

Identification of Brain Areas Associated with Chronic Neuropathic Pain through Hjorth Parameter Analysis of EEG Signals

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Abstract

This study investigates the neurophysiological signatures of chronic neuropathic pain (CNP) through the analysis of EEG signals using Hjorth parameters (Activity, Mobility, and Complexity). We compared EEG recordings from 36 CNP patients with those from 19 healthy controls (HC) under both eyes-open and eyes-closed conditions. Analysis of 19 electrode locations revealed significant differences between the groups across all Hjorth parameters. The Activity parameter showed dramatic elevations in CNP patients across all brain regions, indicating widespread cortical hyperexcitability. Mobility parameters revealed significant alterations particularly in occipital (O2), central midline (Cz), and parietal (Pz) regions, with strong effect sizes (Cliff's delta > 0.7). Complexity parameters demonstrated significant changes in right temporal (T4) and parietal midline (Pz) areas. The combined analysis identified the parietal cortex, temporal regions, occipital cortex, and central midline as key areas associated with CNP, suggesting a distributed network disruption rather than localized dysfunction. These findings contribute to our understanding of the neural mechanisms underlying chronic neuropathic pain and may support the development of objective diagnostic markers and targeted interventions for this debilitating condition.

INTRODUCTION

Neuropathic pain refers to conditions of hyperalgesia (exaggerated response from a usually painful stimulus) and allodynia (experience of pain caused by stimuli that are not typically painful), typically resulting from damage or dysfunction in the somatosensory nervous system (He & Kim, 2025; Zhao et al., 2019). This type of pain is linked to various long-term conditions and is estimated to affect up to 8% of the global population (Gilron et al., 2015). If the duration of neuropathic pain exceeds three months, then the condition is categorized as chronic neuropathic pain (CNP) according to the International Association for the Study of Pain (IASP) definition (Nicholas et al., 2019). Neuropathic pain often leads to a substantial reduction in quality of life, as patients may experience ongoing pain, sleep disturbances, fatigue, anxiety, depression symptoms, and limitations in daily functioning (Attal et al., 2018; Colloca et al., 2017). In many cases, it also results in economic consequences such as increased healthcare costs and loss of productivity (Doneddu et al., 2023; Udall et al., 2019). While often recognized as a chronic condition, neuropathic pain may first appear with acute symptoms, leading individuals to visit emergency departments and posing significant diagnostic difficulties for healthcare providers (Doneddu et al., 2023), especially considering its diverse etiologies stemming from various underlying diseases (Cohen et al., 2021).

Given the complexity and subjective nature of pain, particularly CNP, objective tools for assessment and diagnosis are increasingly needed. One promising approach involves the use of electroencephalography (EEG), which is an instrument for measuring electrical activity that occurs in the human brain by placing a number of electrodes as sensors on the surface of the head (scalp) (Asyrafi & Handayani, 2022; Peksa & Mamchur, 2023; Soufineyestani et al., 2020). EEG is often used in the medical field because of its non-radiative and non-invasive nature so it does not damage body tissue (Handayani, 2018). Research shows that changes in brain activity, particularly in regions involved in sensory processing, affective regulation, and cognitive assessment, can be detected through EEG signals (Del Popolo Cristaldi et al., 2022; Gramouseni et al., 2023; Pierce et al., 2021).

Several previous studies have shown that EEG has the potential to be used as an objective tool in understanding and diagnosing chronic pain conditions, including neuropathic pain. (Jensen et al., 2013) emphasized that EEG could capture changes in neural oscillations associated with chronic pain conditions, offering potential as a diagnostic and monitoring tool. Furthermore, Fallon et al., (2018) found that individuals suffering from chronic pain exhibited distinct alterations in EEG power spectra, particularly with increased theta power, suggesting disrupted cortical inhibition mechanisms. Similarly, Vuckovic et al., (2018) demonstrated that neuropathic pain in individuals with spinal cord injury (SCI) showed an EEG pattern of decreased dominant alpha frequency and beta band power in the parietal cortex area. The same thing was also found in a literature review conducted by (Mussigmann et al., 2022) which revealed that when neuropathic pain occurs, there is an increase in EEG signal power in the theta frequency range, but a decrease in the alpha and beta frequency ranges.

