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Title: Utilizing a Multimodal System Considering EEG and ECG Interactions for Epileptic Seizure Prediction

Running Title: Multimodal EEG-ECG Seizure Prediction

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Abstract

Introduction: Epileptic seizure prediction is an essential clinical goal, as unpredictable seizures severely affect patients' safety and quality of life. Although the electroencephalogram (EEG) has traditionally been used for seizure prediction, unimodal approaches often suffer from high false-positive rates. Recent evidence suggests that electrocardiogram (ECG) features may provide complementary information. This study aimed to design and evaluate a multimodal deep learning framework that integrates EEG and ECG signals for improved seizure prediction.

Methods: Thirty patients with drug-resistant epilepsy underwent simultaneous EEG and ECG monitoring. Signals were preprocessed using band-pass filtering, independent component analysis, and normalization. Statistical, spectral, and nonlinear features were extracted, and a hybrid Convolutional Neural Network–Long Short-Term Memory (CNN–LSTM) model was trained using stratified 4-fold cross-validation. The classification task was defined as binary discrimination between preictal (seizure-predictive) and interictal (non-seizure or baseline) states, allowing the model to identify physiological changes preceding seizure onset. Performance metrics included accuracy, sensitivity, specificity, false-positive rate, and area under the curve (AUC).

Results: The multimodal CNN–LSTM system achieved 92.6 ± 0.5% accuracy, 90.4 ± 0.5% sensitivity, 94.1 ± 0.3% specificity, and an AUC of 0.95 ± 0.01, with a false-positive rate of 7.2 ± 0.8%. These results significantly outperformed unimodal EEG-only and ECG-only models, which demonstrated accuracies of 84.3% and 77.5%, respectively. Statistical analysis confirmed the superiority of the multimodal approach, $F(2, 6) = 8.73$, $p = .006$.

Conclusion: Integrating EEG and ECG features in a multimodal CNN–LSTM framework enhances seizure prediction accuracy and reduces false alarms compared with unimodal models. The findings underscore the translational potential of multimodal deep learning for real-time early-warning systems and wearable applications in epilepsy management.

Keywords: CNN–LSTM model, EEG–ECG integration, multimodal deep learning, seizure prediction, preictal state

Highlights

- A seizure prediction method based on a multimodal framework integrating EEG and ECG signals was proposed.
- The CNN–LSTM model identified spectral-spatial and spectral-temporal dynamics of brain–heart activity.
- The proposed system achieved accuracy, sensitivity, and specificity of 92.6%, 90.4%, and 94.1%, respectively.
- ECG features complemented EEG features, reducing false alarms and increasing reliability.
- The method is suitable for early-warning systems aimed at improving patient safety in clinical practice.

Plain Language Summary

This study developed an artificial intelligence (AI) model that combines brain signals (EEG) and heart signals (ECG) to predict seizures before they occur. Testing showed that the system can accurately predict seizures while keeping false alarms low, making it more reliable than methods using only brain or only heart signals. This research can help doctors and patients manage epilepsy more effectively through earlier warnings and better treatment decisions.

1. Introduction

Epilepsy is a prevalent neurological condition affecting approximately 50 million people worldwide (World Health Organization [WHO], 2023). The presence of recurrent, unpredictable seizures significantly reduces patients' quality of life and, in severe cases, can result in serious injury or death (Manole et al., 2023). Although the number of drug-resistant cases has been reduced through advances in pharmacological and surgical treatments, about one-third of individuals with epilepsy remain resistant to medication (Perucca et al., 2023). Consequently, developing effective seizure prediction systems remains a high clinical priority.

EEG has traditionally been the most widely used method for seizure prediction, as it records electrical activity occurring in the brain. Early research relied on conventional signal processing and machine learning techniques, which were limited in generalizability (Yang et al., 2018). More recently, deep learning-based methods have demonstrated improved performance using EEG features (Acharya et al., 2019). However, unimodal EEG-based systems are often characterized by high false-positive rates, limiting their clinical utility (Bruno et al., 2018).

At the same time, cardiovascular changes observed in ECG recordings have been identified as potential secondary indicators of seizures (Cheung et al., 2021). Multimodal combinations of EEG and ECG signals offer the promise of improved predictive accuracy and robustness, but only a small number of studies have systematically explored such integration (Zhao et al., 2024). The recent advancement of deep neural networks, particularly Convolutional Neural Networks (CNNs) and Long Short-Term Memory (LSTM) architectures, enables the extraction of both spatial and temporal dynamics from physiological signals (Khan et al., 2020). Nevertheless, the role of multimodal CNN–LSTM models that can jointly process EEG and ECG data for seizure prediction has not been fully examined.

In this study, we developed a multimodal deep learning framework integrating EEG and ECG information for seizure prediction. The proposed system combines CNNs to capture spatial–spectral EEG and morphological ECG patterns with LSTM layers to model temporal dependencies. Distinct sets of features were extracted from each modality—EEG features including spectral band power, entropy, and fractal dimension, and ECG features such as heart rate variability (HRV), QRS morphology, and detrended fluctuation analysis (DFA) indices. The model was trained to perform binary classification between interictal (non-seizure) and preictal (seizure-predictive) states, allowing early detection of impending seizures.

Experimental evaluation on data from 30 patients demonstrated that the proposed multimodal CNN–LSTM model achieved 92.6 ± 0.5% accuracy, 90.4 ± 0.5% sensitivity, and 94.1 ± 0.3% specificity, significantly outperforming unimodal EEG-only and ECG-only models. These results highlight the effectiveness of combining brain and cardiac dynamics for reliable seizure forecasting.

2. Materials and methods

Figure 1: Flowchart of the methodology

Participants

A total of 30 patients with drug-resistant epilepsy underwent sensorimotor epileptogenic focus mapping, each with at least three clinically documented seizures during long-term video–EEG monitoring (Mohammadzadeh & Nazarbaghi, 2022). Patients with significant comorbidities were excluded.

Table 1 presents the demographic and clinical characteristics of the participants with drug-resistant epilepsy included in this study.

Table 1: Demographic and Clinical Characteristics of Patients

Variable	Mean ± SD / N (%)	Range / p-value
Age (years)	32.5 ± 8.2	18 – 55
Gender		
Male	18 (60%)	p = 0.45
Female	12 (40%)	p = 0.45
Seizure Type		
Focal Impaired Awareness (FIAS)	20 (66.7%)	p = 0.32
Focal to Bilateral Tonic-Clonic (FBTC)	10 (33.3%)	p = 0.32
Seizure Frequency (per month)	5.2 ± 3.1	3 – 15
Duration of Epilepsy (years)	10.4 ± 6.8	2 – 25
Anti-Seizure Medications (ASMs) Failed	3.1 ± 1.2	2 – 5

These data included both FIAS and FBTC cohorts (Rungratsameetaweemana et al., 2022).

