

Brain imaging results identify structural and vascular abnormalities in type 2 diabetic adults compared to hypertensive controls

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Introduction: Type 2 Diabetes Mellitus (T2DM) is characterized by metabolic dysregulation in the form of hyperglycemia and insulin resistance and can have a profound impact on brain structure and vasculature. Increases in structural atrophy and vascular impairment were previously observed in individuals with T2DM when compared to healthy controls¹. There are still many gaps in our understanding of T2DM impact, one of which is the extent to which T2DM affects brain health on top of common comorbid conditions, especially hypertension (HTN). The primary aim of this study was to elucidate the additional impact of T2DM on the brain over and above that observed in HTN by examining vascular and structural changes in individuals with both conditions (T2DM+HTN) vs. HTN alone.

Methods: Forty participants were scanned using Siemens Trio 3T MRI system (18 with T2DM+HTN, age 71.8±5.6 years, and 22 HTN, age 73.4±6.2 years). Grey matter structure was evaluated using high-resolution T1-weighted three-dimensional magnetization-prepared rapid gradient-echo sequence (3D MPRAGE, TR/TE/T1=2000/2.63/1100ms, matrix=240x191, FOV=240x191 mm², slice thickness=1mm, number of slices=160 and flip angle=9°, total duration=6m30s). Tissue volume was assessed based on cortical thickness (C.Thk) measurements attained using Freesurfer software².

The capacity for brain blood vessels to dilate, cerebrovascular reactivity (CVR), was examined during Blood Oxygenation Level Dependent (BOLD) imaging while participants performed 15s breath hold challenges (BH) (TR/TE=2000/30ms, matrix=64x64, FOV=200x200 mm², slice thickness=5mm, number of slices= 32, flip angle=90°, with 156 volumes, total duration=5m20s). CVR analysis was performed based on the technique introduced elsewhere³. Briefly, images from all participants were entered into temporally-concatenated independent component analysis (MELODIC)⁴ and used to generate 20 spatially independent regions based on the characteristics of their vascular response to BH. CVR maps were identified based on the correlation of component time-series with BH model (box-car function convolved with double-gamma HRF and incorporating a response delay). Two CVR maps within occipital, parietal and frontal lobes were selected as regions of interest because these regions were suspected of having hemodynamic impairment as seen in the T2DM¹ and AD⁵ literature. Group spatial maps were used to generate subject-specific CVR patterns using a dual-regression approach⁶. CVR comparison between the groups was carried out using an FSL permutation method (randomise)⁷ to perform an unpaired t-test. Results were corrected for multiple comparisons including threshold free cluster enhanced algorithm⁸.

Results and Discussion: Two diabetic participants and 2 hypertensive controls were excluded from the analysis due to head motion greater than 1.5 mm during BH. The two maps used for CVR group comparison are shown in Figure I. Group comparison identified a cluster in CVR Map I with decreased CVR in T2DM+HTN when compared to

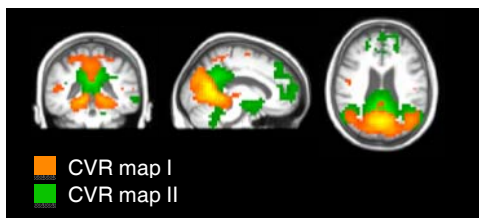


Figure I. CVR maps selected for group comparison

HTN controls. This cluster included right intracalcarine cortex, lingual gyrus and precuneal cortex. No significantly different areas between the groups were detected in CVR map II. Structural analysis revealed a decrease in cortical thickness in the T2DM+HTN, relative to HTN group in right lingual and fusiform gyri. The results of CVR and C.Thk analysis were overlaid on the standard surface map and are shown in Figure II.

Average CVR and C.Thk in ROIs identified in the corresponding analyses showed significant positive correlation ($r=0.471$, $p=0.004$).

Conclusion: This study provides a converging evidence of enhanced damaging effect of two commonly co-occurring conditions, T2DM and HTN, on brain structure and vasculature when compared to individuals with HTN only. Diminished vascular response to a hypercapnia challenge and cortical thinning were detected in the right visual processing regions. Participants recruited in this study had no history of diabetic retinopathy, although these findings might indicate underlying mechanism preceding clinical manifestation. The results of this study provide an insight into the mechanism(s) of T2DM effect on the brain that may help explain the neurodegenerative processes reported in T2DM.

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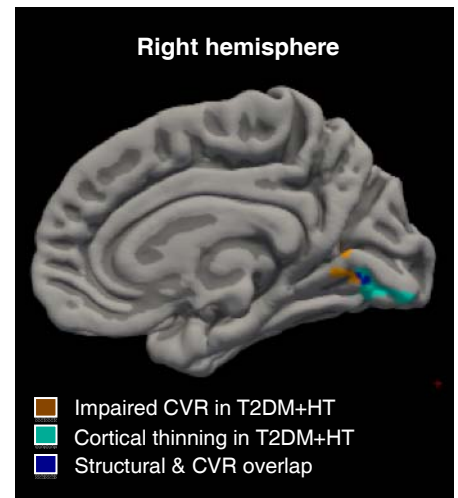


Figure II. Regions identified in structural and vascular group comparison