Gray matter prefrontal changes in type 2 diabetes detected using MRI

A. Kumar[1], E. Haroon[2], C. Darwin[3], O. Ajilore[1], G. Rodriguez[1], and J. Mintz[1]

[1]Department of Psychiatry, UCLA Semel Institute, Los Angeles, CA, United States, [2]Emory University, Atlanta, GA, United States, [3]UCLA Department of Internal Medicine, Los Angeles, CA, United States

Objective. While the cerebrovascular complications of type 2 diabetes are well recognized, the precise neuroanatomical correlates of type 2 diabetes are unknown. The objective of our study was to cross-sectionally examine the volumes of the gray and white matter both globally and regionally in patients diagnosed with type 2 diabetes with and without clinical depression and controls.

Design. All subjects were studied cross-sectionally on a 1.5 Tesla scanner and were recruited from medicine/diabetes clinics. Images were manually masked to remove nonbrain tissue and cerebellum. Brain volumes were corrected for signal intensity inhomogeneities, aligned, and placed into stereotaxic coordinates without scaling to correct for head position. Fully automated tissue segmentation was then applied to the brain volumes, where voxels were classified as gray or white matter or cerebrospinal fluid (CSF). A high-resolution shape representation of the cortex was extracted for each subject using automated software. By using a three-dimensional active surface algorithm, a spherical mesh surface was created that continuously transformed to fit a cortical surface tissue threshold intensity value for individual brain volumes. These surface/shape extractions were used to aid in delineation of three frontal cortical substructures of orbitofrontal (OFC) cortex, anterior cingulate (AC) and gyri recta (GR). Total intracranial volume including sulcal and subarachnoid CSF but not cerebellum was calculated. Details of the written anatomical protocols can be found on the World Wide Web: http://www.loni.ucla.edu/protocols/Prefrontal_cortex.html.

Subjects. Our samples comprised of 26 patients with type 2 diabetes (DC), 26 patients with diabetes and major depressive disorder (DD) and 25 non-diabetic, non-depressed control subjects (HC). Both diabetes and depression were diagnosed using established criteria.

Results. Patients with diabetes with and without depression had smaller total brain gray matter volumes when compared with the control subjects after controlling for age, intracranial volume and years of education, ($p<.05$). The diabetes patients also had smaller gray matter volumes in the anterior cingulate and orbitofrontal regions when compared with the controls after additionally controlling for total gray matter volume, ($p<.05$). The depressed and non-depressed diabetic groups did not differ on any neuroimaging measure. Cerebrovascular risk factors correlated negatively with gray matter volumes.

Conclusions. The findings indicate that type 2 diabetes is associated with specific neuroanatomical abnormalities in the prefrontal gray matter. Vascular disease might contribute to the findings observed in our sample. These observations have implications for the behavioral sequelae of diabetes.

Table 1. *Table shows salient clinical and demographic measures and unadjusted (for age) absolute volumetric brain measures in cc.*

	HC		DC		DD	
	N=25 (M=5, F=20)		N=26 (M=7, F=19)		N= 26 (M=6, F=20)	
	Mean	StDev	Mean	StDev	Mean	StDev
Age	53.24	9.12	57.85	8.53	55.5	9.66
ICV	1283.76	117.56	1232.71	119.54	1235.9	125.16
T_GM	*** 646.21**	**56.59**	***605.91**	**54.9**	605.02	59.69
T_WM	468.66	61.94	458.65	61.46	459.97	58.86
T_AC_GM	*** 18.43**	**3.57**	*** 16.46**	**3.49**	16.39	3.3
T_GR_GM	4.9	0.76	4.52	0.77	4.4	0.7
T_OFC_GM	***25.12**	**2.76**	*** 22.90**	**2.96**	23.37	3.69

**** significantly different from DC and DD, p< .05***

[*Table 1* Legend: **T**=Total; **GM**=Gray matter; **WM**=White matter; **AC**=Anterior Cingulate; **GR**=Gyrus Rectus; **OFC**=Orbitofrontal Cortex]

Figure 1. *Scatter-plot of whole brain gray matter volumes across the 3 groups.*