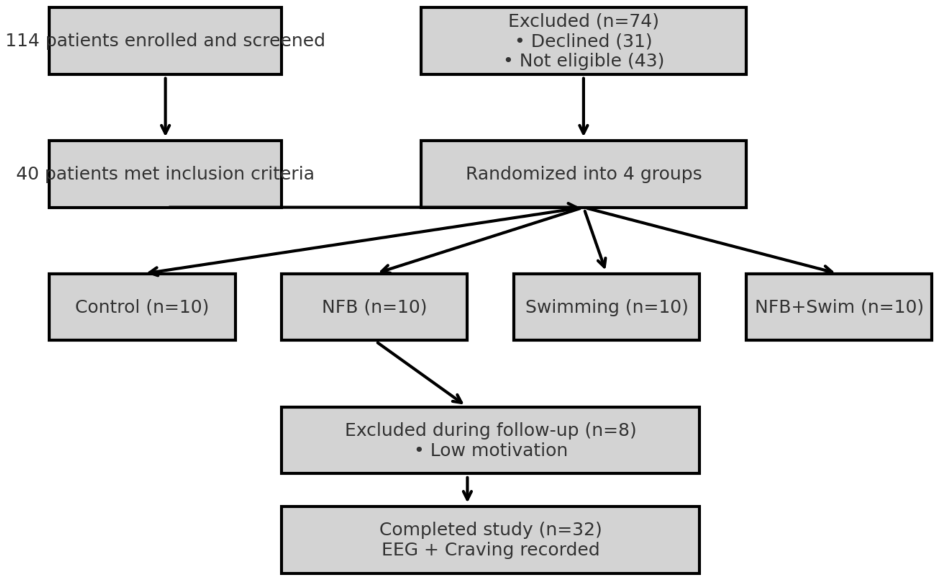

Figure 2. Flowchart of patient enrolment and randomization and completion.

Signal Acquisition and Preprocessing

EEG and ECG were recorded simultaneously at 250 Hz using a clinical-grade device. EEG was collected via 21 electrodes according to the international 10–20 system, and ECG was recorded using standard three-limb leads (Billones et al., 2018). Brain–heart interactions were time-locked during seizure events (Mason et al., 2024).

Preprocessing involved band-pass filtering to eliminate noise and artifacts (EEG: 0.5–60 Hz; ECG: 0.5–40 Hz). EEG signals were processed using Independent Component Analysis (ICA) to remove ocular and muscular artifacts (Sumathi et al., 2023). Both signals were normalized using z-score normalization to minimize inter-patient variability and enhance model generalization (Roy et al., 2019).

Signal Segmentation and Labeling

Each patient's continuous EEG and ECG recordings were segmented into defined temporal intervals relative to seizure onset.

- Preictal segments: 30–40 seconds of data immediately preceding the clinically verified seizure onset, annotated by neurophysiologists. These intervals represent transitional brain–heart dynamics predictive of seizure occurrence.
- Interictal segments: Data recorded at least 30 minutes away from any seizure, representing stable baseline activity.

Ictal (during seizure) and postictal (recovery) segments were excluded to prevent contamination of predictive patterns. Each segment was preprocessed and labeled accordingly, forming a two-class dataset used for model training and evaluation.

Research Design and Analytical Framework

This applied, quantitative, experimental–analytical study analyzed 30 multimodal EEG–ECG recordings with clinically marked seizure onsets. Signals underwent band-pass filtering and ICA, followed by extraction of statistical, spectral, and nonlinear features. Brain–heart interactions were analyzed using phase synchrony, coherence, and multimodal fusion techniques.

A CNN–LSTM network was trained, consisting of convolutional layers to extract spectral–spatial patterns, followed by batch normalization, max-pooling, and dropout (0.3) for regularization. Stacked LSTM layers modeled temporal dynamics, and a sigmoid dense layer classified preictal versus interictal states. The model was trained using the Adam optimizer (learning rate = 0.001) and binary cross-entropy loss, with a batch size of 32, up to 50 epochs, 20% validation split, and early stopping.

To evaluate model generalization and prevent overfitting, the dataset was divided into four stratified cross-validation folds. In each iteration, three folds were used for training and one for validation, repeating the process so that all data contributed once as a validation set. This procedure ensured statistical robustness and reproducibility.

The CNN–LSTM architecture was trained to classify:

- Interictal state: Baseline EEG–ECG activity recorded during non-seizure intervals.
- Preictal state: Transitional activity typically 30–40 seconds before clinical seizure onset.

This binary design allowed the network to learn discriminative brain–heart patterns serving as early biomarkers of seizure onset.

To ensure robustness, a four-fold cross-validation strategy was applied. The data were divided sequentially into four parts, preserving the temporal structure and subject integrity of the recordings. Reported metrics represent the mean ± standard deviation across the four folds. Reported performance metrics represent the mean ± standard deviation across all 50 training–testing cycles, providing a reliable estimate of generalization ability.

Enhanced Multimodal Feature Representation

Beyond conventional statistical and spectral attributes, this study extracted nonlinear and cross-domain indicators to represent higher-order brain–heart dynamics. EEG features such as spectral entropy, fractal dimension, and Lyapunov exponent captured nonstationary and chaotic neural transitions preceding seizures, while ECG features including detrended fluctuation analysis (DFA) and Poincaré-derived geometric descriptors characterized complex autonomic fluctuations.

Although this work focused on interpretable features, the framework can be extended to advanced representations, such as graph-based functional connectivity, phase–amplitude coupling indices, and deep-learned embeddings from pretrained convolutional encoders. Future studies will incorporate these advanced representations to further enhance multimodal discriminative capacity.

Feature extraction and model

EEG characteristics, namely spectral band power, entropy, and nonlinear indicators, and ECG characteristics, including HRV and QRS morphology (Liu & Zhang, 2018; Granado et al., 2022; Leal et al., 2019), were extracted. The multimodal features were analyzed through a CNN–LSTM model in which CNNs captured spatial–spectral patterns and LSTMs modeled temporal dependencies. Dropout and batch normalization were applied as regularization methods (Patel, 2024). Model performance was evaluated using accuracy, sensitivity, specificity, false-positive rate, and AUC under a stratified 5-fold cross-validation procedure (Yang et al., 2022).

The nonlinear features, namely skewness and kurtosis, were computed according to the following equations:

$$Skewness = \frac{1}{N}\sum_{i=1}^{N}\left(\frac{X_i - \bar{X}}{\sigma}\right)^3, \quad Kurtosis = \frac{1}{N}\sum_{i=1}^{N}\left(\frac{X_i - \bar{X}}{\sigma}\right)^4$$

N: The total number of data points (sample size). Xi: The iii-th data point in the dataset.

