Changes in Brain Tissue Distribution and T2 Relaxation Time in Early Onset Type-1 Diabetes

R. M. Wellard[1], G. Pell[1], D. Rankin[2], D. Boyce[2], G. D. Jackson[1], G. Werther[3], E. Northam[2]

[1]Brain Research Isntitute, Melbourne, Victoria, Australia, [2]Psychology, Royal Children's Hospital, Melbourne, Victoria, Australia, [3]Endocrinology and Diabetes, Royal Children's Hospital, Melbourne, Victoria, Australia

Introduction

Despite the use of insulin and regular monitoring to maintain blood glucose concentration within the normal physiological range, abnormal fluctuations do occur, particularly in young patients. The long-term effects on functional outcomes (academic achievement and vocational opportunity) have yet to be determined, although reduced performance in tasks such as IQ, attention, processing speed, long-term memory and executive skills, relative to matched controls, is evident on neuropsychological testing six years after disease onset[1]. While performance changes can be related to altered function in identifiable brain regions, it is unclear as to how the observed changes in performance relate to changes in the structure and function of the brain. Volume changes can be assessed using the voxel-based statistical technique of voxel-based morphometry (VBM)[2]. A voxel-based approach for the analysis of T2 data (voxel based relaxometry, VBR) has also been described[3]. These techniques utilize analysis within a common space for comparison of the images. The relationship of the volume and T2 changes can therefore be studied in the same subjects.

The availability of a large cohort of early-onset diabetic subjects and matched control subjects enabled us to assess the long-term tissue changes associated with type-1 diabetes. The aim of this study was to examine, at least 13 years after diagnosis, regional differences in tissue T2 relaxation time and brain volume.

Methods

Subjects: We studied a group of children with early onset type-1 diabetes (n = 63) 13-15 years after diagnosis, who had previously undergone neuropsychological assessment soon after diagnosis and also two and six years later. Results were compared to a community control group (n = 42) that had been assessed at similar times. All participants underwent an MR examination and completed a battery of neuropsychological measures.

Imaging: Structural and T2 relaxation measurements were performed at 3T (GE Healthcare). Structural scans used a T1-prepared high-resolution FSPGR sequence. T2 mapping utilized a multi-echo CPMG sequence with 8 echoes (TE 29-231 ms; TR 6 sec; slice thickness 5 mm; FOV 24 cm; 256x128 encoding steps).

Analysis: T2 maps were generated by fitting to a mono-exponential model with the inclusion of a baseline that minimizes the contribution of long T2 components (eg CSF) to the fit[4]. VBM (structural) analysis followed the optimised approach of Good *et al.*[2]. Images were spatially normalized, segmented and then smoothed (8mm kernel). VBR analysis was carried out according to the procedure previously outlined[4] (8mm smoothing kernel). Areas of significant grey matter (GM), white matter (WM) volume and T2 change between control and patient groups are reported for $p < 0.00005$ (uncorrected). The correlation between time since diagnosis with the change in volume was also assessed.

Results

Volume based morphometry showed decreased GM in the thalamus (Figure 1a), and a reduction of GM in the medial frontal gyrus that was correlated with years since diagnosis of diabetes. Increased white matter fraction was observed in the inferior temporal gyrus.

A correlation was detected in the precuneus between grey matter change and years since diagnosis.

Analysis of T2 relaxation maps demonstrated increased T2 relaxation times in the superior temporal gyrus (Figure 1b) and a decreased T2 relaxation time in the lentiform nucleus in childhood onset type-1 diabetes, compared to controls.

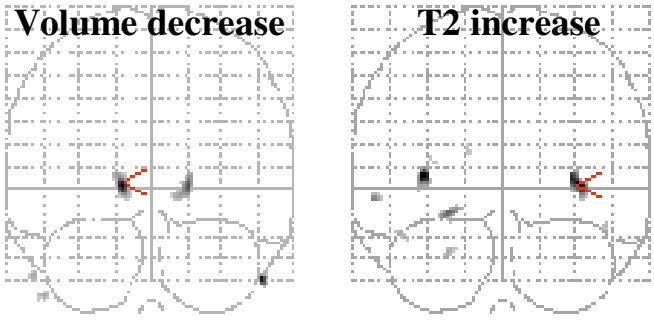

Figure 1: SPM 'glass brain' images showing regions of reduced grey matter in the thalamus (left panel) and increased T2 relaxation time in the superior temporal gyrus (right panel) in early onset type-1 diabetes, compared to controls.

Discussion and conclusions

The areas in which volume changes were observed show some concordance with areas thought to be associated with the neuropsychological functions that are affected by diabetes[1]. The observed volumetric and T2 changes also support our earlier observations of altered metabolite profiles in MR spectra[5] in frontal lobe, temporal lobe and basal ganglia. The regions with altered T2 relaxation times (basal ganglion and superior temporal gyrus) showed changes in opposite directions, suggesting that different processes are occurring at each site. Increased T2 is associated with gliosis and loss of cell density. An explanation for the observed decrease in T2 may be reduced tissue water or a change in cell type. The observed changes in GM, WM and T2 relaxation time provide an indication of regions that contribute to the observed differences in neuropsychological performance of subjects with early onset type-1 diabetes.

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