Chronic Pain-related Clinical Neuropathic Features are not associated to Electroencephalographic Markers.

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1. Introduction

Chronic pain ➔ subjective evaluation and treatment failure ++

For more **complete** assessment + management **improvement**: **subjective** + **objective (e.g. EEG markers)** measures ?

Neuropathic pain (IASP): disease/dysfunction somato-sensory system

Clinical neuropathic features: burning pain, electrical discharges, positive (tingling, pins/needles, itching), negative (numbness) symptoms

?

EEG markers (GABAergic β and γ; α and θ oscillations)

2. Methods

Study design

Multiple case retrospective study
Comparison including previous data (1) and (2) and new data

Participants

Right-handed, chronic pain (< 3 months)
9 chronic peripheral neuropathic patients (CNP1) (1)
(exclusion of 3 patients with polyneuropathy)
16 fibromyalgia patients (FM) (2)
9 chronic peripheral neuropathic patients (CNP2)

Clinical evaluation

Visual Analogue Scale:
- the day of evaluation (**VAS_d**)
- In general the last 1-2 weeks (**VAS_g**)

Hospital Anxiety and Depression sub.scales for
- Anxiety (**HAD_a**)
- Depression (**HAD_d**)

Insomnia Severity Index (**ISI**)
Douleur Neuropathique 4 questions (**DN4**)

EEG recordings

Adapted from: https://imotions.com/blog/what-is-eeg/

Resting-state, eyes-closed
22-minute recording
High density (64-channels)
EEG system (BIOSEMI)

2. Methods (Cont'd)

EEG data analysis: inhouse scripts Matlab, EEGLab, Cartool softwares

Pre-processing

1. Down-sampling ➔ 512 Hz
2. Band-pass filtering (> 0.5 - < 40 Hz) (Finite Impulse Response, FIR)
3. Artefact Subspace Reconstruction EEGlab plugin (ASR)
4. Visual inspection bad channels (≤ 10% rejection) ➔ Spherical spline interpolation
5. Average reference ➔ 2-sec epoch segmentation

Fast-Fourrier transform (FFT)

1. **High beta** (20–30 Hz), **low beta** (13–20 Hz), **alpha** (8–12 Hz), **theta** (5–7 Hz), **delta** (2–4 Hz)
2. 0.5 Hz Frequency resolution
3. 1/f noise removal

Statistical analysis: JAMOVI

Parametric tests

1. Mean (SD)
2. Significance: p<.05 (two-tailed, 95% CI)
3. ANOVA (multiple comparison)
4. Post-hoc Bonferroni
5. Multiple test correction (Bonferroni)
6. Student t-test (two series comparison)
7. Pearson r (correlation)

Exploratory analyses

Back surgery before inclusion

1. CNP1 and CNP2 pooled together
2. **Non Back Surgery (NBS)**: n = 9
3. **Back Surgery (BS)**: n = 10

3. Results

Table 1. General data from CNP1, CNP2, FM; as well as from NBS and BS patients.

	CNP1	CNP2	FM	NBS	BS
Age	51.6 (12.4)	58.4 (13.7)	53.7 (15.4)	56.9 (11.2)	53.6 (15.2)
VAS_d	3.78 (2.12)	3.70 (2.00)	4.75 (2.84)	3.94 (2.07)	3.55 (2.03)
VAS_g	4.22 (1.86)	4.70 (2.00)	6.38 (2.11)	4.00 (1.80)	4.80 (1.93)
DN4	5.44 (1.42)	6.00 (0.94)	5.75 (1.95)	5.44 (1.42)	6.00 (0.94)

Notes: *Data are presented as mean(SD). For abbreviations, see methods. No difference was noticed comparing CNP1 – CNP2 – FM patients and NBS – BS groups respectively (p values not shown).*

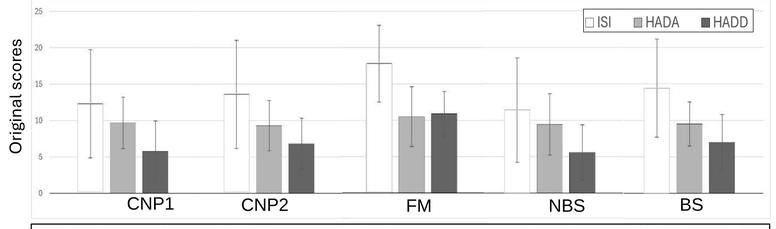

Fig 1. Indicators of mood (HADa for anxiety, HADd for depression) and sleep disorders (ISI for insomnia) in chronic neuropathic pain patients from original (CNP1 and CNP2) and according to back surgery (NBS and BS) groups and in fibromyalgia patients (FM). Respective scores are presented as mean(SD). Color codes are shown in the inset (upper right corner). FM patients showed overall significantly higher HADd (p .002) and tendentially higher ISI scores (p .092) compared to both CNP1 and CNP2 groups. Comparison between NBS and BS showed a slight but non-significant tendency towards higher scores in BS patients (p values not shown).