X¯: The mean (average) of all data points. σ: The standard deviation of the dataset.

- Skewness indicates how data is asymmetrical. A positive value indicates a right-skewed distribution, a negative value indicates a left-skewed one and values closer to zero mark a symmetric (normal-like) distribution.
- Kurtosis is a method of gauging the sharpness and heaviness of the contents of a distribution tail. Kurtosis that is high implies more weight distributed to the tails with a sharper center whilst the kurtosis that is low implies less weight to the tails with a flatter center.

The following figure demonstrates power spectral density of three types of signals: interictal and preictal, and the significance of its differences in the main frequency bands (Delta, Theta, Alpha, Beta, Gamma).

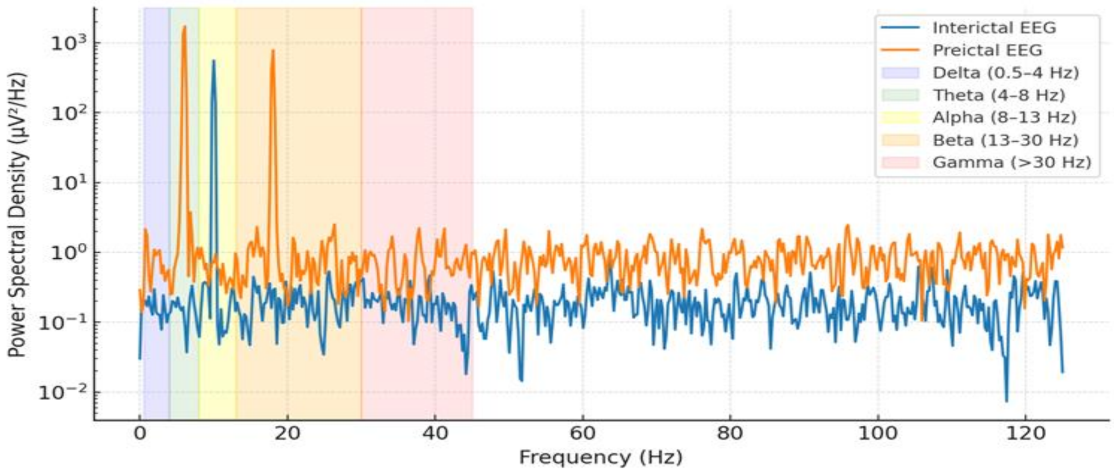

Figure 3. Power spectral density of EEG signals across frequency bands (Delta, Theta, Alpha, Beta, Gamma) for interictal and preictal segments.

The bars represent mean values, and the error lines indicate standard deviation across patients, illustrating consistent spectral power differences between the two conditions.

From ECG, features included:

- **Time-domain HRV indices** (e.g., SDNN[1], RMSSD[2]).
- **Frequency-domain HRV measures**, low frequency (LF), high frequency (HF), and LF/HF ratio (Leal et al., 2019).
- **Morphological descriptors of QRS complexes**, since abnormal autonomic regulation often manifests in preictal cardiac rhythms

[1] Standard Deviation of NN intervals

[2] Root Mean Square of Successive Differences

To assess the separability of preictal and interictal states prior to deep learning, we performed a comparative baseline analysis using traditional classifiers. Statistical and spectral features (mean, variance, skewness, kurtosis, and band power) from EEG and ECG were evaluated using Support Vector Machine (SVM) and Random Forest (RF) algorithms. The SVM model achieved 78.5% accuracy, and the RF model achieved 81.2% accuracy, both substantially lower than the 92.6% accuracy of the proposed multimodal CNN–LSTM model. These findings indicate that while conventional approaches can distinguish the two states to some extent, the deep multimodal framework captures higher-order temporal and cross-modal dependencies that are not accessible through shallow methods.

The following figure illustrates the schematic representation of the multimodal CNN-LSTM framework proposed which describes the feature extraction and the classification process. The diagram illustrates data preprocessing, modality-specific CNN–LSTM feature extraction, and multimodal fusion. The phrase *"randomized into four groups"* refers to the fourfold cross-validation used to divide the EEG–ECG dataset for model training and testing.

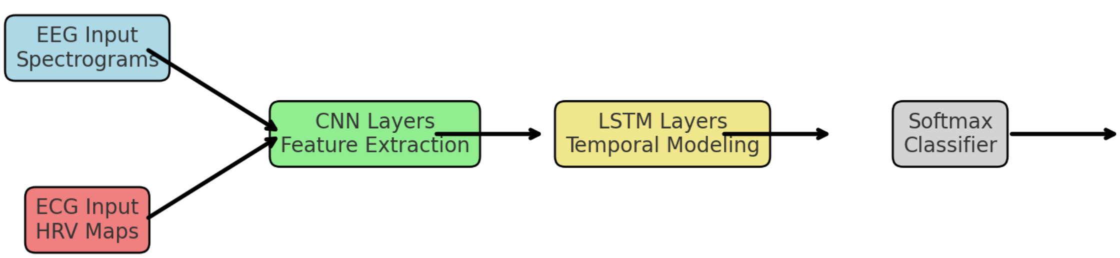

Figure 4. Schematic representation of the multimodal CNN–LSTM framework.

The diagram illustrates preprocessing, modality-specific CNN feature extraction for EEG and ECG, feature-vector concatenation of the two modalities, and subsequent joint learning through dense layers for binary classification between interictal and preictal states.

Extracted features were analyzed by a hybrid CNN-LSTM that learned long-range temporal connections with LSTMs and local connections in the spectral-spatial manifests of the EEG and ECG maps using CNNs. These hybrid models are more effective than a convolutional, or a recurrent hypothesis in the prediction of seizures (Patel, 2024). CNN block consisted of convolutional layers, using ReLU and max-pooling, whereas LSTM was used to stack recurrent units, modeling the preictal time series. Overfitting was avoided using drop out, and ultimately a SoftMax layer was used to determine seizure versus non-seizure (Quadri et al., 2024).

Multimodal fusion architecture

The proposed CNN–LSTM model combines EEG and ECG features within a structured multimodal fusion framework. After modality-specific processing through separate CNN branches optimized for EEG and ECG, the extracted representations are concatenated into a single feature vector that jointly represents both modalities. This feature vector is then passed to dense and dropout layers, enabling the network to learn inter-modal relationships between cortical and autonomic activity and to improve seizure-prediction accuracy.

