

Relationship between serum Inflammatory markers, regional brain volumes, and perfusion in older diabetic subjects

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Background: Type 2 Diabetes Mellitus (DM) is a major risk factor for both large and small vessel atherosclerosis, stroke, and vascular dementia. Hyperglycemia is a common mechanism of endothelial dysfunction and neuronal cell damage. Microvascular disease manifests as white matter hyperintensities on MRI, regional atrophy and functional decline. Inflammation may also contribute to microvascular damage. We investigated the relationship between expression of serum inflammatory markers, regional perfusion and grey and white matter atrophy on MRI.

Methods: 45 type 2 DM (63.3±1.2 yr-old; 51-79 yr) and 59 controls (66.2±1.0 yr-old; 50-83 yr) were studied using high resolution anatomical and perfusion MRI at 3 Tesla. Anatomical MR images (MP-RAGE, FLAIR, GRE) were co-registered to a standard template and segmented to calculate regional volumes of grey (GM) and white (WM) and cerebrospinal fluid (CSF) in the frontal, temporal, parietal and occipital regions. Continuous arterial spin labelling (CASL) was acquired for quantifying cerebral perfusion. The association of brain volumes with plasma inflammatory markers (intracellular adhesion molecule (sICAM), vascular adhesion molecule (sVCAM), C-reactive protein (CRP), tumor necrosis factor (TNF α)) was analyzed using multivariate models and MANOVA.

Results: sICAM was associated with atrophy across all regions in the DM group ($p=0.001$), with the most significant effects in the frontal and parietal regions ($p=0.01$). These effects were independent of age and body mass. In contrast, age had the most significant effects on CSF and GM volumes in the control group, and sICAM was weakly associated with greater GM volume in the frontal ($p=0.03$) and parietal ($p=0.04$) regions. In the control group, bilateral perfusion in the parietal lobe was positively correlated with sICAM ($p=0.03$), and perfusion in the right occipital lobe was positively correlated with sVCAM ($p=0.035$). sICAM and sVCAM levels were correlated and CRP was correlated with TNF α . Associations between regional brain volumes and other inflammatory markers were not prominent. The sICAM levels were not different between the groups.

Conclusions: sICAM is associated with brain atrophy in DM but not control subjects. This may indicate an inflammatory mechanism for microvascular damage in the brain that is specific to DM. Prospective studies are needed to establish causal relationship between DM, inflammation, brain atrophy, and cerebral blood flow.