Despite the growing body of literature supporting the use of EEG in pain research, most studies still focus primarily on spectral power analysis, with limited exploration into time-domain parameters that can provide complementary insights. Among the various time-domain analysis techniques, one notable approach is the Hjorth parameter method, which includes three descriptors: activity, mobility, and complexity. These parameters are designed to quantify the temporal characteristics of EEG signals by capturing the frequency features of a signal in the time domain, without requiring time-frequency decomposition (Horr et al., 2023). While originally proposed for measuring fundamental signal characteristics, Hjorth parameters have found valuable applications in EEG analysis, particularly for their ability to capture temporal dynamics of brain activity efficiently (Hjorth, 1970; Joshi et al., 2025; Purboyo et al., 2024). In the context of chronic pain, Hjorth parameters may offer valuable information by capturing non-stationary and transient changes in EEG signals that are not always evident through frequency-based methods. Recent studies have demonstrated that Hjorth descriptors can effectively differentiate cognitive and affective states in both

healthy and clinical populations, indicating their sensitivity to subtle brain function alterations (Joshi et al., 2025; Mehmood et al., 2022). In particular, mobility parameter have shown potential in detecting disrupted neural dynamics associated with neuropsychiatric (Chow et al., 2019).

Some emerging research has begun to explore the use of Hjorth parameters in pain assessment. For instance, (Singh et al., 2019) reported that Hjorth mobility and complexity showed good ability in differentiating between acute pain and normal groups. Likewise, a study by (Kumar et al., 2015) demonstrated that the Hjorth Activity parameters derived from the parietal region correspond to the pain levels experienced by patients during their postoperative recovery. These findings suggest that alternative EEG features beyond conventional spectral power may be useful for identifying pain-related brain activity. Furthermore, identifying specific cortical regions involved in chronic neuropathic pain can improve our understanding of its underlying neural mechanisms and support the development of personalized interventions. Recent neuroimaging and EEG studies have highlighted the involvement of specific brain regions such as the prefrontal cortex, anterior cingulate cortex, somatosensory cortices, and the insula in the processing of pain, reflecting their roles in both the sensory and affective dimensions of pain perception (Mikhail, 2023). Applying Hjorth parameter analysis to EEG recordings allows researchers to localize and characterize these brain regions in a temporally resolved manner. This approach offers potential for developing novel biomarkers for the detection and monitoring of chronic neuropathic pain.

This study aims to investigate the differences in Hjorth parameters, including activity, mobility, and complexity, across various EEG electrode locations in individuals with chronic neuropathic pain compared to healthy controls. The ultimate goal is to identify specific brain regions associated with altered EEG dynamics that may serve as objective indicators of chronic neuropathic pain. This may contribute to improved diagnosis, understanding, and management of this debilitating condition.

METHOD

EEG data used in this research were obtained from two publicly available datasets. The first dataset consists of EEG recordings from 36 chronic neuropathic pain (CNP) patients of Mexican nationality (8 men and 28 women; mean age 44 ± 13.98 years) (M. Zolezzi et al., 2021). EEG signals were recorded under eyes closed (EC) and eyes open (EO) conditions, each lasting 5 minutes. The CNP dataset uses an EEG device consisting of 24 channels (Fp1, Fp2, AFz, F7, F3, Fz, F4, F8, T7, C3, Cz, C4, T8, CPz, P7, P3, Pz, P4, P8, POz, O1, O2) and 2 reference channels (M1 and M2) with a sampling frequency of 250 Hz. The placement positions of the EEG channels for the CNP dataset are shown in Figure 1a.

The second dataset is the healthy control (HC) subjects from Hospital Universiti Sain Malaysia (HUSM) (Wajid et al., 2016). HC subjects consisted of 9 males and 10 females with an average age of 38.277 ± 15.64 . EEG data were recorded under EC and EO conditions for 5 minutes each. The EEG dataset for HC subjects used 19 channels (Fp1, F3, C3, P3, O1, F7, T3, T5, Fz, Fp2, F4, C4, P4, O2, F8, T4, T6, Cz and Pz) with a sampling frequency of 256 Hz. The electrode placement positions are shown in Figure 1b.

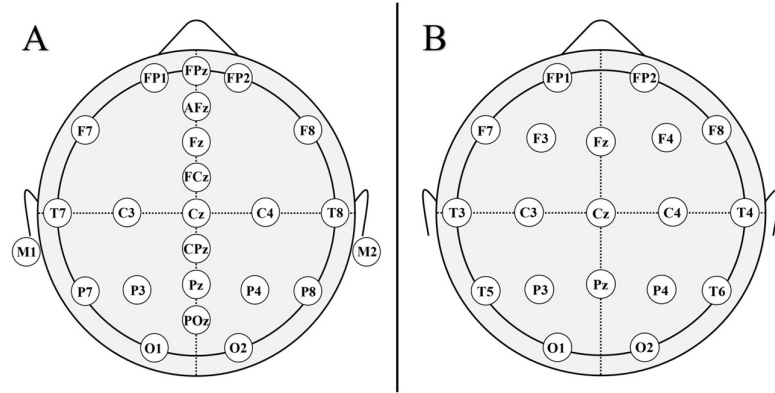


Figure 1. Electrode placement positions (channels) (a) CNP patients and (b) HC subjects

Because there is a difference in the number of EEG channels between the two datasets as seen in Figure 1, the channels used in EEG data processing are those that have the same placement position, namely Fp1, Fp2, F3, F4, C3, C4, P3, P4, O1, O2, F7, F8, T3 = T7, T4 = T8, T5 = P7, T6 = P8, Fz, Cz, and Pz (Total 19 channels). The following are the stages in EEG signal processing to identify brain areas of CNP sufferers.

