Thalamic involment in painful and painless diabetic neuropathy on H-MRS

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Introduction: Although clear pathological abnormalities have been demonstrated in the peripheral nerves in diabetic peripheral neuropathy (DPN), there is only limited understanding about why some patients suffer severe chronic pain whilst others have painless symptoms. As a result, treatment of painful DPN is frequently unsatisfactory. Very little is known about the role of the central nervous system, especially the brain. An understanding of the extent of the disease is crucial for the development of rational treatments. The thalamus, which is the gateway to the somtosensory cortex, may have a role in the pathogenesis of painful DPN.This study used proton magnetic resonance spectroscopy (H^{-}MRS) to determine the neurochemical constitutional make up of the thalamus.

Methods: A total of 64 right handed male type I diabetic patients were selected and underwent detailed neurological evaluation to stage the severity of DPN using Dyck's staging criteria (1). Thirteen patients had no DPN (**No-DPN**), 16 had sub-clinical DPN (**Early-DPN**), 14 had painful DPN (**Painful-DPN**) and 21 had painless DPN (**Painless-DPN**). All subjects underwent H^{-}MRS evaluation of the left posterior lateral nucleus of the thalamus. MR was performed at 1.5T (Eclipse, Philips Medical Systems, Cleveland, Ohio). Proton spectra were obtained from a single voxel (1.5x1.5x2 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 aspartate (NAA) groups. Short TE results are expressed as the areas under the NAA, Cho, Cr and *myo*-inositol (mI) resonances relative to that of unsuppressed water.

Results: At long TE, there was a significantly lower NAA/Cr ratio in patients with **Painless-DN** (mean=1.62 [SD=0.30]) compared to those with **No-DN**(1.90[0.24], ANOVA $p<0.05$). No differences were seen between either group and those with **Early-DN** (1.78[0.31]) or **Painful-DN** (1.73[0.28]), $p>0.3$. Although some trends were noted, there were no significant inter-group differences in any of the normalised metabolite areas obtained at short echo-time.

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), include information about relaxation rates of the neurochemical markers as well as their concentrations. If a change in the NAA resonance is inferred from the significant difference between group mean NAA/Cr ratios, it implies that there is a change in neuronal physiology or function of the ascending pathways within the central nervous system in painless but not painful DN. This suggests that relative preservation of thalamic neuronal function may be necessary for the presence of chronic pain in diabetic neuropathy. The short TE results suggest that there is not lower mean concentration of NAA in the painless DN group, which may in turn indicate that any neuronal damage may be reversible. Further studies are required to determine whether Improved metabolic control or drug therapies can lead to improvement.

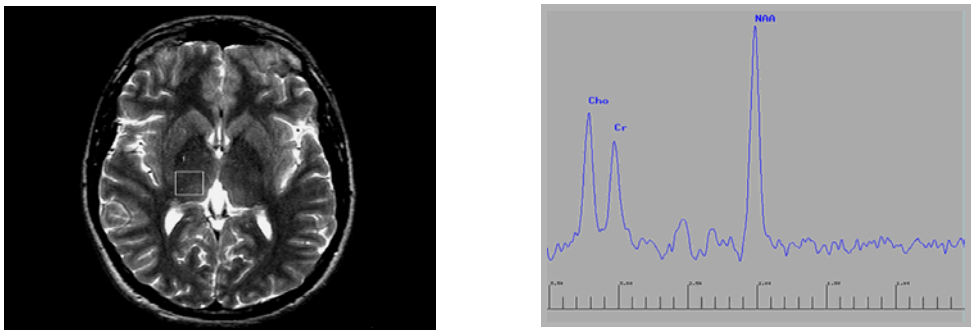

Figure. Spectroscopic voxel placement within the thalamus and example long TE (135ms) spectrum.

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.