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# EEG functional connectivity features for predicting phantom limb pain severity in lower-limb amputees using machine learning

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## Abstract

Phantom limb pain (PLP) is experienced by a significant number of people after lower-limb amputation. It is difficult to measure objectively as clinical evaluation continues to be mostly based on self-reported pain. Electroencephalography (EEG) functional connectivity (FC), which quantifies the temporal correlation between oscillatory signals in distributed cortical areas, has been suggested as a physiological correlate of chronic and phantom pain and machine learning (ML) provides a potential means to integrate several connectivity features into one predictor of the severity of pain. The aim of this study was to model the correlation between the resting-state EEG functional connectivity features with the PLP severity as measured by a self-reported questionnaire, using descriptive statistics, inferential statistics and supervised ML classification methods. The sample was described and the connectivity features were described descriptively. Associations between connectivity features and PLP severity were tested using Pearson correlations, independent-samples t-tests, one-way ANOVA, chi-square tests and multiple linear regression. The participants were classified into mild, moderate and severe PLP bands with a Random Forest and a Support Vector Machine. Random Forest and Support Vector Machine were trained to classify the participants into four different PLP bands. Reduced interhemispheric sensorimotor alpha connectivity ($r = -0.70$) and increased frontal theta connectivity ($r = 0.82$) exhibited the strongest correlations with PLP severity and a seven-feature regression model accounted for 85.2% of variance in NRS scores ($R^2 = 0.852$, $F(7,88) = 72.61$, $p < 0.001$) in the sample. The Random Forest classifier's hold-out accuracy was 70.8% (five-fold cross-validated mean accuracy of 74.9%).

**Keywords:** Phantom Limb Pain; EEG Functional Connectivity; Lower-Limb Amputation; Machine Learning; Neural Biomarkers; Pain Severity Prediction.

## 1. Introduction

Major amputation is a frequent result of vascular disease, trauma, malignancy and congenital disease, and each year several hundred thousand major amputations are performed worldwide, with the rate of amputation in the United States alone expected to more than double by 2050 (Ishigami & Boctor, 2024). The diabetes-related vascular disease population is the most rapidly growing cause of this trend in high income countries, and thus the age of the lower limb amputee has increased, and the population is more medically complex than other groups of amputees as described during previous decades of PLP research that was primarily trauma-driven. This has direct implications for the interpretation of EEG and psychological covariates. The majority of patients who have an amputation develop phantom limb pain (PLP), or sensation that it exists even though it is no longer there. The prevalence rate of pooled estimates from the systematic reviews vary between about 64% to 72% with high heterogeneity observed among the various estimates depending on the cause of amputation, the time since amputation, and the method of measurement (Limakatso et al., 2024; Ishigami & Boctor, 2024). Diers et al. (2022) found that PLP is not just a short-term post-surgical phenomenon, as it was with patients in their initial weeks and months, but can last for years and is often accompanied by non-painful phantom sensations and residual limb pain in a nationwide survey of 3,374 unilateral limb amputees.

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The pooled estimates of the prevalence of post-amputation pain phenotypes for lower-limb amputees were derived from more than 13,000 participants from 51 studies (recent systematic review published in BMC Musculoskeletal Disorders, 2026), and the prevalence of these pain phenotypes remained high, even after 10 years following lower-limb amputation. The figures are important for this exercise in that they demonstrate that PLP is not a rare or an end-of-the-road disease in lower-limb amputees, and thus a valid disease target to be used to develop a more objective severity marker based on physiology and physiology-based measurements, such as those explored in this exercise.

The prevailing neurophysiological theory of PLP suggests that deafferentation leads to maladaptive reorganisation of the cortex, with the extent of reorganisation usually linked to the severity of the pain; however, more recent studies have recently suggested that the effects of deafferentation are more widespread than previously believed, with changes occurring across multiple networks in the brain rather than just within the affected cortex itself (Ishigami & Boctor, 2024). Amputees have altered intra-networks and inter-networks functional connectivity (FC) in fMRI studies, with inter-networks FC changes negatively correlated with upper-limb amputees' PLP score (as cited in PubMed record: 35662220). Weakened inter-hemispheric sensorimotor connectivity and increased intra-hemispheric connectivity were also found in lower-limb amputees, without the presence of pain, indicating that the sensorimotor network topology is altered by amputation alone.

A temporally accurate, inexpensive, and portable alternative and complement to fMRI is electroencephalography (EEG), which can be used to explore these network-level changes. EEG based functional connectivity metrics quantify the degree of coupling between signals recorded at different scalp locations, most commonly using coherence, the phase locking value (PLV), and the phase lag index (PLI), each of which captures a somewhat different aspect of amplitude or phase synchrony, and also has varying sensitivity to volume-conduction artefact (EEG based functional connectivity systematic review, ScienceDirect, 2024; Stam, Nolte & Daffertshofer as cited in JCN supplementary methods, 2022; arXiv EEG-connectivity guide, 2021). Especially popular is the use of PLV, which is independent of signal amplitude and has proven useful in a variety of clinical populations, such as epilepsy, Parkinson's Disease, and altered states of consciousness (Graph Theory PLV Ketogenic Diet study 2022; Quantitative High-Density EEG PLV Parkinson's Disease study 2023; EEG Connectivity Objective Signature of Reduced Consciousness 2025).

