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Background & Objective

- Brain-derived neurotrophic factor (BDNF) is a neuronal growth factor that transported within platelets in the peripheral blood and exerts survival effect on neuronal cells.
- Studies by our group demonstrated BDNF levels in blood and BDNF-val66met-SNP as potential biomarkers in chemotherapy-induced peripheral neuropathy.
- Here we evaluate symptoms of peripheral neuropathy (PN) and depression in patients with type II diabetic mellitus in search of an association with serum BDNF levels and the Val66Met-SNP.

Methods

- In total, 90 patients enrolled in the study; 23 (25.6%) had known PN, as determined by nerve conduction studies (NCS-PN) and 67 (74.4%) were not diagnosed with PN (U-PN).
- PN symptoms were assessed and graded in these groups using the total neuropathy score (TNSr) and DN4 scales.
- Small nerve fiber testing of sensitivity thresholds to cold, warm and hot-pain signals, was performed using the Q-sense device.
- Depression was assessed using the PHQ9 questionnaire.
- BDNF protein levels and Val66Met-SNP were determined with ELISA and Sanger sequencing, respectively

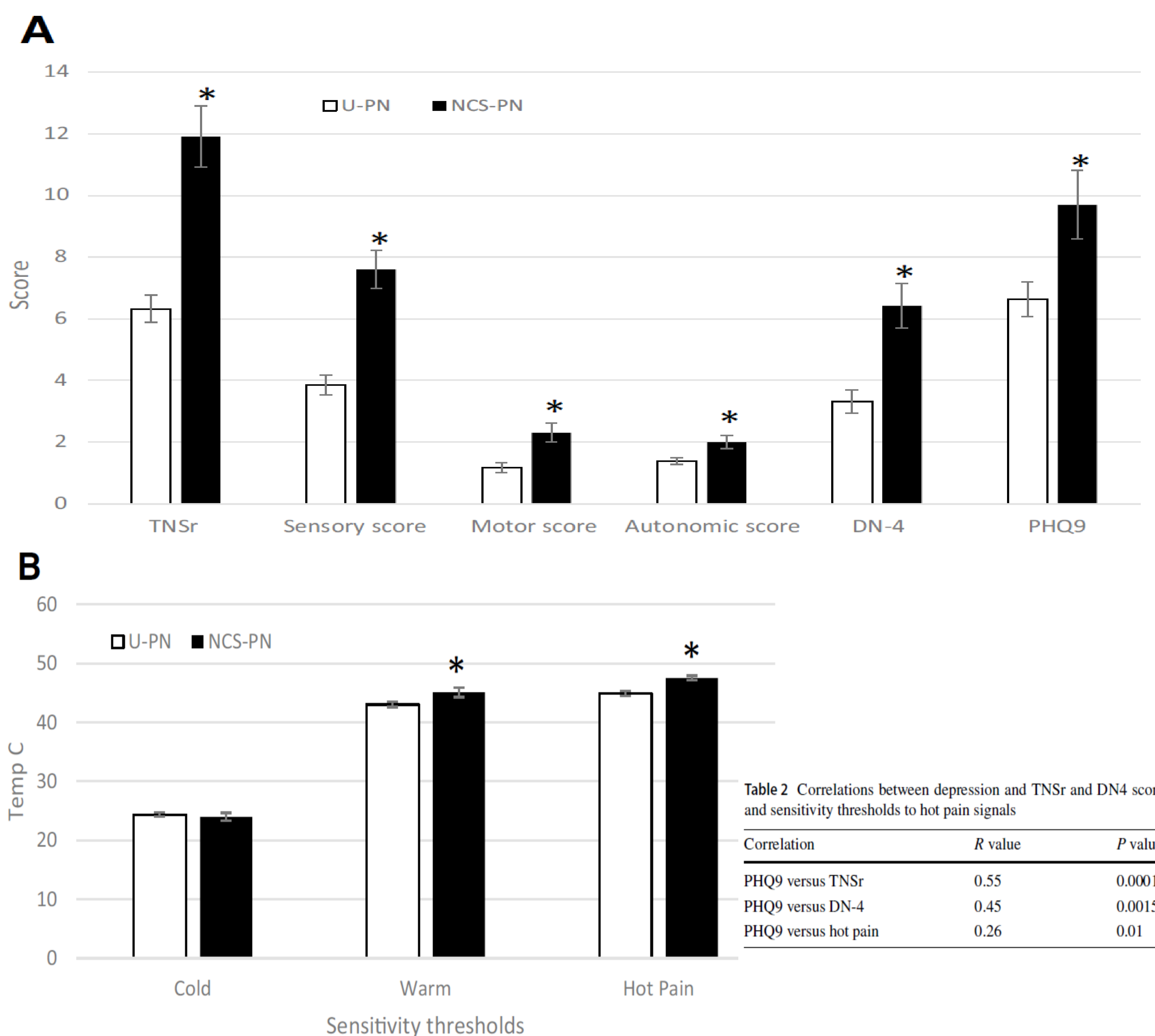
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|--|---------------------------|
| Total participants: N | 90 |
| Gender: F:M (% of total) | 34(38): 56(62) |
| Age (years): mean ± SD (range) | 60.51 ± 10.1 (26–75) |
| Disease duration (years): mean ± SD (range) | 10.42 ± 5.75 (2.5–32) |
| A1c (%): mean ± SD (range) | 8.15 ± 2.1 (5–13.7) |
| Glucose (mg/dL): mean ± SD (range) | 181.13 ± 69.27 (74–402) |
| Active vitamin B12 (pmol/L): mean ± SD (range) | 111.89 ± 65.83 (19–388) |
| Insulin treated: N (% of total) | 40 (44) |
| Metformin treated N (% of total) | 68 (75) |
| NCS-PN: N (% of total) | 23 (25.5) |
| PN treated: N (% of total) | 14 (15.5) |
| PN treatment: N (% of treated) | |
| Cymbalta | 3 (21.4) |
| Elatrolet | 2 (14.3) |
| Gabapentin | 3 (21.4) |
| Lyrica | 6 (42.8) |
| Serum BDNF (ng/mL): mean ± SD (range) | 16.75 ± 6.02 (0.99–28.06) |
| Val66Met-SNP: N of total genotyped | 87 |
| GG: N (% of total) | 58 (66.7) |
| GA: N (% of total) | 25 (28.7) |
| AA: N (% of total) | 4 (4.6) |
| Met-BDNF: N (% of total) | 29 (33.33) |