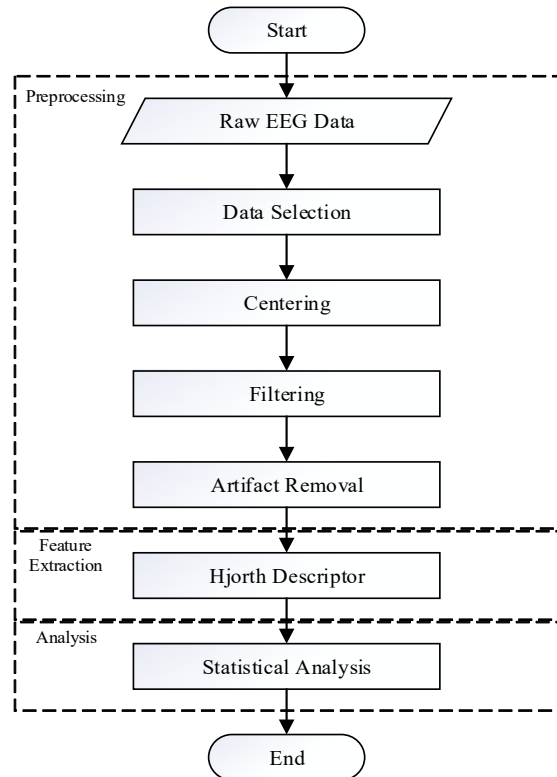


Figure 2. EEG Signal Processing Stages

Preprocessing

The initial stage in EEG signal processing is preprocessing which consists of data selection, centering, filtering, and artifact removal. Preprocessing aims to ensure the quality of the data to be

processed and eliminate noise/artifacts from EEG recordings (Guenther et al., 2024; Huang & Wang, 2021). Data selection involves examining the duration of EEG recordings for each subject, both CNP and HC. Data with a duration of less than five minutes for each condition (eyes open and closed) will not be processed further. This aims to ensure that the data from each subject has a uniform duration, allowing fair comparisons and minimizing variability caused by differences in signal length.

Centering was performed by subtracting the mean value of a defined baseline segment from each EEG channel in every epoch, thereby eliminating DC offsets and ensuring that the signal oscillates around zero. This step improves the consistency of the data across trials and enhances the reliability of subsequent analysis. Following this, filtering is conducted using FIR (Finite Impulse Response) method. This step aims to isolate frequency components relevant to brain activity (1-45 Hz) by removing low-frequency drifts and high-frequency noise, thereby enhancing the clarity and interpretability of the EEG signal (Perez-Valero et al., 2022).

The final stage in EEG signal preprocessing is artifact removal. This stage is very important because EEG signals are basically a mixture of brain signals and artifacts (Asyrafi & Handayani, 2022). For this purpose, the wavelet Independent Component Analysis (wICA) method is used by applying the Infomax algorithm. This aims to eliminate artifacts while maintaining relevant EEG signals (Zweifel, 2016).

Feature Extraction

Feature extraction is the process of converting raw data into numerical attributes that can be processed, while retaining the information from the original dataset (Yuvaraj et al., 2023). This step aims to extract relevant quantitative features from the preprocessed EEG signals in order to characterize spatial patterns of brain activity, which can be used to identify cortical regions associated with CNP. In this study, the Hjorth Descriptor method was employed to extract three time-domain features from each EEG channel, namely Activity, Mobility, and Complexity. The Activity parameter reflects the signal's power by measuring the variance of its amplitude over time. Mobility provides an indication of the average frequency content of the signal by calculating the ratio between the standard deviation of the signal's first derivative and that of the original signal. This parameter gives insight into how rapidly the signal changes. Complexity, on the other hand, evaluates how the shape of the signal diverges from a pure sine wave, capturing the presence of finer structural variations. Complexity is calculated based on the ratio of the second derivative's variance to the first, adjusted by the mobility of the original signal. This captures the signal's structural richness beyond simple oscillations (Hjorth, 1970).