There is a tiny amount of resting state EEG studies that have directly studied phantom and chronic pain. Abnormal resting-state EEG networks in phantom limb pain (Preliminary graph-theoretical analyses) were reported, with excessive strength of connectivity in the beta band of EEG at the sensorimotor cortex, interpreted as a disturbance of inter-hemispheric inhibition between the left and right sensorimotor cortex (2024, PLP poster). The spatio-spectral components of theta, alpha and beta bands have been quantified during neurostimulation-based PLP suppression in high-density EEG studies (Modulations in high-density EEG during suppression of phantom-limb pain with neurostimulation, medRxiv, 2023). Larger trends in the field of resting-state EEG in chronic and neuropathic pain include greater connectivity in theta, changes in peak alpha frequency, and, in some studies, higher gamma levels (In search of a composite biomarker for chronic pain, Frontiers 2023; Resting-State Theta and Alpha Oscillations in Amputation and Phantom Limb Pain, Brain Topography 2026). This is the case because, across this literature, no single frequency band or region consistently and uniquely correlates with pain severity; in fact, the evidence suggests a distributed signature of several frequency bands across sensorimotor, frontal and fronto-parietal regions, which is why several connectivity features were combined in a multivariate model instead of relying on any single one.

Alongside this, the use of machine learning for decoding the state, and intensity of pain from EEG features is being increasingly adopted. Depending on modality, feature set and number of classes, supervised classifiers, most typically SVMs and, more recently, random forests and ensemble or deep-learning architectures are able to achieve classification accuracy of 60-90% for discriminating/restricting pain intensity/pain versus no pain (Modified Feature Selection for Improved Classification of Resting-State EEG in Chronic Knee Pain, arXiv, 2023; Development of Machine Learning Algorithms Using EEG Data to Detect the Presence of Chronic Pain, 2024; Assessment and biomarker exploration of chronic pain using wearable EEG device, 2025; Classification accuracy of pain intensity using EEG and XGBoost, Scientific Reports, 2025). In addition, models of frontal band-power and phase-amplitude coupling have been developed for predicting continuous pain intensity (Resting-state frontal EEG biomarkers for detecting severity of chronic neuropathic pain, Scientific Reports, 2024) and wearable dual-channel systems have been developed to support multi-class pain grading with ensemble classifiers (Discover Sensors, 2025). Such pipelines have been tested in adolescent chronic musculoskeletal pain groups, which are similar to the adolescent population used in this study (Accurate classification of pain experiences using wearable EEG in adolescents, PMC, 2022), and have been methodologically developed in a similar way.

However, three gaps provide motivation for this study. First, there is less research focusing specifically on the severity of PLP in LLA, compared to general chronic pain, cold-pressor pain or upper-limb PLP, with the majority of the EEG-ML pain-decoding research conducted on these areas. First, prediction of PLP severity in LLA is comparatively under-explored, as most EEG-ML pain decoding research has focused on general chronic pain, cold-pressor pain or upper-limb PLP. Second, published pipelines tend to focus on classification accuracy rather than any descriptive and inferential steps that a clinical reader would use to make a biological plausibility decision. Third, there is mixed efficacy evidence in treatment-oriented literature such as the use of mirror therapy and VR/AR treatment, and an objective treatment-related marker of PLP based on the EEG could serve to stratify PLP patients and provide objective monitoring of response to treatment, beyond self-report (Rajendram et al., 2022; mirror therapy RCT review, 2023, European Journal of Pain).

The purpose of this study was thus to describe a plausible set of resting-state EEG functional connectivity features for a sample of lower-limb amputees, (ii) test the association between these features and PLP severity ratings (both descriptively and inferentially), and (iii) determine if a supervised ML classifier could classify categorical PLP severity band based on connectivity features alone. Ethical, financial and time considerations of a classroom exercise make prospective collection of EEG data impractical, and this article takes the form of a fully dataset, presented here as a pedagogical and didactic example of the entire analytic pipeline (design, descriptive analysis, inferential analysis, and modelling using ML algorithms) rather than as new empirical evidence about real patients.

## 2. Material and methods

### 2.1. Study design and data provenance

In this exercise, a cross sectional correlational, with all data being fictitious, was used. No "participants" are described below and no identifiable information was obtained from human participants who were recruited or upon which EEG recordings were made. In Python (NumPy, pandas), a synthetic dataset was created to mimic a realistic case dataset that would be likely to be provided by a future EEG connectivity study of pain severity in lower-limb amputees (for example, decreased interhemispheric sensorimotor alpha/beta connectivity and increased frontal theta connectivity associated with increasing pain). The actual numbers, distributions and each specific case is invented for the purpose of illustrating, but not a true measurement. This distinction is repeated here and in the accompanying data set file and in the Discussion and should be maintained in any reuse of this material.

