Abnormal H-MRS suggests involvement of the thalamus in diabetic neuropathy

D. Selvarajah[1], S. Tesfaye[1], P. D. Griffiths[2], I. D. Wilkinson[2]

[1]Diabetes Research Unit, Royal Hallamshire Hospital, Sheffield, United Kingdom, [2]Academic Radiology, University of Sheffield, Sheffield, United Kingdom

Introduction: Although clear pathological abnormalities have been demonstrated in the peripheral nerves in distal symmetrical diabetic polyneuropathy (DN), there is little information with regard to the involvement of the brain. An understanding of the extent of the disease is crucial for the development of rational treatments. This study uses proton magnetic resonance spectroscopy (H^-MRS) to determine the neurochemical constitutional make up of deep grey matter in DN.

Methods: A total of 16 right handed male type I diabetic patients were randomly selected and underwent detailed neurological evaluation to stage the severity of DN using Dyck's staging criteria (1). Eight patients were found to be normal diabetics with no DN (**No-DN**). And the remaining 8 had established DN (**Est-DN**). These patients together with 8 age and sex matched healthy volunteers (**HV**) underwent H^+MRS evaluation of the right posterior lateral nucleus of the thalamus. MR was performed at 1.5T (Eclipse, Philips Medical Systems). Proton spectra were obtained from a single voxel (2x2x2 cm^3) using short (STEAM: TE = 20ms, TR = 300ms) and long (PRESS: TE = 135ms, TR = 1600ms) echo-time techniques. Long TE results are expressed as ratios under the three prominent resonances: Choline (CHO), Creatine (Cr) and N-acetyl (NA) groups. Short TE results are expressed as the areas under the NA, Cho, Cr and *myo*-inositol (mI) resonances relative to that of unsuppressed water.

Results: At long TE there was a significant reduction in NA/Cho ratio in patients with **Est-DN** compared to the other two groups (**Est-DN** vs **No-DN**, p = 0.036; **Est-DN** vs **HV**, p = 0.015). There was no significant difference between the **No-DN** and **HV** groups (p = 0.596). There were no significant inter-group differences in any of the normalised metabolite areas obtained at short echo-time ($p>0.05$).

Discussion: The posterior lateral thalamic nucleus was studied since all ascending sensory nerve fibre tracts (spinothalamic and dorsal columns) terminate in this nucleus before projections are sent to higher cortical centres (SI/SII). Spectra acquired at short TE / long TR (20/3000ms) provide information regarding metabolite densities thereby reflecting metabolite concentrations. Spectra acquired at long TE / intermediate TR (135/1600ms), yield information about relaxation rates of the neurochemical markers as well as their concentrations. If a change in the NA resonance is inferred from the significant difference between group mean NA/Cho ratios, it implies that there is a change in neuronal physiology or function of the ascending pathways within the central nervous system in DN. The short TE results suggest that this is not due to a lower mean concentration in the **Est-DN** group, which may in turn indicate that the neuronal damage is reversible. Further studies are required to determine at what stage these abnormalities occur in the natural history of DN and whether Improved metabolic control can lead to direct neuronal improvement.

Reference:

1. P.J. Dyck, J.L. Davies, W.J. Litchy, P.C. O'Brien. Longitudinal assessment of diabetic polyneuropathy using a composite score in the Rochester Diabetic Neuropathy Study cohort. Neurology(1997), 49, 229-239.