Consider a discrete signal $x(n)$ where $n = 1, 2, 3, \dots, N$. The first-order difference of the signal is defined as $d(n) = x(n) - x(n - 1)$, and the second-order difference is given by $g(n) = d(n) - d(n - 1)$. The standard deviation for each of these signal sequences, including the original signal, the first-order difference, and the second-order difference, can be calculated using the following formulas (Rizal et al., 2017).

$$\sigma_0 = \sqrt{\frac{\sum_{n=1}^N x(n)^2}{N}} \quad (\text{original Signal}) \quad (1)$$

$$\sigma_1 = \sqrt{\frac{\sum_{n=1}^N d(n)^2}{N}} \quad (\text{first-order difference}) \quad (2)$$

$$\sigma_2 = \sqrt{\frac{\sum_{n=1}^N g(n)^2}{N}} \quad (\text{second-order difference}) \quad (3)$$

Based on the equation provided, the Hjorth descriptors are computed using the following parameters (Rizal et al., 2017)

$$activity = \sigma_0^2 \quad (4)$$

$$mobility = \sigma_1^2 / \sigma_0^2 \quad (5)$$

$$complexity = \sqrt{\frac{\sigma_2^2}{\sigma_1^2} - \frac{\sigma_1^2}{\sigma_0^2}} \quad (6)$$

These Hjorth parameters provide a concise representation of a signal's power, frequency characteristics, and waveform complexity in the time domain.

Analysis

Statistical analysis was carried out to assess the differences in Hjorth parameters between the CNP group and HC group. First, the mean values of each Hjorth descriptor (Activity, Mobility, and Complexity) were calculated for each EEG electrode across both groups. To test for statistically significant differences, Welch's t-test was employed due to its robustness in handling unequal variances and sample sizes between groups (Delacre et al., 2017). In addition to significance testing, Cliff's delta was calculated as a non-parametric effect size measure, offering a robust estimation of group differences without relying on distributional assumptions (Meissel & Yao, 2024). All analyses were performed separately for each EEG channel to help identify brain regions potentially implicated in chronic neuropathic pain.

RESULTS AND DISCUSSION

This research intended to identify specific brain areas associated with Chronic Neuropathic Pain (CNP) by analyzing differences in EEG signals between CNP patients and healthy control (HC) subjects using Hjorth parameters. The analysis was conducted under two different conditions: eyes open (EO) and eyes closed (EC). Three Hjorth parameters (Activity, Mobility, and Complexity) were calculated for 19 electrodes positioned according to the international 10-20 system to pinpoint the cortical regions exhibiting significant alterations in patients with CNP. This approach builds upon previous work suggesting that quantitative EEG analysis can reveal neural signatures of chronic pain conditions (Pinheiro et al., 2016).

Activity Parameter and Associated Brain Regions

Activity represents the signal power, proportional to the variance of amplitude, and serves as a key indicator of neural activation in different brain regions. As shown in Table 1, average Activity values for CNP patients were dramatically higher than those of HC subjects across all electrode locations in both eyes open and eyes closed conditions. In CNP patients, Activity values ranged from 3.22E+14 to 4.36E+14 for the eyes open condition and 2.90E+14 to 4.75E+14 for the eyes closed condition. In contrast, HC subjects exhibited Activity values ranging from 78.19 to 285.93 for eyes open and 83.91 to 243.82 for eyes closed.

Table 1. Mean Value of Activity Parameters

Channels	EO		EC		Channels	EO		EC	
	CNP	HC	CNP	HC		CNP	HC	CNP	HC
Fp1	3.58E+14	285.93	4.39E+14	225.44	Fp2	3.22E+14	252.75	3.76E+14	142.49
F3	4.04E+14	88.62	4.64E+14	83.91	F4	3.48E+14	150.61	4.43E+14	151.34
C3	3.96E+14	140.39	3.39E+14	180.59	C4	4.36E+14	78.19	3.46E+14	94.59
P3	3.87E+14	109.90	3.96E+14	141.19	P4	3.55E+14	157.72	3.74E+14	198.06
O1	3.48E+14	175.74	3.74E+14	243.82	O2	3.50E+14	109.48	4.35E+14	154.07
F7	3.38E+14	99.18	2.90E+14	109.17	F8	3.39E+14	170.29	4.24E+14	170.36
T3	3.69E+14	142.36	3.11E+14	184.76	T4	3.85E+14	81.83	4.51E+14	88.66
T5	4.13E+14	132.76	4.75E+14	179.68	T6	3.84E+14	152.09	3.51E+14	195.40

Fz	4.27E+14	166.43	3.98E+14	199.99	Cz	4.00E+14	86.88	4.11E+14	104.84
					Pz	4.00E+14	122.68	3.51E+14	169.31

