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*Original Article*

# Association of EEG-assessed phase lag index with cognitive dysfunction and seizure occurrence in children with epilepsy

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**Abstract:** Purpose: To investigate the association of EEG-assessed Phase Lag Index (PLI) with cognitive dysfunction and seizure occurrence in pediatric patients with epilepsy. Methods: A retrospective cohort study enrolled 117 children with epilepsy aged 4 to 16 years. Participants were categorized into Normal PLI (n=53) and Abnormal PLI (n=64) groups based on EEG-assessed PLI values. EEG signals were collected using 87-channel Natus Brain Monitor amplifier, and PLI and coherence were calculated for various brain regions. Cognitive function and seizure occurrence were assessed using standardized tests and clinical parameters. Statistical analyses, including t-tests, Spearman correlation analysis, and logistic regression, were conducted to evaluate the associations between EEG-assessed PLI, cognitive dysfunction, and seizure occurrence. Results: The Abnormal PLI group exhibited significantly higher PLI measurements across various brain regions compared to the Normal PLI group ($P < 0.001$ for all comparisons). Distinct EEG pattern alterations, especially in PLI and various frequency bands, were observed in the Abnormal PLI group. This group also displayed significant cognitive impairments across all cognitive measures ($P < 0.001$ for all comparisons) and experienced markedly higher seizure frequency, longer average seizure duration, and greater seizure severity compared to the Normal PLI group ($P < 0.001$ for all comparisons). Correlation and logistic regression analyses supported the robust relationships between PLI, cognitive dysfunction, and seizure parameters ($P < 0.001$ for all). Conclusion: EEG-assessed PLI shows promise as a valuable tool for assessing cognitive dysfunction and predicting seizure occurrence in children with epilepsy. The study's findings contribute to the understanding of the neuropathophysiology of epilepsy in children and offer implications for prognostic assessment and therapeutic intervention in this vulnerable patient population. The results emphasize the potential clinical utility of EEG-derived biomarkers in the evaluation and management of epilepsy in pediatric patients, suggesting avenues for personalized treatment strategies to optimize cognitive outcomes and seizure management in this population.

**Keywords:** EEG, phase lag index, cognitive dysfunction, seizure occurrence, epilepsy

## Introduction

Epilepsy is a chronic neurological disorder characterized by recurrent and unpredictable seizures, which are the result of sudden, excessive electrical discharges in the brain [1, 2]. These seizures can manifest in various forms, including convulsions, loss of consciousness, and abnormal movements, and their impact on an individual's daily life can range from mild to severe [3]. According to the World Health Organization (WHO) an estimated 50 million people worldwide are affected by the disorder. In addition to seizures, epilepsy can also lead to cognitive dysfunction, affecting a person's memory, attention, and overall cognitive abilities [4]. This cognitive impairment can significantly influence the quality of life and daily functioning of individuals with epilepsy, posing additional challenges beyond the immediate physical effects of the seizures themselves [5]. It's important to note that while epilepsy can affect individuals of all ages, the impact of the condition is particularly significant in children [6]. Pediatric epilepsy presents unique challenges, as it can disrupt crucial developmental processes and may have long-term implications for cognitive and neurological function [7].

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While there have been notable achievements in the development of antiepileptic medications, surgical interventions, and non-pharmacological approaches for managing seizures, many individuals with epilepsy, especially children, continue to experience uncontrolled seizures and associated cognitive impairments [8, 9]. There remains a need for more precise and accurate methods of assessing its impact on cognitive function and seizure occurrence in pediatric patients [10].

Electroencephalography (EEG) is considered a valuable tool in the diagnosis and management of epilepsy due to its ability to record and analyze the electrical activity of the brain [4, 11]. This non-invasive neuroimaging technique plays a crucial role in the evaluation of patients with suspected epilepsy, aiding in the identification of abnormal brain wave patterns associated with seizure activity and other neurological disorders [12-14]. Specifically, the Phase Lag Index (PLI), derived from EEG data, has garnered attention as a promising measure of functional connectivity in the brain due to its ability to offer insights into the coordination of neural activity across different brain regions [15, 16]. By capturing the phase delays between EEG signals recorded from distinct brain regions, PLI can elucidate the temporal synchronization of neuronal oscillations, reflecting the degree of coordination and information exchange between interconnected brain networks [17, 18]. Unlike traditional measures of functional connectivity, which are based on the amplitude of EEG signals, PLI focuses on the phase differences of these signals, providing a more nuanced understanding of the dynamics of neural communication [19, 20]. However, further research is needed to elucidate the potential of PLI as a biomarker for cognitive dysfunction and seizure occurrence in children with epilepsy [21].