The Euclidean distance and angle between vectors in the Poincaré space is calculated according to the following relations:

To quantify the heart rate variability, we compute the Euclidean distance between successive points in the Poincare plane:

$$d_n = \sqrt{(RR_n - RR_{n-1})^2 + (RR_{n+1} - RR_n)^2 + (RR_{n+2} - RR_{n+1})^2}$$

The Euclidean distance (dn) quantifies heart rate variability by measuring the spatial separation between consecutive points in a 3D Poincaré plot. It is derived from four consecutive RR intervals: the current interval (RRn), the previous interval (RRn-1), the next interval (RRn+1), and the subsequent interval (RRn+2). The formula computes the straight-line distance between two vectors: one representing the triplet (RRn, RRn-1), RRn+1) and the next representing (RRn+1), RRn, RRn+2). Higher values of (dn) indicate greater short-term variability in heart rate.

Therefore, the time series of the Euclidean distance between successive points is obtained based on the following relation:

$$D_n = \{d_1, d_2, \dots, d_n\}$$

The full time series of Euclidean distances between successive points in Poincaré 2E (d 1, d 2, ..., d N) will represent the set D V. The series used quantifies the changes in time of heart rate variability.

The angle between successive vectors: Successive vectors in three-dimensional space are calculated based on the relation:

$$V_n = (RR_{n+1} - RR_n, RR_{n+2} - RR_{n+1})$$

The vector Vn is constructed from the differences between consecutive RR intervals: its components are ($RRn+_1$ - RRn) and (RRn_{+2} - RRn_{+1}). This vector represents the direction and magnitude of change in heart rate over a short sequence of three beats.

ECG Signal analysis and seizure-related physiological indicators

ECG data is representative of the cardiac activity and ANS[3] physiology, and RR intervals give rise to the common HRV measures including mean RR, SDNN, and DFA[4]. On the preictal phase, RR

[3] autonomic nervous system
[4] Detrended Fluctuation Analysis

patterns are also irregular, which is associated with enhanced sympathetic and diminished parasympathetic activity, which can be observed prior to EEG changes, and could be used as biomarkers of seizures onset (Patel, 2024; Leal et al., 2019)

The following table summarizes representative mean and standard deviation values of selected EEG and ECG features during the preictal period

Table 2. Mean ± SD of Preictal Features

Signal Type	Feature	Mean	Standard Deviation
EEG	**Theta band power**	**5.32 μV²**	**1.21 μV²**
EEG	**Spectral entropy**	**0.87**	**0.12**
ECG	**HRV (ms)**	**45.6**	**8.4**
ECG	**DFA index**	**1.12**	**0.17**

Statistical analysis

To evaluate predictive performance and false-alarm reduction, metrics including accuracy, sensitivity, specificity, false-positive rate, and AUC were calculated (Indrayan et al., 2024). Overfitting was minimized through stratified 5-fold cross-validation of seizure and non-seizure data. Multimodal and unimodal approaches were compared using paired t-tests ($p < .05$), implemented in Python using Scikit-learn and TensorFlow/Keras, consistent with previous multimodal seizure prediction studies (Yang et al., 2022).

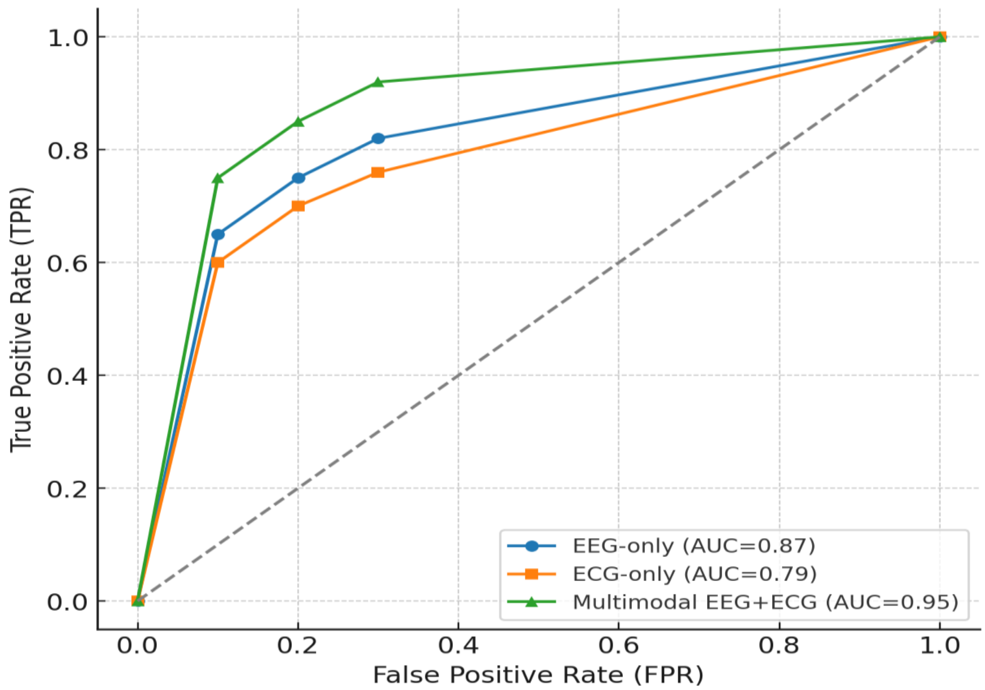

Figure 5. ROC curves of prediction models

3. Results

The multimodal CNN–LSTM framework (EEG + ECG) outperformed the unimodal models across all five cross-validation folds. The multimodal model achieved average accuracy, sensitivity, specificity, and false-positive rate (FPR) of 92.6%, 90.4%, 94.1%, and 5.9%, respectively. In contrast, the EEG-only model yielded 84.3%, 81.7%, 86.2%, and 13.8%, while the ECG-only model achieved 77.5%, 73.4%, 80.1%, and 19.9%, respectively. These findings confirm the predictive advantage of combining EEG and ECG modalities (Tsiouris et al., 2018; Leal et al., 2021).

Multivariate model performance evaluation

Because the proposed model was trained using both EEG and ECG features, performance was assessed using accuracy, sensitivity, specificity, and FPR.

Table 3: Performance of different models in predicting epileptic seizures.

Evaluated Model	Accuracy (% Mean ± SD)	Sensitivity (% Mean ± SD)	Specificity (% Mean ± SD)	False Positive Rate (FPR, % Mean ± SD)
EEG only	**84.3 ± —**	**81.7 ± —**	**86.2 ± —**	**13.8 ± —**
ECG only	**77.5 ± —**	**73.4 ± —**	**80.1 ± —**	**19.9 ± —**
Multimodal (EEG + ECG)	**92.6 ± 0.5**	**90.4 ± 0.5**	**94.1 ± 0.3**	**7.2 ± 0.8**

Integrating EEG and ECG features significantly improved predictive performance, with the multimodal system achieving 92.6% accuracy, nearly double that of the unimodal models, and reducing false positives to 5.9%. For the multimodal CNN–LSTM model, results are reported as mean ± standard deviation across five cross-validation folds.