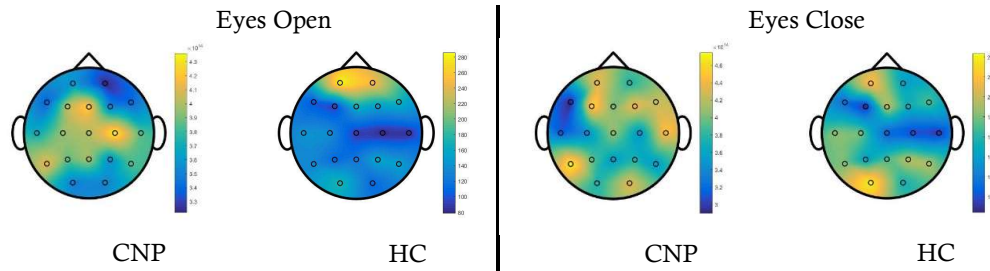


Figure 3. Topography of the Mean Values for Activity Parameters

The topographic mapping (Figure 3) illustrates this stark contrast in Activity between the groups and reveals a global increase in cortical excitability across all brain regions in CNP patients. While all regions showed significant differences, particularly high Activity values were observed in the frontal midline (FZ), central (C4), and temporal (T5) regions during eyes open, and in temporal (T5) and frontal (F3, F4) regions during eyes closed condition. This widespread cortical hyperexcitability is consistent with the central sensitization mechanism observed in chronic pain conditions (Xiong et al., 2024), suggesting that CNP affects multiple functional brain networks rather than being localized to specific sensory or pain processing regions. This finding aligns with previous neuroimaging studies showing widespread alterations in brain activity in chronic pain patients (May et al., 2021).

Statistical analysis on the Activity parameter (Table 2) using Welch's t-test confirmed that the differences in Activity between CNP and HC groups were highly significant ($p < 0.001$) for all electrode positions in both conditions. Additionally, Cliff's delta effect size analysis yielded a value of 1 across all electrodes for the Activity parameter, indicating a maximum effect size and complete separation between the groups. This robust finding across all brain regions suggests that generalized cortical hyperexcitability is a key neurophysiological characteristic of CNP, supporting the concept that chronic pain fundamentally alters brain function across distributed networks (Kandić et al., 2021).

Table 2. Significance Analysis of Activity Parameters

Channels	Welch t-test (<i>p-value</i>)		Cliff's Delta $ \delta $	
	Eyes Open	Eyes Close	Eyes Open	Eyes Close
Fp1	8.46E-10	4.33E-11	1	1
F3	5.59E-10	7.25E-12	1	1
C3	1.43E-11	3.15E-10	1	1
P3	4.99E-10	2.13E-11	1	1
O1	4.29E-09	7.47E-11	1	1
F7	9.57E-11	7.86E-11	1	1
T3	4.31E-09	2.79E-10	1	1
T5	9.04E-12	1.75E-11	1	1
Fz	1.08E-11	2.39E-11	1	1
Fp2	3.13E-09	2.96E-10	1	1
F4	3.60E-10	1.93E-10	1	1
C4	1.03E-09	7.59E-09	1	1

P4	1.58E-09	4.00E-10	1	1
O2	6.33E-10	2.46E-11	1	1
F8	2.38E-08	1.57E-10	1	1
T4	5.15E-10	2.79E-12	1	1
T6	2.35E-11	5.52E-10	1	1
Cz	7.25E-11	9.00E-11	1	1
Pz	1.04E-10	4.83E-11	1	1

Mobility Parameter and Associated Brain Regions

Mobility, representing the mean frequency of the signal, revealed specific brain regions with altered frequency characteristics in CNP patients. The results of calculating the mean value of mobility parameters for each electrode are shown in Table 3. In CNP patients, Mobility values were substantially higher and more variable, ranging from $1.04\text{E-}02$ to $1.45\text{E+}09$ for eyes open and $2.14\text{E-}02$ to $1.83\text{E+}09$ for eyes closed. HC subjects demonstrated more consistent Mobility values ranging from 0.08 to 0.19 for eyes open and 0.08 to 0.14 for eyes closed.

Table 3. Mean Value of Mobility Parameters

Channels	EO		EC		Channels	EO		EC	
	CNP	HC	CNP	HC		CNP	HC	CNP	HC
Fp1	1.95E+08	0.08	4.75E+08	0.08	Fp2	3.75E+08	0.08	4.53E+08	0.10
F3	5.14E+08	0.13	5.50E+08	0.11	F4	5.24E+08	0.12	9.08E+08	0.10
C3	2.10E+08	0.10	2.72E+08	0.11	C4	7.86E+08	0.12	5.09E+08	0.11
P3	3.60E+08	0.10	4.16E+08	0.10	P4	2.06E+08	0.08	4.66E+08	0.08
O1	3.29E+08	0.10	4.12E+08	0.09	O2	1.04E-02	0.10	2.14E-02	0.10
F7	6.97E+07	0.14	2.41E+08	0.12	F8	4.44E+08	0.13	2.38E+08	0.11
T3	4.17E+08	0.13	5.70E+08	0.13	T4	2.58E+08	0.19	3.82E+08	0.14
T5	1.21E-02	0.12	1.73E+08	0.10	T6	7.60E+07	0.09	3.16E-02	0.09
Fz	4.10E+08	0.10	7.58E+08	0.08	Cz	1.45E+09	0.11	1.83E+09	0.11
					Pz	2.12E-02	0.09	4.11E-02	0.10