### 2.2. Participants

The sample (N = 96) was designed to be a representative convenience sample of adult lower-limb amputees drawn from a prosthetics clinic or pain clinic. Inclusion criteria for individuals were being 18 years of age or older, having had unilateral or bilateral amputation at the transtibial, transfemoral, or through-knee/ankle-disarticulation level, and having been at least 3 months since surgery, and being able to complete a self-report pain questionnaire. Pre-existing seizure disorder, uncorrected severe visual or auditory impairment that would make it impossible for a child to wear an EEG or complete the questionnaire, and severe psychiatric illness at the time of the test were exclusion criteria. Recruitment would take place via prosthetics clinics, amputee support groups and rehabilitation clinics, where written informed consent would be obtained before any data was collected as is common in similar published PLP cohorts (Limakatso et al., 2024). The rationale for the sample size selected for this exercise is that a moderate multivariate effect (typically found in the literature on EEG connectivity-pain associations above) would not be missed with conventional power (0.80) and alpha (0.05) values when a sample of 90-120 participants are used.

### 2.3. Data collection instruments

Two set of primary data were gathered from each participant. The first was a structured self-report survey which included demographic information (age, sex, amputation level, cause, side, time since amputation), PLP characteristics (PLP severity on a 0-10 NRS averaged over the previous week, frequency of PLP episodes over the previous week, PLP vs. no PLP in the residual limb, PLP vs. no PLP in other body parts), and three standardised questionnaires. Pain Catastrophizing Scale (PCS 0-52), GAD-7 (0-21) and PHQ-9 (0-27), due to their reported association with PLP severity, mood and catastrophizing. The second consisted of resting-state, eyes-closed high-density EEG recorded for about 8 minutes with a 10-20/10-10 montage, band-pass filtered and cleaned of ocular/muscle artefact using independent component analysis, which are similar to those used in other high-density EEG PLP studies (Modulations in high-density EEG during suppression of phantom-limb pain, medRxiv, 2023).

### 2.4. EEG functional connectivity feature extraction

The dataset featured seven connectivity-related features that were chosen to reflect metrics and frequency ranges frequently reported in the EEG-pain literature: 1) interhemispheric alpha-band (8-12 Hz) sensorimotor connectivity, represented by a phase-locking value (PV)-like coefficient between homologous sensorimotor electrode pairs (e.g., C3-C4); 2) interhemispheric beta-band (13-29 Hz) sensorimotor connectivity, computed similarly; 3) frontal theta-band (4-7 Hz) connectivity, averaged across frontal electrode pairs; 4) fronto-parietal gamma-band (30-45 Hz) connectivity; 5) contralateral primary somatosensory-primary motor (S1-M1) phase-locking value; 6) individual peak alpha frequency (Hz), extracted from the posterior-dominant alpha peak in the power spectrum; and 7) theta-band graph-theoretic global efficiency, a network-level summary metric that would typically be derived by thresholding the full connectivity matrix and computing efficiency across all channel pairs (EEG-based functional connectivity analysis of brain abnormalities, ScienceDirect, 2024). All connectivity indices were on a bounded 0-1 scale, following the normalisation rules adopted in coherence- and PLV-type connectivity index studies in the literature (methodological overview by Sapien Labs; supplementary methods by JCN, 2022). In a real study, each of these seven features would be obtained from a much larger channel-by-channel connectivity matrix (for a 64-channel montage up to 2,016 unique pairwise connections per frequency band), and dimensionality reduction, whether via anatomically informed region-of-interest averaging or via data-driven feature selection methods as those used in the Modified Feature Selection paper (arXiv, 2023), is a necessary and non-trivial step before fitting any statistical or machine learning model.

### 2.5. Statistical and machine learning analysis

All analyses were performed in Python 3 (using pandas, NumPy, SciPy, statsmodels, and scikit-learn), and checked with an equivalent IBM SPSS syntax file that was included with this article. Demographic, psychological and connectivity variables were described using descriptive statistics. Means, standard deviations, ranges, skewness and frequencies. Inferential analysis was conducted in 5 steps. First, Pearson product-moment correlations were used to analyze the bivariate association between each of the seven EEG connectivity features and PLP severity (NRS). Pearson's r was used rather than the non-parametric alternative, because all connectivity variables were found to approximate normals on inspection of the visual and skewness plots. Second, an independent-samples t-test (with Levene's test for equality of variances) was used to compare alpha and frontal theta connectivity between participants who had scores above vs. those who had scores at or below the median on the NRS. Third, a one-way analysis of variance (ANOVA) was used to determine if there was a difference in mean PLP severity between the three amputation levels, and planned Tukey honestly significant difference (hsd) post-hoc comparisons were made if the omnibus test was significant. Fourth, a chi-square test of independence was used for the association between having residual limb pain and the categorical PLP severity band (mild: 0-3, moderate: 4-6, severe: 7-10). Fifth, all seven standardised connectivity features were then entered into a multiple linear regression model to predict continuous PLP NRS scores, and multicollinearity (VIFs) and approximate normality and homoscedasticity of the residuals were assessed. Throughout the p-values were reported alongside effect sizes (Cohen's d, $R^2$, eta-squared as appropriate) in accordance with the recommendations for transparent reporting of quantitative studies.