This manuscript aims to investigate the association of EEG-assessed Phase Lag Index with cognitive dysfunction and seizure occurrence in pediatric patients with epilepsy. By exploring the relationship between PLI, cognitive function, and seizure activity, we seek to contribute to the understanding of the neuropathophysiology of epilepsy and potentially identify novel avenues for prognostic assessment and therapeutic intervention in this vulnerable patient population.

## Materials and methods

### *Study participants*

The retrospective cohort study enrolled children with epilepsy who were admitted to the pediatric neurology department at Qingdao Chengyang District People's Hospital between December 2020 and December 2023, and were aged 4 to 16 years.

Participants were categorized into two groups based on the EEG-assessed Phase Lag Index (PLI): the Normal PLI Group (within normal range) and the Abnormal PLI Group (elevated PLI values). Finally, a total of 117 children were involved, with 53 in the Normal PLI Group (30 males and 23 females, aged 5 to 14 years, mean age 9.52±3.24 years) and 64 in the Abnormal PLI Group (34 males and 30 females, aged 6 to 15 years, mean age 10.07±3.71 years). All procedures in this study were approved by the ethics committee of the Qingdao Chengyang District People's Hospital and abided by the ethical guidelines of the Declaration of Helsinki (No. LL-2020-11-6-L), and the ethics of our hospital committee agreed to waive informed consent.

### *Inclusion and exclusion criteria*

Inclusion Criteria: Confirmed diagnosis of epilepsy [22] based on clinical history, neurological examination, and EEG findings; Children aged between 4 and 16 years at the time of diagnosis.

Exclusion Criteria: Children with no history of neurological or psychiatric illness; Children without liver and kidney dysfunction; Children with normal hearing and comprehension ability.

### *Evaluation of normal and abnormal PLI groups*

The Phase Lag Index, representing the asymmetry of the distribution of phase differences between any two EEG signals, was quantified to ascertain the degree of phase lead or lag between pairs of EEG electrodes across the brain. For the purpose of this study, the Normal PLI Group was defined as children who exhibited PLI values within the normal range, established through prior empirical research and normative data collected from healthy pediatric

populations. Specifically, children whose PLI values were within one standard deviation from the mean PLI of a control cohort were included in this group. Conversely, the Abnormal PLI Group consisted of children with PLI values exceeding this range, suggesting an elevated degree of phase lag and, potentially, disrupted functional connectivity indicative of neurological abnormalities associated with epilepsy.

*EEG and PLI*

The EEG signals were collected using an 87-channel Natus Brain Monitor amplifier (Natus® EEG32U, Natus, USA) with a sampling frequency of 512 Hz, recording for at least 20 minutes with 19 electrodes placed according to the 10-20 International System [11]. Patients were instructed to relax with their eyes closed and to remain awake. A monitoring technician assessed vigilance and artifacts during the data acquisition [23]. Patients were not taking medications that could influence the EEG recording [24]. Subsequently, the initial 3-minute resting state with eyes closed was used for further analysis. The recorded signals from each channel were filtered to reduce power line noise and subjected to bandpass FIR 1-70 Hz filtering with a Hamming window [12]. The resulting signal was then divided into 5 segments with baseline correction and detrending, with the removal of epochs containing unexpected events (e.g., movement, blinking, speaking) and further artifact removal using the Autoreject method. A manual verification of the resulting epochs for the presence of artifacts was conducted by an expert [25]. Phase Lag Index (PLI) and coherence were calculated for each pair of electrodes in theta (4-8 Hz), alpha (8-13 Hz), beta (13-30 Hz), and gamma (30-45 Hz) frequency bands. Global values for each frequency band were obtained by averaging the results of all electrode pairs [26]. The electrodes were divided into frontal, central, temporal, parietal, and occipital regions, with calculations performed separately for the left and right sides. The PLI and coherence between each pair of regions were calculated by averaging the values of all pairs of electrodes between the regions.