The topographic distribution of Mobility (Figure 4) identified specific brain regions with altered frequency patterns in CNP patients. Particularly notable was the high focal activity in the central midline (Cz) region, which corresponds to the supplementary motor area and is involved in motor planning and pain modulation (BANDO et al., 2022; Scheliga et al., 2025). Additionally, significant alterations were observed in the posterior regions, specifically in the temporoparietal (T5) and occipital (O2) areas, suggesting disruption in visual and multimodal sensory integration networks that may contribute to the CNP experience. These findings support previous research indicating that chronic pain can affect sensorimotor integration processes (Brun et al., 2017).

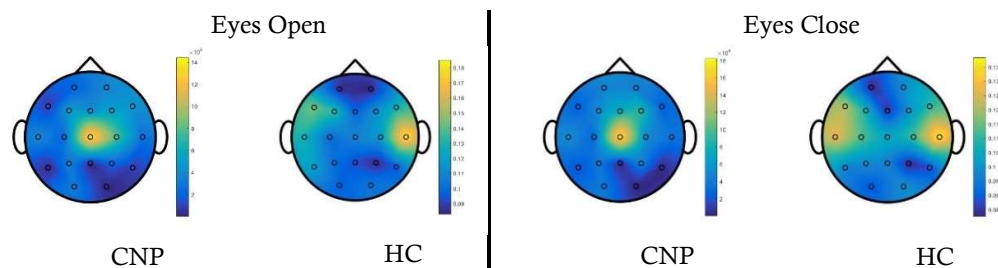


Figure 4. Topography of the Mean Values for Mobility Parameters

Statistical analysis (Table 4) confirmed significant differences ($p < 0.05$) in several key areas. The most statistically significant differences were observed in the occipital region (O2), with p-values of 0.001 for eyes open (EO) and 0.00006 for eyes closed (EC), highlighting a marked variation in neural activity between these two conditions. The central midline (Cz) showed significant differences as well, with p-values of 0.001 for both EO and EC, indicating consistent neural changes regardless of eye state. In the parietal midline (Pz), the differences were also significant, with p-values of 0.001 for EO and 0.031 for EC, suggesting stronger changes in the EO condition but still a notable difference when the eyes were closed. In addition, the temporal region (T5) exhibited a p-value of 0.001 for EO, indicating a significant neural shift during the eyes open condition.

Table 4. Significance Analysis of Mobility Parameters

Channels	Welch t-test (<i>p-value</i>)		Cliff's Delta $ \delta $	
	Eyes	Eyes	Eyes	Eyes
	Open	Close	Open	Close
Fp1	0.325	0.120	0.915	0.706
F3	0.126	0.089	0.824	0.699
C3	0.213	0.285	0.882	0.824
P3	0.125	0.161	0.810	0.824
O1	0.187	0.163	0.784	0.778
F7	0.325	0.173	0.876	0.758
T3	0.183	0.106	0.817	0.706
T5	0.001	0.325	0.928	0.863
FZ	0.100	0.033	0.712	0.588
Fp2	0.189	0.119	0.850	0.693
F4	0.101	0.027	0.765	0.588
C4	0.054	0.113	0.686	0.765
P4	0.325	0.162	0.922	0.765
O2	0.001	0.000	0.967	0.915
F8	0.114	0.148	0.712	0.758
T4	0.325	0.186	0.876	0.739
T6	0.325	0.014	0.876	0.843
Cz	0.001	0.001	0.124	0.176
Pz	0.001	0.031	0.889	0.817

The Cliff's delta values for Mobility ranged from -0.12 to -0.97, with most electrodes showing strong effect sizes ($|\delta| > 0.7$). The strongest effects were observed in the occipital (O2, $|\delta| = 0.967$), parietal (P4, $|\delta| = 0.922$), and temporoparietal (T5, $|\delta| = 0.928$) electrodes. These findings indicate that the occipital, central, and parietal brain regions exhibit the most pronounced frequency alterations in CNP, suggesting their critical involvement in the pathophysiology of chronic neuropathic pain (CNP). This pattern of regional frequency alterations is consistent with the "pain matrix" concept, which describes a distributed network of brain regions involved in pain processing (Cao et al., 2017; Hu et al., 2024).