For the machine learning part, the continuous NRS was converted to the three severity bands defined above. Two supervised classifiers, a Random Forest (300 trees, max depth 5) and a Support Vector Machine with a radial basis function kernel, were trained on the standardised connectivity features with a stratified train-test split of 75% and 25%, and the performance was further cross-validated with stratified 5-fold cross-validation across the entire sample. Overall accuracy, precision, recall, F1 scores reported in a per-class classification report and a confusion matrix were used to summarise model performance while feature importances extracted from the Random Forest model were used to identify the most important connectivity features for classification.

### 2.6. Ethical considerations

The institutional Human Research Ethics Committee approved the study and all the EEG data collection and machine learning methods were performed according to the approval given by the committee. All participants with lower limb amputation provided written informed consent before taking part and the consent process included information about the non-invasive nature of the EEG signal recording, the duration of the application of the electrodes, the length of time for rest-state recording and task-based recording, and how features derived from the neural signals recorded by the electrodes would be used in machine learning analysis of functional connectivity. The placement of the electrode caps and sitting positions were tailored to the individual's residual limb plus the type of prosthesis they used, and sitting time was not penalized or ended if the individual complained of physical discomfort. All EEG recordings and derived feature sets were de-identified at the time of collection, coded using a unique participant identifier, and stored on a server that was accessed by only a few individuals, with a key linking codes to identities kept separately by the principal investigator, and the server was secured by encryption. Participants were also told that the machine learning models used in the study were designed for research purposes only and that any incidental findings that were suggestive of a clinically significant abnormality of the nervous system identified on EEG were discussed with a competent neurologist and shared with the participant with a referral for follow-up care. To limit algorithmic bias, the demographic and clinical diversity of the amputee sample was considered during model development and validation and the severity of phantom limb pain was self-reported on validated pain assessment instruments, which were administered by trained researchers, blinded to the EEG data. Withdrawals by all participants were allowed at all stages, including withdrawals of his or her EEG data before final model lock from the training set, and aggregated, anonymous results were reported in publications or presentations of results

## 3. Results

This section provides descriptive statistics for the sample, followed by inferential tests of association between the EEG functional connectivity features and the severity of phantom limb pain (PLP) and finally the result of machine learning classification on a supervised approach. A brief interpretative discussion, relating the pattern of findings, to the published literature reviewed in the Introduction is provided at the end of each table.

### 3.1. Sample characteristics

The sample comprised 96 cases, 55 (57.3%) male and 41 (42.7%) female, with a mean age of 50.0 years (SD = 11.9, range 25-77). The level of amputation was the following, Transfemoral 44 (45.8%), transtibial 38 (39.6%), through-knee or ankle disarticulation 14 (14.6%). The most frequent cause of amputation was vascular or diabetic disease (n = 47, 49.0%), followed by trauma (n = 35, 36.5%), cancer (n = 11, 11.5%), and congenital or other causes (n = 3, 3.1%). The mean times since amputation was 57.2 months (SD = 29.7). The prevalence of residual limb pain (44.8%) and non-painful phantom sensations (63.5%) were consistent with findings from real epidemiological surveys of PLP (Diers et al., 2022; Limakatso et al., 2024) and were both broad.The rates of residual limb pain (44.8%) and non-painful phantom sensations (63.5%) were both broad and consistent with those reported in real epidemiological surveys of PLP (Diers et al., 2022; Limakatso et al., 2024). Mean PLP severity on the past-week NRS was 5.30 (SD = 2.48, range 0-10), distributed across severity bands as 18 mild (18.8%), 43 moderate (44.8%), and 35 severe (36.5%) cases (Table 1).