Conclusions

- Diminished peripheral BDNF resources and Met-BDNF-SNP genotype are associated with augmented symptoms of PN in patients with type II diabetes mellitus.
- Sensitivity thresholds to hot pain signals may be less influenced by depression and possibly more accurately detect PN symptoms in diabetic patients.

Results

NCS-PN patients show significantly higher TNSr, DN4 and PHQ9 scores and lower hot-pain sensitivity thresholds as compared to U-PN patients.



NCS-PN patients show significantly lower serum BDNF as compared to U-PN patients.

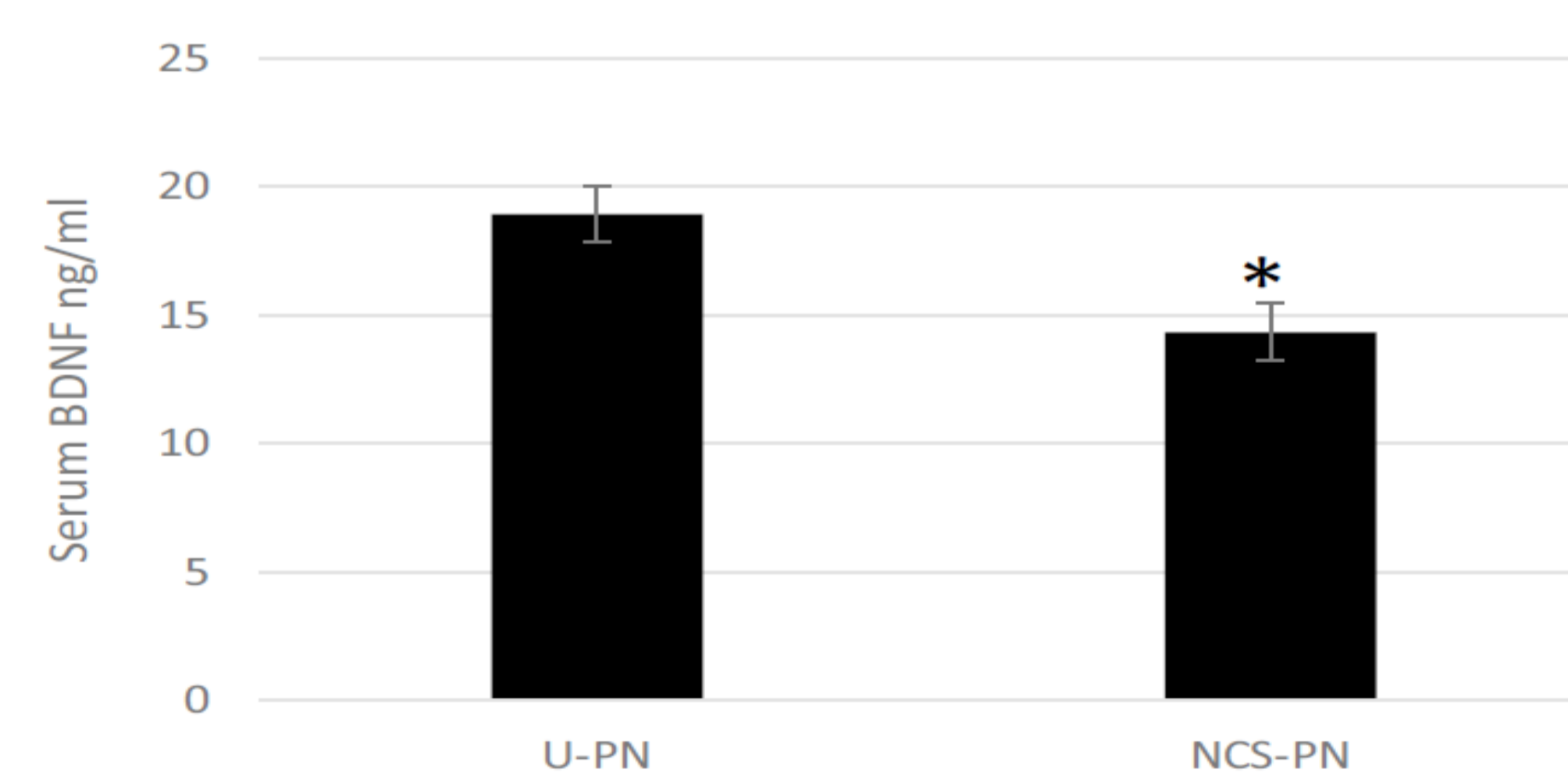


Fig. 2 Serum BDNF protein levels in patients with NCS-PN and U-PN. The bars show mean (±SEM) of serum BDNF levels in patients with NCS-PN or U-PN. **p* value < 0.05

Patients with Met-BDNF-SNP show increased TNSr scores and lower hot-pain sensitivity thresholds as compared to patients with Val-BDNF-SNP