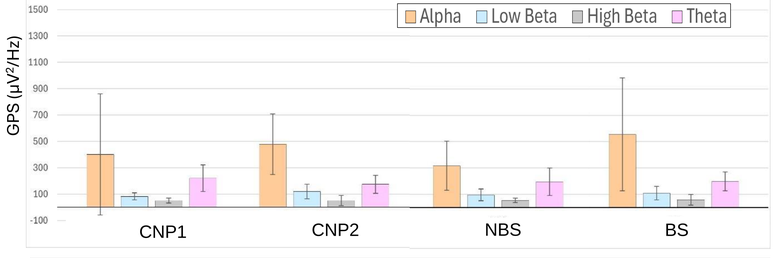

Fig 2. Global power spectra (GPS) of chronic neuropathic pain patients from original (CNP1 and CNP2) and according to back surgery (NBS and BS) groups. Data are presented as mean(SD). Frequency domains (see methods for frequency limits) are presented according to color codes mentioned in the upper right inset. No difference was noticed between CNP1 and CNP2 patients, as well as between NBS and BS patients (p values not shown).

3. Results (Cont'd)

Correlations clinical indicators

CNP1:
- **DN4**: VASg (r 0.809, p .008); HADa (r 0.693, p .039); HADd (r 0.823, p .006); ISI (r 0.752, p .019)
- **VADd**: VASg (r 0.791, p .011); HADa (r 0.830, p .006);
- **HADd**: HADa (r 0.812, p .008)

CNP2:
- **HADa**: ISI (r 0.727, p .017), HADd (r 0.558, p .025)

FM:
- **DN4**: VASg (r 0.694, p .003)

NBS:
- **DN4**: VASg (r 0.779, p .013); HADa (r 0.701, p .035); HADd (r 0.732, p .025)
- **VADd**: VASg (r 0.922, p < .001); HADa (r 0.756, p .019); HADd (r 0.750, p .020)
- **ISI**: HADa (r 0.887, p .001); HADd (r 0.828, p .006); ISI (r 0.752, p .019)
- **HADd**: HADa (r 0.823, p .006);

BS:
- **VASd**: HADa (r 0.636, p .048)

Correlations clinical indicators – EEG markers

CNP1:
- **HADa**: High beta (r -0.702, p .035); Low beta (r -0.722, p .028)

CNP1 (VASd ≥ 3):
- **VASd**: High beta (r -0.878, p .032), Low beta (r -0.909, p .032)
- **HADa**: Low beta (r -0.893, p .041)

CNP2 and FM : None

NBS:
- **DN4**: High beta (r -0.690, p .040)
- **VADd**: High beta (r -0.682, p .043)
- **ISI**: High beta (r -0.666, p .050); Low beta (r -0.666, p .050)
- **HADa**: High beta (r -0.827, p .006); Low beta (r -0.837, p .005)
- **HADd**: High beta (r -0.689, p .040)

BS: None

4. Discussion and Conclusion

1. The CNP1 – CNP2 and NBS – BS comparison disclose no significant difference regarding both clinical and EEG data.
2. Previous results of correlations (between clinical variables and between clinical and EEG indicators) in CNP1 are reproduced (**only GABAergic markers**), but not regarding pain clinical neuropathic features.
3. The NBS – BS discrimination shows comparable clinical correlations with CNP1 – CNP2, but more accurate and extensive (**including DN4 – high beta GPS**) clinical – EEG correlations
4. The history of back surgery could be the most impacting element for clinical – EEG correlations in neuropathic pain as such, but also in clinical neuropathic features of pain

5. References

1. Teixeira M et al. Front Neurosci. 2021
2. Mory LN et al. J Clin Med. 2022.
3. Mussigmann T et al. Neuroimage. 2022.
4. Mouraux A et al. Brain. 2018.
5. Bouhassira D. et al. Pain.2005