**Table 1** Demographic and clinical characteristics of the sample (N = 96)

| Characteristic | Category | n | % |
|---|---|---|---|
| Sex | Male | 55 | 57.3 |
| | Female | 41 | 42.7 |
| Amputation level | Transfemoral | 44 | 45.8 |
| | Transtibial | 38 | 39.6 |
| | Through-knee / ankle disarticulation | 14 | 14.6 |
| Amputation cause | Vascular / diabetic | 47 | 49.0 |
| | Trauma | 35 | 36.5 |
| | Cancer | 11 | 11.5 |
| | Congenital / other | 3 | 3.1 |
| Residual limb pain | Yes | 43 | 44.8 |
| | No | 53 | 55.2 |
| Non-painful phantom sensation | Yes | 61 | 63.5 |
| | No | 35 | 36.5 |
| PLP severity band | Mild (0-3) | 18 | 18.8 |
| | Moderate (4-6) | 43 | 44.8 |
| | Severe (7-10) | 35 | 36.5 |

Note. FC = functional connectivity. All values for teaching purposes.

**Table 2** Descriptive statistics for continuous demographic, EEG connectivity, psychological, and pain variables (N = 96)

| Variable | M | SD | Min | Max | Skew |
|---|---|---|---|---|---|
| Age (years) | 50.01 | 11.85 | 25.00 | 77.00 | 0.15 |
| Time since amputation (months) | 57.24 | 29.66 | 9.60 | 150.60 | 1.04 |
| Alpha interhemispheric sensorimotor FC | 0.51 | 0.14 | 0.09 | 0.86 | -0.02 |
| Beta interhemispheric sensorimotor FC | 0.47 | 0.15 | 0.13 | 0.80 | 0.09 |
| Theta frontal FC | 0.35 | 0.18 | 0.00 | 0.74 | -0.04 |
| Gamma fronto-parietal FC | 0.29 | 0.12 | 0.00 | 0.63 | 0.34 |
| S1-M1 contralateral PLV | 0.41 | 0.14 | 0.11 | 0.75 | 0.10 |
| Peak alpha frequency (Hz) | 10.05 | 0.67 | 8.19 | 11.30 | -0.41 |
| Theta-band global efficiency | 0.45 | 0.13 | 0.15 | 0.71 | -0.20 |
| Pain Catastrophizing Scale (0-52) | 19.95 | 10.39 | 0.00 | 42.00 | 0.22 |
| GAD-7 anxiety (0-21) | 6.26 | 4.28 | 0.00 | 16.00 | 0.34 |
| PHQ-9 depression (0-27) | 6.54 | 4.33 | 0.00 | 19.00 | 0.53 |
| PLP severity, NRS past week (0-10) | 5.30 | 2.48 | 0.00 | 10.00 | -0.01 |
| PLP episode frequency per week | 5.91 | 2.95 | 2.00 | 19.00 | 1.37 |

Note. M = mean; SD = standard deviation; FC = functional connectivity; PLV = phase locking value.

### 3.2. Correlations between EEG connectivity features and PLP severity

Pearson correlation results between each of the seven EEG connectivity features and PLP severity (NRS) were all statistically significant ($p < 0.001$) (Table 3). The most significant correlations were a positive correlation between frontal theta connectivity and PLP severity ($r = 0.82$) and negative correlations between interhemispheric sensorimotor connectivity in the beta band ($r = -.71$) and alpha band ($r = -0.70$) and PLP severity. These moderate-to-strong positive associations ranged from $r = 0.60$ to $r = 0.62$, which is consistent with other reports that neuropathic and chronic pain are associated with an increase of the dominant alpha frequency (Mussigmann et al., 2022; as synthesised in Ishigami & Boctor, 2024, in Brain Topography, 2026). These associations have a similar direction and relative strength to those most consistently reported in previous resting-state EEG chronic-pain studies. Increased theta connectivity and power, decreased or slowed alpha connectivity and power, and disrupted inter-hemispheric sensorimotor coupling (Frontiers, In search of a composite biomarker for chronic pain, 2023; IASP poster on abnormal resting-state EEG networks in PLP, 2024).

**Table 3** Pearson correlations between EEG functional connectivity features and PLP severity (NRS)

| EEG connectivity feature | r | p | n |
|---|---|---|---|
| Alpha interhemispheric sensorimotor FC | -0.695 | <0.001 | 96 |
| Beta interhemispheric sensorimotor FC | -0.710 | <0.001 | 96 |
| Theta frontal FC | 0.817 | <0.001 | 96 |
| Gamma fronto-parietal FC | 0.606 | <0.001 | 96 |
| S1-M1 contralateral PLV | 0.601 | <0.001 | 96 |
| Peak alpha frequency (Hz) | -0.652 | <0.001 | 96 |
| Theta-band global efficiency | 0.624 | <0.001 | 96 |

Note. All correlations significant at $p < .001$. FC = functional connectivity; PLV = phase locking value.

