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Diabetic polyneuropathy does not exclusively start with small fiber damage, is not invariably progressive and may even regress: a prospective study from the GDS group

Aim: To assess whether small and large fibre damage due to diabetic sensorimotor polyneuropathy (DSPN) in type 1 (T1D) and type 2 diabetes (T2D) could develop in parallel and whether it may be reversible.
Methods: Prospective observational study of subjects from German Diabetes Study with recent-onset T1D/T2D (n = 350/570) and age-matched healthy controls (Control 1/Control 2: n = 114/190) for 5 years. Assessment of DSPN based on nerve conduction studies (NCS), thermal detection thresholds, vibration perception threshold (VPT), Neuropathy Symptom Score (NSS), Neuropathy Disability Score (NDS) and intraepidermal nerve fibre density (IENFD) in skin biopsies.
Results: At baseline, DSPN was present in 8.1% and 13.3% of T1D and T2D groups, respectively. The most frequently abnormal tests in the lower limbs below or above the 2.5th and 97.5th centiles of the controls were the IENFD (13.7%) and individual NCS (up to 9.4%) in participants with T1D, and IENFD (21.8%), malleolar VPT (17.5%), and individual NCS (up to 11.8%) in those with T2D. After 5 years, the highest progression rates from the normal to the abnormal range in T2D participants were found for IENFD (18.8%), malleolar VPT (18.6%) and NCS (15.0%), while vice versa the highest regression rates were observed for NDS (11.2%), sural nerve amplitudes (9.1%), IENFD (8.7%) and NSS (8.2%). In participants with T1D, no major progression was seen after 5 years, but subclinical DSPN regressed in 10.3%. Multivariate analyses in the present study did not reveal any predictors for the course of nerve function tests over 5 years in both diabetes groups.
Conclusions: This study demonstrates an early parallel dysfunction or pathology to both small and large nerve fibres in well-controlled recent-onset T2D and, to a lesser degree, T1D. In individuals with T1D, small and large fibre dysfunction did not progress over 5 years, but noticeable regression of subclinical DSPN was found. In participants with T2D, further peripheral nerve pathology and dysfunction developed after 5 years despite good glycaemic control, but initial nerve alterations were also reversible to a meaningful degree.

Comments: This is a unique parallel and prospective evaluation of the progression or regression of small as well as large nerve fibre damage in patients with both T1D and T2D. The study helps to understand the course of diabetic neuropathy. In the T2D group, the rates of progression from the normal to the abnormal range from baseline to 5 years were considerably higher than in participants with T1D. Early DSPN is not necessarily a continuously progressive condition, but a dynamic one with ongoing degenerative and preserved regenerative processes, contradicting the notion of sequential small and large fibre damage in T2D. The results might help to identify subjects at higher risk for progression of nerve pathology.

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Reference: Ziegler D, Bönhof GJ, Strom A, Straßburger K, Karusheva Y, Szendroedi J, Roden M. Progression and regression of nerve fibre pathology and dysfunction early in diabetes over 5 years. Brain. 2021 Nov 29;144(10):3251-3263. doi: 10.1093/brain/awab330.
https://academic.oup.com/brain/article-abstract/144/10/3251/6367771?redirectedFrom=fulltext