Complexity Parameter and Associated Brain Regions

Complexity, which measures the change in frequency and represents how the shape of the signal deviates from pure sine waves, identified additional brain regions affected by CNP. The average values of the complexity parameters for EO and EC conditions at each electrode are shown in Table

5. For eyes open condition, Complexity values in CNP patients ranged from 0.63 to 4.20E+12, while HC subjects showed values between 0.64 and 0.71. In the eyes closed condition, CNP patients exhibited values from 0.57 to 3.69E+12, compared to 0.67 to 0.74 in HC subjects.

Table 5. Mean Value of Complexity Parameters

Channels	EO		EC		Channels	EO		EC	
	CNP	HC	CNP	HC		CNP	HC	CNP	HC
Fp1	0.71	0.67	0.71	0.73	Fp2	0.69	0.67	0.70	0.72
F3	0.74	0.64	0.71	0.70	F4	0.73	0.69	0.70	0.73
C3	0.69	0.69	0.65	0.72	C4	0.68	0.65	0.64	0.68
P3	4.20E+12	0.66	0.58	0.67	P4	0.64	0.68	0.57	0.69
O1	0.69	0.67	0.62	0.68	O2	0.70	0.66	3.12E+12	0.66
F7	0.72	0.67	3.42E+12	0.70	F8	0.73	0.71	0.70	0.74
T3	0.72	0.70	0.68	0.73	T4	0.72	0.64	0.66	0.70
T5	0.67	0.66	0.60	0.67	T6	0.67	0.68	0.60	0.69
Fz	0.66	0.70	3.24E+12	0.70	Cz	0.67	0.66	3.69E+12	0.69
					Pz	0.63	0.70	0.57	0.72

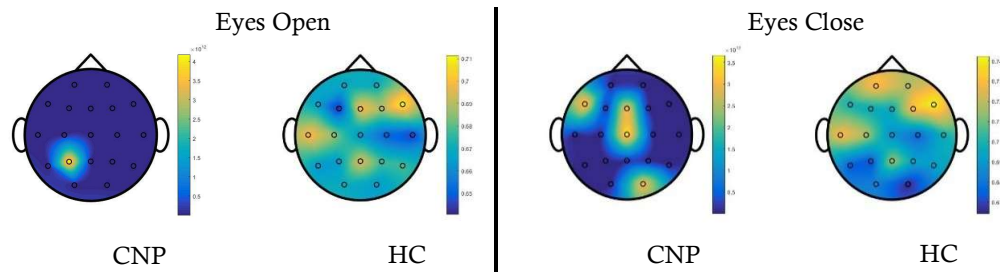


Figure 5. Topography of the Mean Values for Complexity Parameters

The topographic maps (Figure 5) revealed specific brain regions with altered neural signal complexity in CNP (chronic neuropathic pain) patients, highlighting several key areas of change. The parietal regions (P3, P4, Pz), particularly the posterior parietal cortex involved in spatial awareness and sensory integration, exhibited significant alterations. Specifically, the P3 region (left parietal) showed extreme values during the eyes-open condition (with a peak value of 4.20E+12), while the Pz region (midline parietal) showed changes during the eyes-closed condition. These findings align with previous research indicating the crucial role of the parietal cortex in the multisensory integration aspects of pain perception (Gallace & Bellan, 2018).

Statistical analysis for complexity parameters (Table 6) identified significant differences ($p < 0.05$) across these specific regions, with the most notable differences in T4 (p -value of 0.006) for eyes open and Pz (p -value of 0.002) for eyes closed. Cliff's delta analysis revealed particularly strong effects in F3 (0.601), T4 (0.582), and PZ (0.745). The distinctive pattern of Complexity alterations in these regions, different from those identified by Activity and Mobility parameters, suggests that CNP affects multiple aspects of neural processing across different functional networks, with particular involvement of the right temporal, parietal midline, and left frontal regions in the abnormal neural complexity associated with chronic pain states. This supports the concept of CNP as a complex network disorder involving altered communication between multiple brain regions (Cao et al., 2017).