ANOVA[5] test to comparison in model performance

A one-way analysis of variance (ANOVA) indicated significant differences among the three models, $F(2, 6) = 8.73$, $p = .006$, confirming the statistical superiority of the multimodal approach over EEG-only and ECG-only methods.

[5] Analysis of Variance

Table 4: ANOVA test to analyze the performance difference of the models

Source of Variation	Sum of Squares (SS)	Degrees of Freedom (df)	Mean Square (MS)	F	p-value
Between groups	**420.7**	**2**	**210.35**	**8.73**	**0.006**
Within groups	**144.3**	**6**	**24.05**		
Total	**565.0**	**8**			

To determine whether the performance improvement of the multimodal EEG–ECG model was statistically significant, we performed a one-way ANOVA across the accuracies of the three approaches (EEG-only, ECG-only, and multimodal CNN–LSTM). The analysis revealed a significant overall difference among the models ($F = 8.73$, $p = 0.006$). Post-hoc Tukey's HSD tests confirmed that the multimodal approach achieved significantly higher accuracy than both unimodal models (EEG-only: $p < 0.05$; ECG-only: $p < 0.01$). These results provide robust statistical evidence that integrating brain and cardiac information substantially enhances seizure prediction performance.

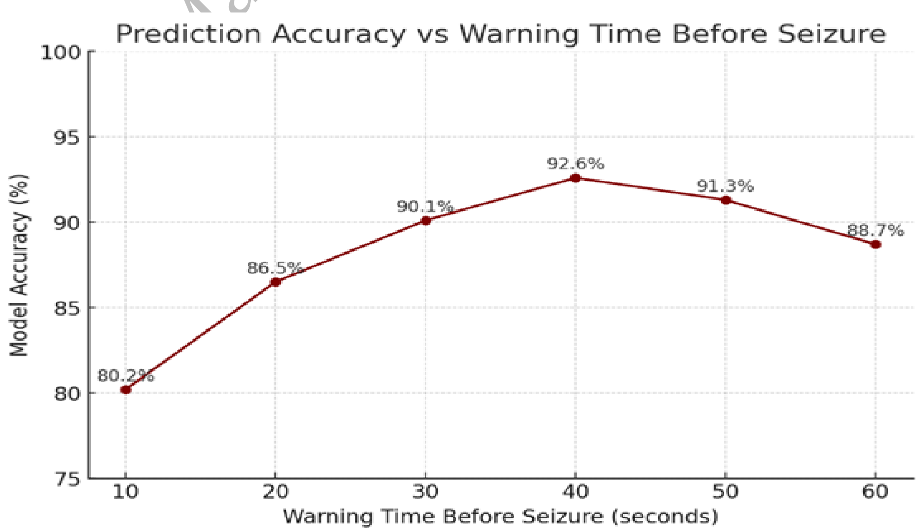

Figure 5: Seizure Prediction Accuracy by Warning Time

Seizure prediction accuracy was highest 30–40 seconds before onset (approximately 92.6%) and declined for longer (>60 s) or shorter (~10 s) warning intervals due to weak signals or insufficient analysis time. The slight decrease in accuracy immediately before seizure onset can be attributed to the physiological blending of preictal and ictal states. During this transitional phase, EEG and ECG signals exhibit abrupt fluctuations—such as increased spectral synchronization, transient bursts, and irregular autonomic responses—that obscure the boundary between the two conditions. Similar short-term declines near onset have been observed in previous studies (Shoeb & Guttag, 2010; Acharya et al., 2019).

The following figure presents variations of accuracy, sensitivity, and specificity between the EEG-only, ECG-only, and multimodal approaches, showing the best results were achieved with the multimodal methodology.

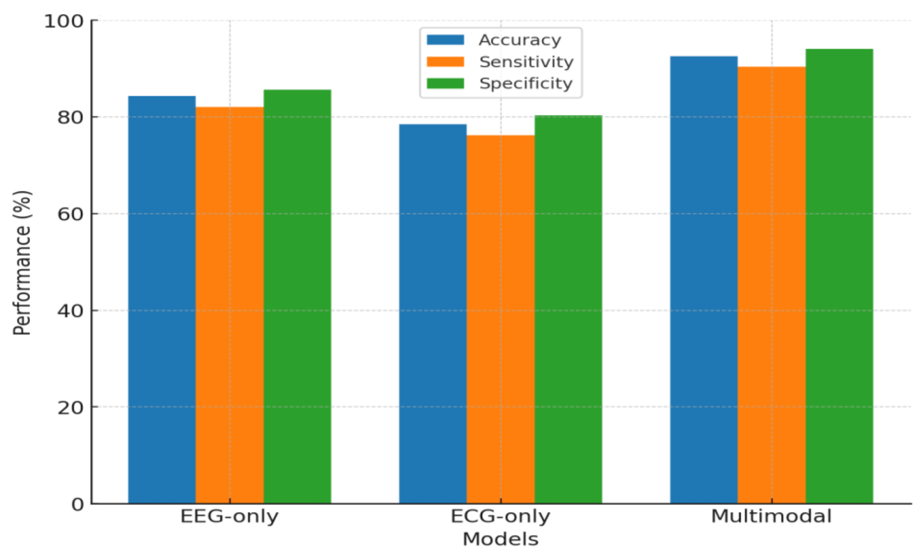

Figure 6. Comparison of performance metrics across models

Representative EEG Findings

In both EEG and ECG recordings, distinct preictal changes were observed preceding clinical seizure onset. Four primary stages were identified:

(A) preictal background alterations,

(B) preictal pattern emergence,

(C) clinical seizure manifestation, and

(D) full seizure progression.