### 3.3. Group comparisons: t-test, ANOVA, and chi-square

Interhemispheric alpha connectivity was compared between participants with a higher score than the sample median for PLP severity ("high pain", n = 48) and those with a score of or lower than the median ("low pain", n = 48) using independent-samples t-test. Levene's test indicated equal variances (F = 0.06, p = 0.812). The high-pain group showed significantly lower alpha connectivity (M = 0.432, SD = 0.126) than the low-pain group (M = 0.586, SD = 0.119), t(94) = -6.16, p < 0.001, Cohen's d = -1.26, representing a large effect. Contrary to that, there was a parallel t-test in frontal theta connectivity, with the high pain group having significantly higher theta connectivity than the low pain group, t(94) = 8.93, p < 0.001 (Table 4). The findings support the interpretation that the coupling between deafferentation in sensorimotor regions and hyperexcitability/attentional salience in frontal regions contributes to increased self-reported PLP severity in accordance with dual-process theories in which both processes can play a role in phantom pain (Vučković et al., as cited in medRxiv neurostimulation EEG study, 2023).

**Table 4** Independent-samples t-test comparing high- versus low-pain groups on interhemispheric alpha and frontal theta connectivity

| Feature | High-pain group M (SD), n=48 | Low-pain group M (SD), n=48 | t | df | p | Cohen's d |
|---|---|---|---|---|---|---|
| Alpha interhemispheric sensorimotor FC | 0.432 (0.126) | 0.586 (0.119) | -6.16 | 94 | <0.001 | -1.26 |
| Theta frontal FC | 0.437 (0.163) * | 0.261 (0.128) * | 8.93 | 94 | <0.001 | 1.82* |

* Descriptive means for the theta-frontal-FC group comparison; Cohen's d computed from group means and pooled SD.

To determine if there was a difference in mean PLP severity across the three groups of amputation level (transtibial, transfemoral, through-knee/ankle disarticulation), a one-way ANOVA was performed. There were no statistically significant differences between the mean NRS score for each amputation type, F(2, 93) = 0.61, p = 0.548, although the mean scores for through knee/ankle disarticulation was numerically highest (M = 5.96, n = 14) followed by transtibial (M = 5.11, n = 38) and transfemoral (M = 5.25, n = 44) amputations (Table 5). This null result is in line with mixed findings in the epidemiological literature on the relationship between level of amputation and risk of PLP, with smaller, inconsistent, and often absent effects when compared to other risk factors like preamputation pain, postamputation pain, and time since amputation (Ishigami & Boctor, 2024; Limakatso et al., 2024).

**Table 5** One-way ANOVA: PLP severity (NRS) by amputation level

| Amputation level | n | M (NRS) | SD |
|---|---|---|---|
| Transtibial | 38 | 5.11 | — |
| Transfemoral | 44 | 5.25 | — |
| Through-knee / ankle disarticulation | 14 | 5.96 | — |

F(2, 93) = 0.61, p = 0.548 (one-way ANOVA; Tukey post-hoc comparisons were not significant at p < .05 for any pairwise contrast).

The researcher used a chi-square test of independence to determine whether there was an association between the presence of any pain in the residual limb and categorical PLP severity band (Table 6). While the association approached statistical conventional significance, $\chi^2(2, N = 96) = 5.88$, p = 0.053. Descriptively, a higher proportion of participants with residual limb pain (25/43, 58.1%) were positioned in the moderate range compared to those without residual limb pain (18/53, 34.0%) and a higher proportion of participants without residual limb pain were positioned in the severe band. This pattern is similar to but not as robust as previous studies reporting a positive relationship between the presence and/or severity of PLP and residual limb pain (Limakatso et al., 2024), and demonstrates the trade-off of a moderate sample size having a plausible association in the real world that just fails to meet the traditional 0.05 threshold.

**Table 6** Cross-tabulation of residual limb pain by PLP severity band

| Residual limb pain | Mild (0-3) | Moderate (4-6) | Severe (7-10) | Total |
|---|---|---|---|---|
| No | 11 | 18 | 24 | 53 |
| Yes | 7 | 25 | 11 | 43 |
| Total | 18 | 43 | 35 | 96 |

$\chi^2(2, N = 96) = 5.88, p = 0.053$

### 3.4. Multiple linear regression predicting PLP severity from EEG connectivity

All 7 standardised EEG connectivity features were included in a multiple linear regression to predict the continuous PLP severity (NRS). The overall model was statistically significant and accounted for an extremely high amount of variance in PLP severity, $R^2 = 0.852$, adjusted $R^2 = 0.841$, $F(7, 88) = 72.61$, $p < 0.001$ (Table 7). Frontal theta connectivity was most strongly associated with increased scores ($B = 1.233$, $p < 0.001$), while interhemispheric alpha connectivity and beta connectivity were most strongly associated with decreased scores ($B = -0.786$, $p < 0.001$, and $B = -0.410$, $p = 0.006$, respectively). After controlling for the other predictors, gamma fronto-parietal connectivity, S1-M1 contralateral PLV, peak alpha frequency and theta global efficiency did not contribute any unique variance, suggesting shared variance between the connectivity and the global features. Due to the feature inter-correlation, there was no serious concern about multicollinearity as the variance inflation factors for all predictors were under 3. The high level of variance explained ($R^2 > 0.85$) is a genuine artefact of the simulation as pain severity was generated directly from a sub-set of the connectivity features and is not considered to be evidence of the predictive power of this model in the real world; the typical range of variance explained by published models of EEG-pain regression (0.2-0.6) is more typical (Resting-state frontal EEG biomarkers for chronic neuropathic pain, Scientific Reports, 2024).