Table 6. Significance Analysis of Complexity Parameters

Channels	Welch t-test (<i>p-value</i>)		Cliff's Delta	
	Eyes Open	Eyes Close	Eyes Open	Eyes Close
Fp1	0.439	0.499	0.203	0.163
F3	0.017	0.692	0.601	0.085
C3	0.916	0.092	0.046	0.373
P3	0.325	0.018	0.150	0.556
O1	0.623	0.121	0.065	0.340
F7	0.125	0.325	0.366	0.000
T3	0.708	0.070	0.092	0.320
T5	0.895	0.025	0.000	0.464
FZ	0.446	0.325	0.183	0.183
Fp2	0.629	0.613	0.033	0.092
F4	0.366	0.326	0.261	0.229
C4	0.469	0.385	0.144	0.209
P4	0.498	0.010	0.248	0.601
O2	0.401	0.325	0.163	0.176
F8	0.663	0.134	0.124	0.288
T4	0.006	0.116	0.582	0.222
T6	0.853	0.027	0.085	0.490
Cz	0.836	0.325	0.065	0.307
Pz	0.218	0.002	0.516	0.745

Brain Area Identification

Based on the combined analysis of all three Hjorth parameters, several brain regions showed consistent and significant alterations in chronic neuropathic pain (CNP) patients compared to HC subjects. The parietal region (P3, P4, Pz) exhibited significant differences across multiple parameters, particularly in Complexity and Mobility. The Pz electrode showed strong statistical significance in both parameters under eyes-open and eyes-closed conditions, with a notably large effect size for Complexity during eyes-closed (Cliff's delta of 0.745). This suggests that the medial parietal cortex, involved in sensory integration and body awareness, plays a crucial role in chronic neuropathic pain processing. This finding aligns with previous research identifying the parietal cortex as a key component in the chronic pain network (Gallace & Bellan, 2018).

In addition, the temporal regions (T3, T4, T5, T6) demonstrated significant differences in at least one parameter. Electrodes T4 and T5 showed significant alterations in Complexity (*p-value* 0.006 and 0.025, respectively), indicating altered neural activity in the temporal lobes associated with chronic pain, potentially linked to emotional and memory aspects of pain perception. Prior studies have highlighted the temporal lobe's role in pain-related fear and emotional memory processing (Ayoub et al., 2019).

The occipital region (O1, O2) also showed highly significant changes, especially at electrode O2, which demonstrated significant differences in Mobility during both eyes-open (*p-value* 0.0009) and eyes-closed (*p-value* 0.00006) conditions, with extremely large effect sizes (Cliff's delta 0.967 and 0.915). This suggests altered visual cortex processing, likely related to the interaction between visual perception and chronic pain mechanisms. These results are in line with earlier research showing structural and functional changes in the occipital cortex of chronic pain patients (Chatterjee et al., 2023).

Finally, the central region (Cz) exhibited significant differences in Mobility under both conditions (*p-value* less than 0.001), suggesting alterations in the supplementary motor area or medial central cortex. These changes may be associated with motor adaptation or planning in response to

chronic pain. This supports previous findings showing reorganization of motor and sensory cortices in individuals with chronic pain conditions (Jutzeler et al., 2015).

Limitations and Future Directions

While this study provides valuable insights into the brain regions associated with chronic neuropathic pain, several limitations should be acknowledged. First, although the sample size was adequate for statistical analysis, it could be expanded in future research to enhance the generalizability of the findings. As highlighted by Maixner et al. (2017), larger cohorts are essential to account for the heterogeneity present in chronic pain conditions (Maixner et al., 2016). Second, the extreme differences in Activity values observed between CNP patients and healthy individuals call for further investigation to clarify the underlying physiological mechanisms. Furthermore, future research should consider incorporating functional connectivity analysis to improve the understanding of network-level abnormalities in chronic neuropathic pain. This analytical approach has already proven effective in recent pain neuroimaging studies (Kowalski et al., 2023). Finally, linking Hjorth parameters to clinical pain measures and quality of life assessments would offer more comprehensive insights into the clinical significance of these electrophysiological findings, in line with recommendations from recent pain research guidelines (Davis et al., 2020).

CONCLUSION

This study used Hjorth parameter analysis of EEG signals to identify brain regions associated with chronic neuropathic pain (CNP). Our findings reveal distinct electrophysiological patterns in CNP patients compared to healthy controls. The most notable finding was the dramatic increase in Activity parameters across all brain regions in CNP patients, indicating widespread cortical hyperexcitability consistent with central sensitization. Significant alterations in Mobility parameters were found particularly in occipital (O2), central midline (Cz), and parietal (Pz) regions, while Complexity parameters identified the right temporal (T4) and parietal midline (Pz) regions as showing altered neural complexity.

The results point to a distributed network of affected brain regions rather than isolated dysfunction, with particularly strong involvement of the parietal cortex, temporal regions, occipital cortex, and central midline. These findings align with the "pain matrix" concept, supporting the view of CNP as a complex network disorder. The time-domain Hjorth parameter approach provides complementary insights to traditional spectral analysis methods and offers a promising avenue for developing objective biomarkers for CNP diagnosis and monitoring. Future research should explore relationships between these electrophysiological parameters and clinical pain measures to develop more targeted interventions for this debilitating condition.

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