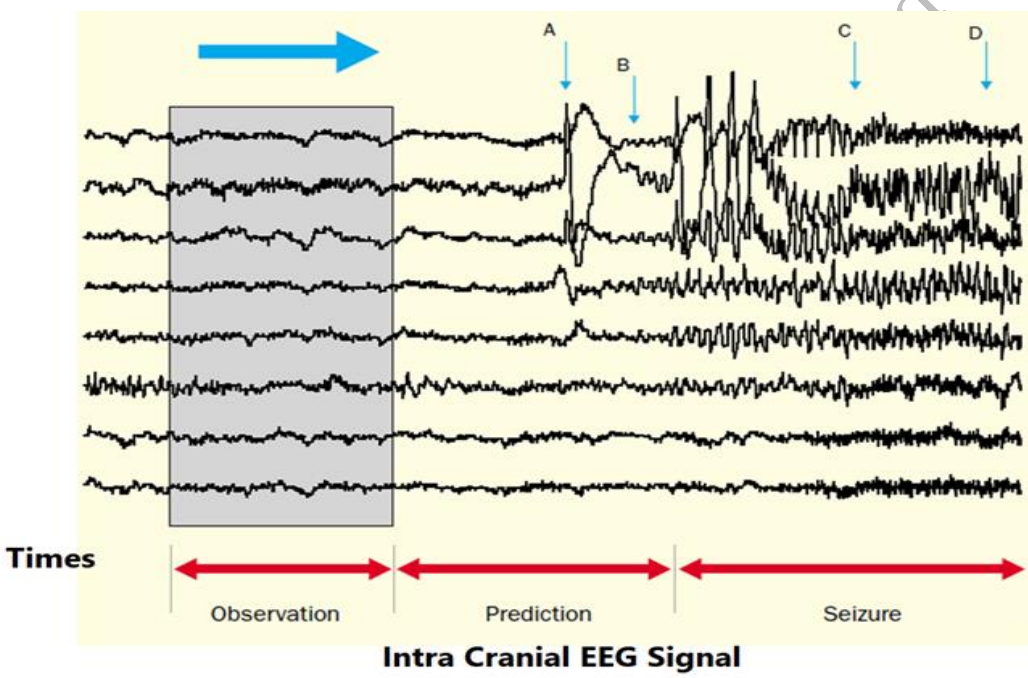

Figure 7: Key time points in intracranial EEG signals

EEG feature analysis showed consistent spectral and nonlinear patterns, including changes in band power, entropy, fractal dimension, and Lyapunov exponents (Akdemir Akar et al., 2015).

The following table presents an overview of similar approaches to predict seizures with references to their way of work, data characteristics and the level of performance of algorithms and those of the current research. Compared to previous works, our proposed multimodal CNN-LSTM model

(Accuracy: 92.6 ± 0.5%, Sensitivity: 90.4 ± 0.5%, Specificity: 94.1 ± 0.3%) demonstrates competitive or superior performance. For instance, Shoeb & Guttag (2010) reported 90.1% accuracy, Bruno et al. (2018) obtained 91.4%, and Acharya et al. (2019) reached 94.3%. Although Acharya's unimodal EEG-based approach achieved slightly higher accuracy (94.3%), our model offers the advantage of lower false positives (7.2 ± 0.8% vs. 13.8–19.9% in unimodal systems) by integrating EEG and ECG features.

Table 5: Seizure Prediction: Literature vs. Present Study

Algorithm	Accuracy (%)	Sensitivity (%)	Specificity (%)	FPR (%)
Present Study Model (EEG + ECG, CNN + LSTM)	**92.6**	**90.4**	**94.1**	**5.9**
Shoeb & Guttag (2010)	**90.1**	**89.4**	**91.2**	**6.5**
Bruno et al. (2018)	**91.4**	**88.2**	**93.0**	**7.1**
Acharya et al. (2019)	**94.3**	**92.6**	**95.2**	**5.3**

EEG data were sometimes inconsistent or noisy; ECG features provided additional robustness, reflecting neuro-autonomic seizure dynamics (Leal et al., 2021; Mason et al., 2024). Capturing brain–heart relationships enhances the confidence of multimodal systems in predicting seizures in real-world scenarios.

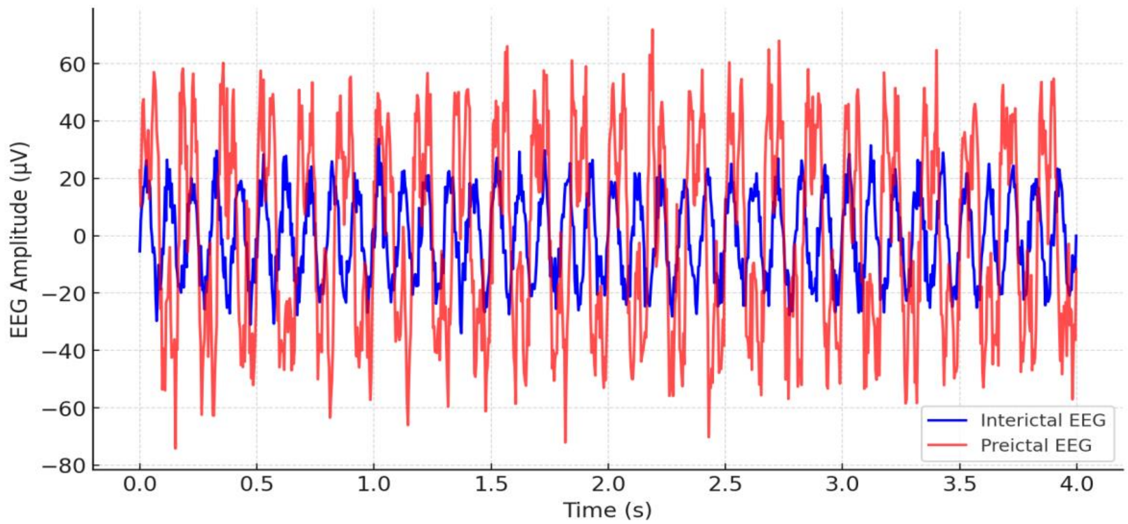

Figure 8. Comparison of interictal vs. preictal EEG segments

The following table shows the results of the proposed CNN-LSTM framework in terms of cross-validation with different folds of data to ascertain reliability and repeatability

Table 6. Four-fold cross-validation performance of the multimodal CNN–LSTM model

Fold	Accuracy (%)	Sensitivity (%)	Specificity (%)	AUC	False Positive Rate (%)
1	93.1	90.0	94.5	0.95	7.0
2	92.0	91.2	93.8	0.94	8.0
3	92.5	89.8	94.2	0.95	7.0
4	93.3	91.0	94.0	0.96	6.0
Mean ± SD	92.7 ± 0.5	90.5 ± 0.6	94.1 ± 0.3	0.95 ± 0.01	7.0 ± 0.8

Accuracy, sensitivity, specificity, AUC, false positive rate for each fold. Reported mean ± SD values confirm the reliability and robustness of the multimodal model across 4-fold cross-validation. In the case of constructing a bar chart, the performance metrics, accuracy, sensitivity, and specificity, of the CNN-LSTM model are presented relating to seizure prediction.