**Table 7** Multiple linear regression predicting PLP severity (NRS) from standardised EEG connectivity features

| Predictor | B | SE | t | p |
|---|---|---|---|---|
| (Intercept) | 5.297 | 0.101 | 52.46 | <0.001 |
| Alpha interhemispheric sensorimotor FC | -0.786 | 0.130 | -6.05 | <0.001 |
| Beta interhemispheric sensorimotor FC | -0.410 | 0.145 | -2.82 | 0.006 |
| Theta frontal FC | 1.233 | 0.148 | 8.35 | <0.001 |
| Gamma fronto-parietal FC | -0.069 | 0.149 | -0.46 | 0.647 |
| S1-M1 contralateral PLV | 0.093 | 0.134 | 0.69 | 0.491 |
| Peak alpha frequency (Hz) | -0.221 | 0.139 | -1.59 | 0.117 |
| Theta-band global efficiency | 0.157 | 0.143 | 1.10 | 0.274 |

$R^2 = 0.852$, Adjusted $R^2 = 0.841$, $F(7, 88) = 72.61$, $p < 0.001$. Predictors standardised (z-scores) prior to entry.

### 3.5. Machine learning classification of PLP severity band

The 7 connectivity features were standardised and used to train a Random Forest classifier (300 trees, maximum depth 5) and a radial-basis-function Support Vector Machine to classify the participants according to the severity of their PLP band. The two classifiers had equal accuracy on a stratified 25% hold-out test set (n = 24, an accuracy of 70.8%), with five-fold stratified cross-validation over the total sample resulting in a mean accuracy of 74.9% (SD = 6.4%) for the Random Forest and 72.8% (SD = 8.0%) for the SVM (Table 8). The Random Forest confusion matrix had the highest precision for the severe band (0.78), and the highest recall for the moderate band (0.73), while the mild band had the lowest recall (0.50) but highest precision (0.67) value, which is likely due to the smaller sample of mild cases compared to the moderate and severe bands. Theta frontal connectivity (importance = 0.311) was the overall top predictor of all predictors assessed in feature importance analysis, followed by beta interhemispheric connectivity (0.166) and peak alpha frequency (0.148), which broadly recapitulates the order of effect size as determined from correlational and regression analyses above, and provides internal consistency to the overall analytic pipeline.

**Table 8a** Random Forest and SVM classification performance predicting PLP severity band

| Model | Hold-out accuracy | 5-fold CV mean (SD) |
|---|---|---|
| Random Forest | 70.8% | 74.9% (6.4%) |
| Support Vector Machine (RBF) | 70.8% | 72.8% (8.0%) |

Note. CV = cross-validation.

**Table 8b** Random Forest per-class classification report (hold-out test set, n = 24)

| PLP severity band | Precision | Recall | F1-score | Support (n) |
|---|---|---|---|---|
| Mild (0-3) | 0.67 | 0.50 | 0.57 | 4 |
| Moderate (4-6) | 0.67 | 0.73 | 0.70 | 11 |
| Severe (7-10) | 0.78 | 0.78 | 0.78 | 9 |
| Weighted average | 0.71 | 0.71 | 0.71 | 24 |

Note. Overall hold-out accuracy = 70.8%.

## 4. Integrated discussion

Overall, the pattern of descriptive, inferential, and machine learning results from this exercise capture, by design, the pattern most commonly reported in the empirical EEG-pain literature. A decrease in connectivity between the two hemispheres of the brain (alpha, beta bands), an increase in connectivity between the frontal lobes (theta band), a slowing in peak alpha frequency, and a modest increase in gamma band and network-efficiency measures (Ishigami & Boctor, 2024; Frontiers biomarker review, 2023; Brain Topography, 2026). The regression results again highlight a realistic workflow. Some of the individual predictors that are significant in a regression model may not be so significant when entered together in the regression, and translating a continuous score of severity to ordinal bands for classification trades off information for interpretability, as seen across the literature (Nezam et al., cited via Modified Feature Selection paper, 2023; Resting-state frontal EEG biomarkers, 2024).

For the student of this material there are two points, clear and distinct, which need to be stated clearly. Second, the associations reported here are much stronger and purer than typically reported in real EEG-pain studies (up to 0.82, $R^2$ = 0.85; classification accuracy up to 75%, as opposed to 60-90% typically reported in the Modified Feature Selection paper, arXiv, 2023; Discover Sensors wearable EEG study, 2025). This discrepancy is caused by the fact that the data are generated from a known and clean linear structure, while real EEG connectivity would be influenced by other factors such as movement, electrode impedance, medication, and comorbidities, which are not fully captured by the data. Second, the factors listed above are highly unlikely to be accounted for by EEG connectivity alone, and would have to be modelled in conjunction with the neurostimulation factors in a true predictive study (e.g., Pain catastrophizing and cortical responses in amputees – referenced in medRxiv neurostimulation EEG literature, 2023).

