Serum Neurofilament Light Chain and Structural and Functional Nerve Fiber Loss in Painful and Painless Diabetic Polyneuropathy

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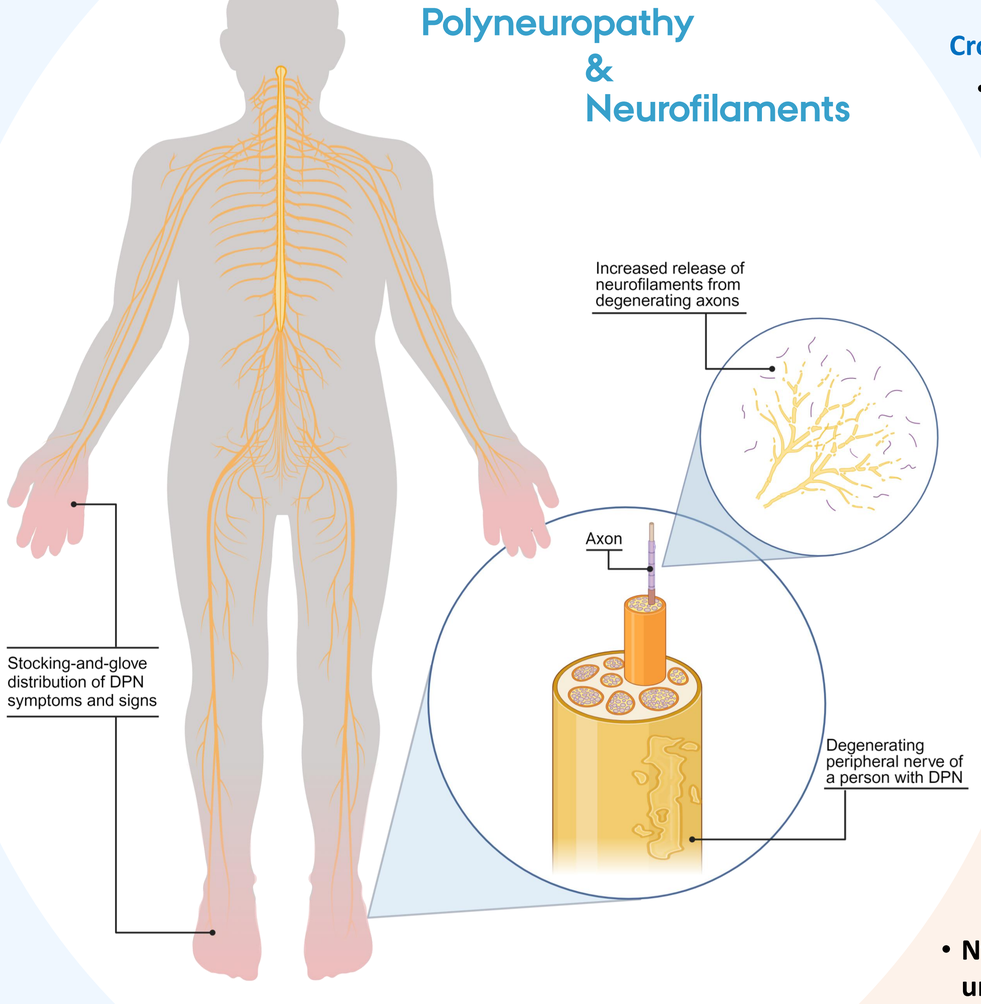
BACKGROUND

Diabetic polyneuropathy (DPN) is a common complication of diabetes

- Often diagnosed late in the disease trajectory
- Symptoms: numbness, pain, dysesthesias
- No targeted treatment
- Objective tools for early diagnosis & follow-up are needed

Neurofilament light chain (NfL)

- Neuron-specific axonal cytoskeletal protein
- Marker of neuronal damage & degeneration
- Proposed as a possible biomarker for DPN
- How well does NfL reflect the severity of DPN?



