Early involvement of the spinal cord in 'peripheral' diabetic neuropathy

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Introduction: Distal symmetrical polyneuropathy (DSP) is a common complication affecting 40 percent of diabetic patients. The pathogenesis of DSP however remains poorly understood and there are no effective treatments. Hitherto been considered a disease of the peripheral nerves, involvement of the central nervous system has been largely over looked. We have recently reported a significant reduction in spinal cord cross sectional area (CSA) in established DSP. However the relevance of this to the pathogenesis of DSP depends on whether these changes occur early in its natural history of the disease.

Methods: Seventy-seven Type I male diabetic patients and 15 healthy volunteers (**HV**) have been studied to date. A detailed neurological evaluation that included neurophysiological tests (quantitative sensory testing, autonominc function tests and nerve conduction studies) was performed to diagnose and stage the severity of DSP (Dyck's neuropathy staging criteria) (2). It was found that 27 diabetic patients had no DSP (**Non-DSP**; Dyck's Stage N0), 20 had early DSP (**Subclinical-DSP**; Dyck's Stage N1a) and 30 had established DSP (**Established-DSP**; Dyck's N1b/N2). All patients and **HV** underwent MR imaging of their cervical spine using a standard spinal phased-array receive-only RF coil on a system operating at 1.5 T (Eclipse, Philips Medical Systems). T2*-weighted imaging was performed axially from C1-T2 using a gradient echo technique (TE = 17.9ms, TR = 800ms; $\alpha = 40^{o}$; slice thickness = 4mm; in-plane resolution = 0.78mm x 0.96mm). Cord cross-sectional area (CSA) was measured at the level of disk space C2-C3 in all 77 patients.

Images were post-processed using a previously described semi-automated computerised technique on a Sun Workstation with the image display program Dispimage (3). Calculated CSA were then corrected for errors in slice positioning and as this is a cross-sectional study, corrections for shrinkage over time were also made. Inter- and intra-observer variations were determined.

Results: A scatter-plot depicting the cord CSA within each group is presented in Figure 1. Mean cord area measurements were significantly lower in both **Subclinical-DSP** and **Established-DSP** groups compared to **Non-DSP** group ($p < 0.0001$). No significant difference was found between the two DSP groups (**Subclinical-DSP** vs **Established-DSP**; $p = 0.80$) and between **Non-DSP** and **HV** groups ($p = 0.71$). Furthermore 15% of **Subclinical-DSP** and 16% of **Established-DSP** had spinal cord atrophy (defined as CSA < 2 SD of the mean CSA of **HV**). In addition there was an early reduction in cervical cord medio-lateral diameter compared to antero-posterior diameter ($p = 0.025$), in **Subclinical–DSP** groups.

The coefficient of variation for inter-observer measurement was x% and for intra-observer measurement was y%.

Discussion: We have demonstrated early involvement of the central nervous system in the pathophysiology of DSP, reflected in marked reduction in cervical cord CSA. An early reduction in cord medio-lateral diameter seen in **Subclinical-DSP** suggests a preferentially early involvement of the spinothalamic (small fibre; pain and temperature) tracts. Furthermore, this non-invasive, reproducible, rapid test may serve as an early marker and allow the identification of subjects that are more likely to resp ond to therapeutic intervention.

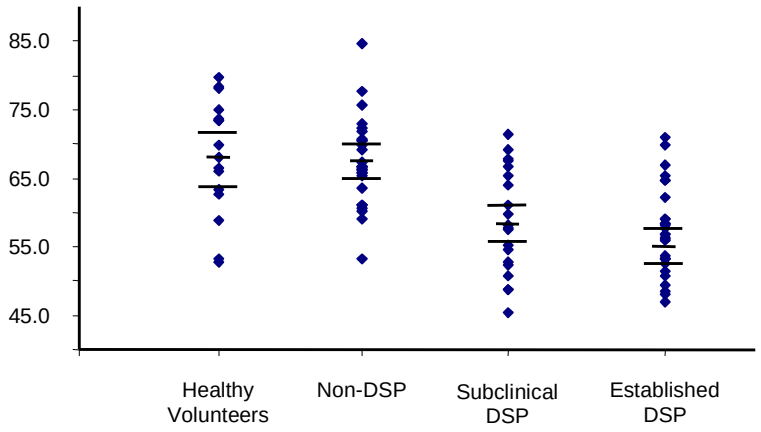

Figure 1: Corrected cord cross-sectional area as a function of subject group.
Horizontal bars represent means ± 2 standard error of mean.

Reference:

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