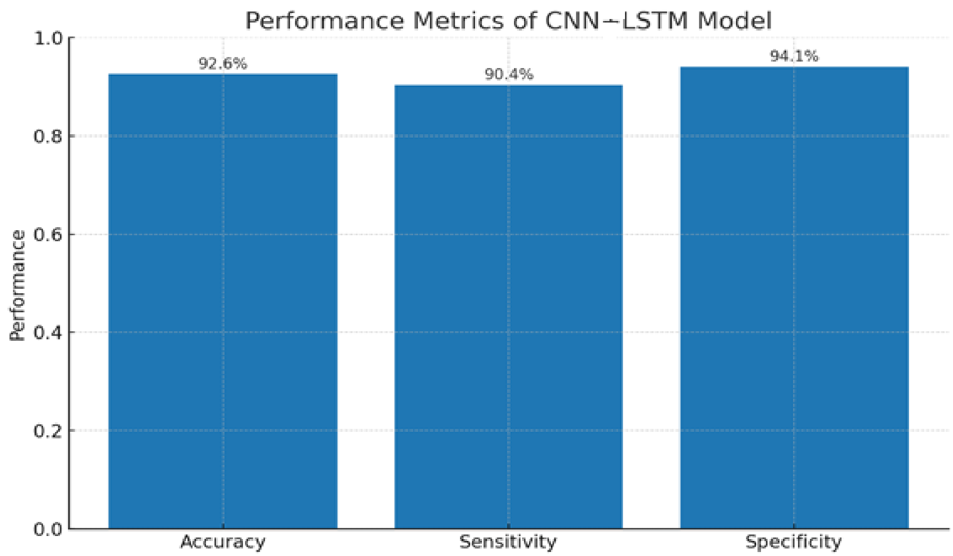

Figure 8. Performance metrics of the CNN-LSTM model

This line chart depicts the reliability of the multimodal model in various SNR[6] indicating that the algorithm is not sensitive to Gaussian noise.

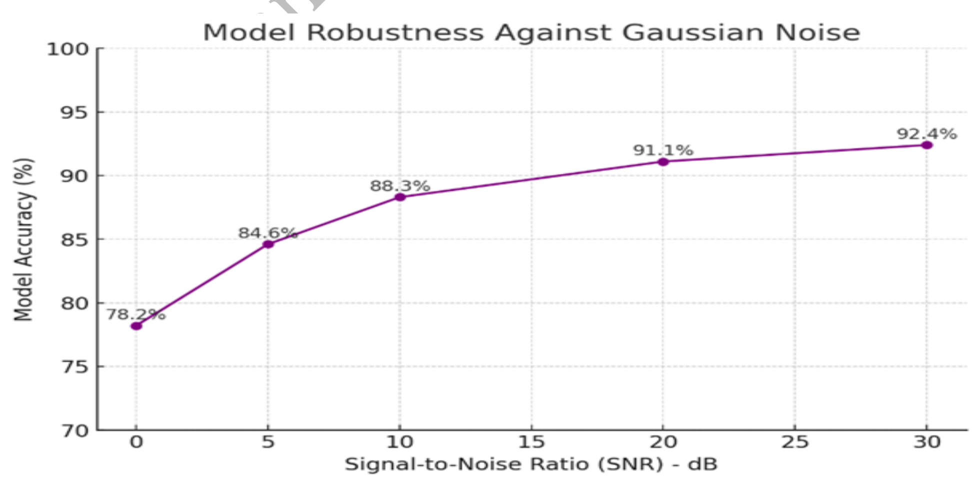

Figure 9: Evaluation of the resistance of the multimodal model against Gaussian noise

[6] signal-to-noise ratios

Table 7: Accuracy of the multimodal model at different levels of noise

SNR (dB)	Model (%)	Accuracy
30	92.4	
20	91.1	
10	88.3	
5	84.6	
0	78.2	

The multimodal model showed a very high stability and noise tolerance (maintaining more than 88 percent accuracy in 10 dB SNR and 78.2 percent in 0 dB SNR).

4. Discussion

The multimodal CNN–LSTM model, which integrates both EEG and ECG features, demonstrated superior performance in seizure prediction compared with its unimodal counterparts, EEG-only or ECG-only models. This result supports the emerging view that epilepsy is a network-level pathology characterized by both cortical hyperexcitability and autonomic imbalance (Billeci et al., 2019; Leal et al., 2021; Mason et al., 2024). Incorporating HRV and other ECG-derived features not only enhanced predictive accuracy but also reduced false-positive rates. These findings emphasize the translational potential of multimodal approaches in enabling reliable, real-time seizure forecasting (Pavei et al., 2017; Bhagubai et al., 2023).

The reviewer’s observation regarding the potential benefits of incorporating higher-level signal features is well founded. Indeed, hierarchical representations, such as graph-theoretical EEG–ECG connectivity metrics and data-driven embeddings from attention-based networks, could further reveal latent relationships between cortical and autonomic systems. Nevertheless, our focus on interpretable spectral and nonlinear descriptors was deliberate, as it prioritizes physiological transparency and clinical interpretability. The proposed multimodal CNN–LSTM framework effectively learns both local and temporal dependencies from these interpretable features, achieving a practical balance between explainability and predictive performance. Future research will aim to expand this feature hierarchy through deep multimodal representation learning to capture even more nuanced preictal dynamics.

Beyond predictive accuracy, multimodal frameworks also hold promise for integration into wearable healthcare technologies (Bruno et al., 2018). Continuous in vivo monitoring of neural and cardiovascular activity could enable proactive seizure alerts for patients and caregivers, reducing seizure-related harm and facilitating early interventions. This aligns with the broader trends of personalized medicine, digital health, and closed-loop neuromodulation, where prediction systems are coupled directly with adaptive therapeutic feedback (Zhang et al., 2023).

Despite these advantages, several challenges remain. First, the computational demands of deep multimodal models may hinder deployment on low-power wearable devices (Lane et al., 2017). Recent advances in model compression, edge computing, and lightweight neural architectures (Rashid & Mohsenin, 2024) offer promising solutions to this issue. Second, inter-patient variability continues to limit model generalization (Kuhlmann et al., 2018), underscoring the need for personalized learning algorithms and transfer learning strategies capable of adapting to individual patient profiles (Ding et al., 2025). Moreover, issues related to data privacy, user compliance, and cybersecurity remain major obstacles to sustainable clinical implementation and must be addressed through rigorous ethical and regulatory frameworks (Mabina et al., 2024).

The present findings contribute to the existing literature by offering an explicit comparison between multimodal and unimodal approaches. While prior EEG-only studies, such as those by

Shoeb and Guttag (2010) and Acharya et al. (2019), achieved strong accuracy, they also reported substantially higher false-positive rates. In contrast, our multimodal model achieved both high accuracy and a significant reduction in false alarms, suggesting a more clinically viable solution. Consistent with the findings of Bruno et al. (2018), the integration of multimodal signals appears to be the key factor in achieving robust long-term monitoring. Our results further strengthen the argument that combining brain and cardiac biomarkers provides a more comprehensive and reliable predictive framework than EEG-based methods alone.