METHODS

Cross-sectional analysis of biobank samples & clinical data

- 201 participants from the British PiNS/DOLORisk cohort
  - Type 1 or 2 diabetes with DPN +/-neuropathic pain
    - Serum NfL (s-NfL) levels quantified by Single molecule array technology

DPN definition & measures

- Toronto criteria for probable or confirmed DPN
- IASP NeuPSIG criteria for painful DPN
- Clinical DPN scales
- Nerve conduction studies
- Skin biopsies for intraepidermal nerve fiber density (IENFD)
- Quantitative sensory testing (QST)

HYPOTHESIS

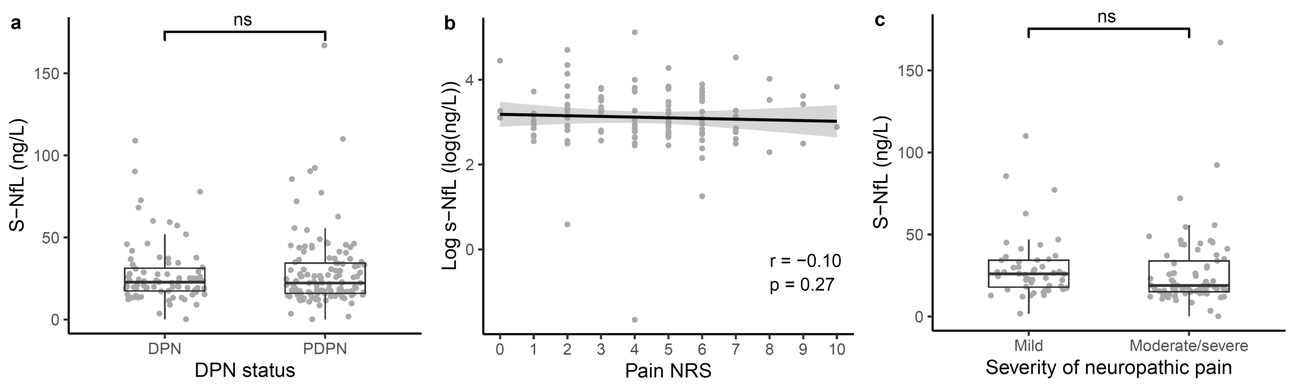
NfL is associated with higher DPN severity as reflected by clinical scales, objective loss of nerve fiber function and structure, and pain presence and severity.

CONCLUSION

- **Higher NfL is associated with nerve fiber dysfunction and loss, but not with pain or clinical DPN scales.**
- **NfL may reflect the severity of the nerve fiber damage underlying DPN and have value as an objective marker of DPN severity.**

RESULTS

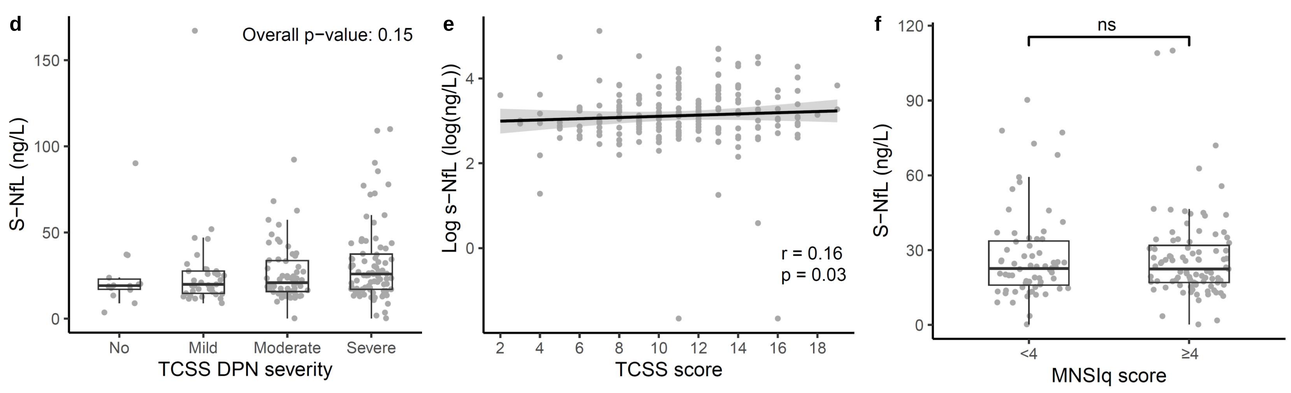
Figure 1 – NfL levels by DPN status, pain severity and clinical DPN scales



a) S-NfL levels (ng/L) by DPN status (DPN vs. PDPN)

b) The association between s-NfL (log(ng/L)) and continuous average pain severity (NRS) in participants with PDPN.