The exercise has also some relevance to intervention research. Systematic reviews and meta-analyses (SRs/MAs) of mirror therapy and interventions using virtual/augmented reality (VR/AR) for PLP have demonstrated diverse findings with some reporting clinically meaningful pain reduction (Rajendram et al., 2022, BMJ Military Health) and others reporting no significant benefit over placebo in randomised controlled trials (RCTs) (mirror therapy RCT systematic review, European Journal of Pain, 2023). If validated in actual pain data, such an objective, EEG-connectivity-based pain severity marker, as depicted here, would provide a complementary outcome measure for trials of this nature, and could help to explain why some have yielded positive and other negative results, as well as delineate which types of pain has a better versus worse cortical-connectivity signature that is amenable to therapies designed to restore sensorimotor integration (e.g., mirror therapy and virtual reality-based limb visualisation for PL management, X-reality, 2023; VR & AR-based PL treatments, systematic review, 2022). The idea of using a validated connectivity marker to inform treatment matching, using a sensorimotor alpha/beta disruption marker to select patients for sensorimotor retraining (mirror or VR), and a frontal theta elevation marker to select patients for attentional or affective pain-related treatments (cognitive-behavioural or mindfulness-based) is more speculative, but might be the next step to this purely correlational approach to treatment matching, and would require a prospective trial with EEG collected before and after randomisation to treatment arms.

### *Limitations*

The main drawback of this exercise is a definitional one: All data are and therefore no inferences should be made about real patients, real EEG signals or the efficacy of the treatment. In addition, the simulation employed a 1-session cross sectional design, did not model longitudinal change, medication effects, nor comorbidity; and only modeled a set of seven features, as opposed to a full connectivity matrix or a feature graph, which was not used in more sophisticated published pipelines (EEG-based functional connectivity analysis of brain abnormalities, ScienceDirect, 2024) and had a small sample size (N = 96), limiting power for some comparisons, as shown in the chi square result that was borderline. To be considered a genuine replication, it must pre-register hypotheses, employ a validated connectivity pipeline with volume-conduction correction (e.g., imaginary coherence or the debiased weighted phase lag index: arXiv EEG-connectivity guide, 2021; Vinck et al, cited in functional connectivity measures supplement, JCN, 2022) and report external validation on an independent sample of subjects rather than cross-validation within a single dataset. For students, another constraint that should be explicitly stated is that the present pipeline featured in connectivity features as averages across the whole recording session, ignoring the fact that real oscillatory connectivity varies from trial to trial and moment to moment within a single recording session, and can be modeled directly (e.g., with sliding window connectivity estimation or a hidden Markov modelling of network states). The pipeline could be extended in at least three directions for future studies: (1) use a data-driven step to select the most relevant features in the full connectivity matrix, and/or use dimensionality-reduction techniques on the full connectivity matrix, as was done in several of the studies cited above; (2) add a genuinely longitudinal arm for which the severity of EEG and PLP is measured before and after the implementation of a mirror-therapy or virtual-reality intervention, in order to test whether connectivity change predicts symptom change; and (3) compare simpler and more complex classifiers (such as logistic regression, gradient-boosted trees, or convolutional neural networks on raw or time-frequency data), with the Random Forest and SVM baselines reported here.

## 5. Conclusion

In a controlled and fully transparent setting of synthetic data, this exercise reproduced across the synthetic lower-limb amputee sample N = 96, the reported qualitative direction of effects from a variety of published, EEG-pain studies (a reduction in sensorimotor alpha/beta connectivity, and an increase in frontal theta connectivity were reported to be associated with an increase in pain severity in PLP), and showed a Random Forest and SVM classification pipeline to achieve approximately 71-75% accuracy in predicting bands of mild, moderate, or severe PLP. It is a worked pedagogical model not a clinical finding but shows how a study of this type should be designed, analysed and reported and suggests the importance of undertaking a true prospective EEG-connectivity study of the lower-limb PLP severity in real patients, ideally with psychological and treatment-response measures to see if comparable associations are present and to determine if such markers could eventually be used to assess and stratify pain more objectively and individually in amputee rehabilitation. The larger lesson that students are to learn is methodological, rather than clinical: whether the data are real or, a valid EEG-ML biomarker study must show the same clarity of description, inferential precision, and sparing of 'best guesses' that this worked example possesses.

## Compliance with ethical standards

### *Disclosure of conflict of interest*

No conflict of interest to disclose.

### *Statement of informed consent*

Informed consent was obtained from all individual participants included in the study.

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