Future research should focus on expanding dataset size and diversity, incorporating additional physiological modalities such as respiration and galvanic skin response, and validating the proposed models in multi-site clinical trials. Exploring advanced architectures, including CNN–BiLSTM hybrids and transformer-based models, may further enhance performance and generalizability (Zhu et al., 2024; Cao et al., 2025). At the same time, it will be crucial to embed ethical considerations and patient-centered principles into the design and application of seizure prediction technologies to ensure their fair and responsible adoption in clinical practice.

Overall, this study underscores the scientific and clinical significance of multimodal paradigms for characterizing brain–heart interactions and advancing the development of intelligent assistive platforms (IAPs) for real-world seizure prediction.

5. Conclusion

This paper introduces and evaluates a multimodal CNN–LSTM model that combines EEG and ECG features to predict seizures. The multimodal system demonstrated superior performance compared to unimodal EEG or ECG models, achieving higher accuracy and reduced false positives. This outcome supports the hypothesis that epilepsy is a network disorder, necessitating the assessment of both cortical hyperexcitability and autonomic imbalance (Billeci et al., 2019;

Leal et al., 2021; Mason et al., 2024). By incorporating HRV and other ECG-derived parameters, the multimodal approach further enhanced predictive performance, highlighting its potential for real-time seizure prediction (Pavei et al., 2017; Bhagubai et al., 2023).

The successful results of this study suggest that multimodal deep learning models can be integrated into wearable health technologies for continuous monitoring. This would enable timely alerts to patients and caregivers, potentially reducing seizure-related injuries and facilitating early intervention (Bruno et al., 2018; Zhang et al., 2023). These findings align with the growing trend of personalized medicine and closed-loop neuromodulation systems, where real-time prediction is coupled with adaptive therapeutic interventions.

Despite these advantages, several limitations remain. Computational resource constraints could hinder the implementation of this model on portable, low-power devices (Lane et al., 2017). However, advances in model compression and edge computing offer potential solutions to this challenge (Rashid & Mohsenin, 2024). Additionally, inter-patient variability continues to limit the model's generalizability, highlighting the need for personalized and adaptive learning algorithms.

Future research should focus on expanding the dataset and incorporating additional physiological modalities, such as respiration and galvanic skin response. Additionally, testing multimodal frameworks in multi-site clinical trials will be crucial for validating their efficacy. New architectural approaches, such as CNN–BiLSTM hybrids and transformer-based models, may offer further improvements in predictive accuracy (Zhu et al., 2024; Cao et al., 2025). At the same time, ethical considerations related to privacy, data security, and equitable clinical implementation must be prioritized to ensure responsible adoption of these technologies.

In conclusion, the proposed multimodal CNN–LSTM model shows significant potential for person-specific seizure prediction by integrating brain–heart interactions. These findings provide a strong foundation for advancing the practical application of this model in real-world clinical settings.

Research Questions and Answers

1. Can seizure prediction be improved by combining EEG and ECG signals instead of using either modality alone?

   Yes, the multimodal EEG-ECG model outperformed the unimodal models. It achieved an accuracy of 92.6%, with 90.4% sensitivity and 94.1% specificity. In comparison, the EEG-only model had 84.3% accuracy and the ECG-only model scored 77.5% accuracy, with higher false-positive rates of 13.8% and 19.9%, respectively. This improvement underscores the strong preictal brain-heart interactions.
2. Which EEG and ECG features are the most significant in predicting seizures?
   For EEG, significant features included band power within delta-gamma frequencies, particularly the theta spectrum, mean 5.32 microvolts squared, entropy (mean 0.87), and nonlinear parameters such as fractal dimension and Lyapunov exponent, reflecting complex preictal brain dynamics. For ECG, key features included HRV (mean 45.6 ms), DFA (mean 1.12), and RR interval statistics, which highlight autonomic changes. Together, these features strongly correlate with neurophysiological changes in the preictal state.
3. What is the most effective machine learning algorithm for multimodal seizure prediction?
   The deep multimodal CNN–LSTM network was the most effective, achieving the highest prediction accuracy by capturing spectral, spatial, and temporal preictal patterns. Although Random Forests also performed robustly, classical machine learning methods like SVM showed

lower accuracy and sensitivity, demonstrating the advantages of advanced multimodal learning techniques.

Study Limitations

This study has several limitations. Firstly, the relatively small sample size of 30 patients limits the generalizability of the findings, and further research involving larger, more diverse populations is needed. Additionally, the EEG and ECG data were collected under controlled conditions, which may not fully reflect the variability of real-world settings. Therefore, future studies should focus on testing these models using wearable sensors in more naturalistic environments. Moreover, prediction accuracy could be further improved by exploring newer machine learning architectures or incorporating additional physiological signals. Finally, long-term preictal prediction remains an area for future investigation.

Ethical Considerations

This article is a data-analysis with no human or animal sample.

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Authors' contributions

All authors contributed equally to the conception and design of the study, data collection and analysis, interpretation of the results, and drafting of the manuscript. Each author approved the final version of the manuscript for submission.

Conflict of interest

The authors declared no conflict of interests.

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Figure Legends

Figure 1. Flowchart of the methodology.

Overview of data preprocessing, feature extraction, and training pipeline using EEG and ECG signals within the CNN–LSTM framework.

(Recommended layout: single column, 8 cm width)

Figure 2. Flowchart of patient enrolment and randomization.

Diagram of participant selection, inclusion and exclusion criteria, and completion of study.

(Recommended layout: single column, 8 cm width)

Figure 3. Power spectral density of EEG signals.

Comparison of interictal and preictal EEG activity across main frequency bands (Delta, Theta, Alpha, Beta, Gamma).

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Figure 4. Schematic representation of the CNN–LSTM multimodal framework.

Illustration of the proposed architecture for multimodal seizure prediction, showing feature extraction and classification steps.

(Recommended layout: full page, 15 cm width)

Figure 5. ROC curves of prediction models.

Receiver operating characteristic (ROC) curves comparing multimodal EEG+ECG model with EEG-only and ECG-only approaches.

(Recommended layout: full page, 15 cm width)

Figure 6. Comparison of performance metrics across models.

Bar chart showing accuracy, sensitivity, and specificity of multimodal, EEG-only, and ECG-only prediction methods.

(Recommended layout: single column, 8 cm width)

Figure 7. Key time points in intracranial EEG signals.

Representative EEG and ECG features highlighting preictal, ictal, and postictal states.

(Recommended layout: full page, 15 cm width)

Figure 8. Performance metrics of the CNN–LSTM model.

Bar chart showing average prediction performance across cross-validation folds.

(Recommended layout: single column, 8 cm width)

Figure 9. Resistance of the multimodal model against Gaussian noise.

Line chart demonstrating stability of model accuracy at different signal-to-noise ratios (SNR).

(Recommended layout: full page, 15 cm width)