Publication News 111 – 26 February 2024

Brain alterations are present in people with well-controlled diabetes: evidence from a large Biobank study in the UK

Aims: To investigate grey matter volumetric and microstructural white matter alterations in a large community-based cohort of people with diabetes (DM) compared to a control cohort without (NDC).
Methods*:* Data was analysed from participants recruited into the UK Biobank cohort, comprising of participants aged 40-69 between 2006 and 2010. A total of 38,444 participants were included, with NDC matched by age and sex at baseline with a 1:1 ratio to DM participants (~15% T1DM, 85% T2DM). All participants completed self-reported outcomes, and had physical measures and blood tests, and 2,404 underwent brain MRI (NDC n=1,803, DM n=601) for volumetric analysis, of whom 830 underwent tractography analysis (NDC n=600, DM n=230). Data was extracted relating to cognition and pain measures. Volumetric analysis was performed using Freesurfer software and tractography using TractSeg.
Results*:* Focusing on those who underwent neuroimaging, participants with DM had an HbA1c of 51.9 mmol/mol (SD 12.6), duration of diabetes of 18 (11) years and 0.2% had renal and 5.8% ophthalmic complications according to ICD-10 coding. Compared with NDC there was no difference in cognitive measures in the DM group, but there was a greater proportion of people with diabetes who experienced pain (not specific to painful-diabetic peripheral neuropathy, pain locations included headache, back, stomach etc.). Volumetric brain analysis revealed a reduction in whole brain, subcortical grey matter, and total grey matter volume in DM relative to NDC (-3.71% whole brain volume difference in DM vs. NDC). Widespread volume reduction was found in cortical and subcortical regions, including regions associated with somatomotor (precentral and postcentral gyri and the thalamus) and visual function (occipital gyri). Reductions in fractional anisotropy were present again in regions associated with somatosensory function (e.g. thalamocortical radiations) and those associated with motor (cerebellum) and visual function (occipitofrontal fascicle).
Conclusions: In this cohort of participants with a reasonably long duration of diabetes, but good glycaemic control and low prevalence of microvascular complications there was evidence of volumetric grey matter and microstructural white matter changes in regions of the brain associated with visual and sensorimotor networks. The authors hypothesize that central nervous system alteration may occur early in the natural history of microvascular complications.

Comments. With the advent of advanced MR scanning and analysis techniques it is increasingly recognised that the central nervous system is not an innocent bystander in diabetes complications, particularly in diabetic peripheral neuropathy. This study adds to the growing body of evidence indicating brain involvement in diabetes complications. It is the largest volumetric and tractometric study to be performed in people with diabetes and provides the interesting insight of significant brain changes in people with relatively well-controlled diabetes, without a high burden of complications. Thus, central nervous system alterations may occur concurrently with, or even predate, end-organ dysfunction. However, within this, and all database/Biobank studies, it was not feasible to perform highly detailed diabetes complication phenotyping (particularly neuropathy/pain) and microvascular complication diagnoses rely on ICD-10 coding information. Therefore, further, ideally longitudinal, studies are necessary to elucidate the role of central nervous system alterations in microvascular complications.

Gordon Sloan

Reference. Burgess J, de Bezenac C, Keller SS, Frank B, Petropoulos IN, Garcia-Finana M, Jackson TL, Kirthi V, Cuthbertson DJ, Selvarajah D, Tesfaye S, Alam U. Brain alterations in regions associated with end-organ diabetic microvascular disease in diabetes mellitus: A UK Biobank study. Diabetes Metab Res Rev. 2024 Feb;40(2):e3772. doi: 10.1002/dmrr.3772. PMID: 38363054.
https://onlinelibrary.wiley.com/doi/10.1002/dmrr.3772