c) S-NfL levels by dichotomized pain severity in participants with PDPN.



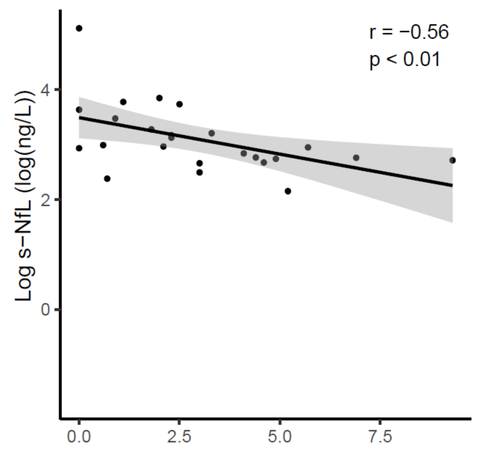
d) S-NfL levels (ng/L) by DPN severity groups as defined by TCSS scores

e) The association between s-NfL (log(ng/L)) and continuous TCSS score.

f) S-NfL levels (ng/L) by MNSIq abnormality.

Moderate/severe pain was defined as pain NRS ≥4. DPN: Diabetic polyneuropathy. PDPN: Painful diabetic polyneuropathy. NRS: Numerical rating scale. TCSS: Toronto Clinical Scoring System. MNSIq: Michigan Neuropathy Screening Instrument questionnaire. p: p-value. r: Spearman correlation coefficient.

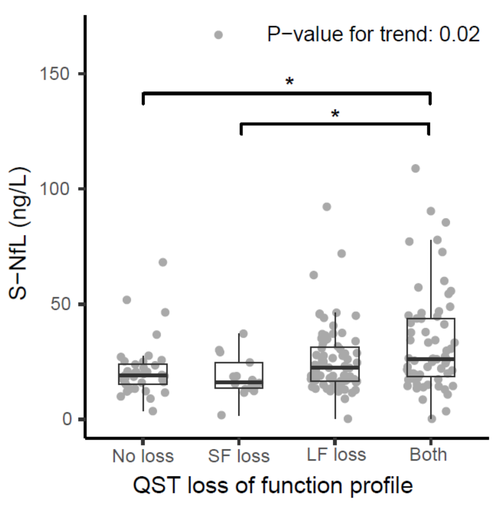
Figure 2 – Association between NfL levels and IENFD



13.6% (3.1; 22.9) ↑**s-NfL** for each 1 fiber/mm decrement in IENFD

Association between s-NfL levels (log(ng/L)) and intraepidermal nerve fiber density (fibres/mm). IENFD: Intraepidermal nerve fiber density. p: p-value. r: Spearman correlation coefficient.

Figure 3 – Association between NfL levels and the extent of loss of nerve fiber function as evaluated by QST



↑**s-NfL** with more extensive loss of function

↑**s-NfL** with combined loss of function compared to no loss and SF loss

"No loss": normal CDT, WDT, MDT and VDT; "small fiber (SF) loss": abnormal CDT and/or WDT, normal MDT and VDT; "large fiber (LF) loss": abnormal MDT and/or VDT, normal CDT and WDT; "both" (combined SF and LF loss): abnormal CDT and/or WDT, abnormal MDT and/or VDT. QST: Quantitative sensory testing. CDT: Cold detection threshold. WDT: Warm detection threshold. MDT: Mechanical detection threshold. VDT: Vibration detection threshold

Illustration (top center) created with BioRender.com