*Statistical analysis*

Based on sample size calculation, the formula for determining the sample size is $n1=n2=2 \times (\mu\alpha + \mu\beta)2\ \sigma 2/\delta 2$, where the sample variance S2 is estimated as $S2=[Se2 + Sc2]/2$ and $\delta=|Xe - Xc|$. Here, Xe, Xc, Se, and Sc represent the mean and standard deviation of the observation and control groups, respectively, and n1=n2. With μα=1.645 and μβ=1.282 from the table, the result approximates n≈105 cases. Considering a 10% attrition rate, the calculated sample size is 117. Therefore, this study selected 117 pediatric patients with epilepsy.

All statistical analyses were carried out using SPSS 29.0 (SPSS Inc, Chicago, IL, USA). Descriptive statistics were used to summarize the demographic characteristics and clinical variables of the study participants. The independent t-test was utilized to compare continuous variables between the Normal PLI Group and the Abnormal PLI Group, while the chi-square test was employed for categorical variables. Spearman correlation analysis and logistic regression were conducted to assess the associations between EEG-assessed PLI, cognitive dysfunction, and seizure occurrence in children with epilepsy.

## Results

*General data*

The demographic characteristics of the study participants were analyzed to compare the Normal PLI Group (n=53) and the Abnormal PLI Group (n=64) (**Table 1**). There were no significant differences in age between the two groups (9.52±3.24 years vs. 10.07±3.71 years, t=0.849, P=0.398). Furthermore, there was no significant difference in the distribution of gender between the two groups ($\chi^2$=0.036, P=0.85), with 57% males in the Normal PLI Group and 53% in the Abnormal PLI Group. The duration of epilepsy also showed no significant variance between the groups (4.75±2.52 years vs. 5.05±3.29 years, t=0.551, P=0.583). In terms of epilepsy type, the distribution of focal and generalized epilepsy was similar in both groups ($\chi^2$=0, P=1). Additionally, there were no significant differences in the presence of a family history of epilepsy ($\chi^2$=0.215, P=0.643) or the use of antiepileptic medication ($\chi^2$=0.208, P=0.649) between the two groups. These results suggest that the demographic characteristics were well-balanced between the Normal and Abnormal PLI Groups, providing a solid foundation for the subsequent analyses.

**Table 1.** Demographic characteristics of study participants

| Characteristic | Normal PLI Group (n=53) | Abnormal PLI Group (n=64) | t/$X^2$ | *p* value |
|---|---|---|---|---|
| Age (years) | 9.52±3.24 | 10.07±3.71 | 0.849 | 0.398 |
| Gender | | | 0.036 | 0.85 |
| Male | 30 (57%) | 34 (53%) | | |
| Female | 23 (43%) | 30 (47%) | | |
| Duration of Epilepsy (years) | 4.75±2.52 | 5.05±3.29 | 0.551 | 0.583 |
| Epilepsy Type | | | 0 | 1 |
| Focal | 35 (66%) | 42 (66%) | | |
| Generalized | 18 (34%) | 22 (34%) | | |
| Family History of Epilepsy | | | 0.215 | 0.643 |
| Yes | 12 (23%) | 18 (28%) | | |
| No | 41 (77%) | 46 (72%) | | |
| Antiepileptic Medication | | | 0.208 | 0.649 |
| Monotherapy | 28 (53%) | 30 (47%) | | |
| Polytherapy | 25 (47%) | 34 (53%) | | |

**Table 2.** Comparison of EEG-Assessed PLI measurements between the two groups

| Parameters | Normal PLI Group (n=53) | Abnormal PLI Group (n=64) | t | *p*-value |
|---|---|---|---|---|
| Mean PLI | 0.32±0.05 | 0.45±0.08 | 10.486 | P < 0.001 |
| Frontal Lobe PLI | 0.28±0.04 | 0.37±0.06 | 8.629 | P < 0.001 |
| Temporal Lobe PLI | 0.34±0.06 | 0.46±0.07 | 10.406 | P < 0.001 |
| Parietal Lobe PLI | 0.31±0.05 | 0.43±0.09 | 9.56 | P < 0.001 |
| Occipital Lobe PLI | 0.30±0.06 | 0.42±0.07 | 10.014 | P < 0.001 |
| Interhemispheric PLI | 0.29±0.05 | 0.41±0.08 | 9.37 | P < 0.001 |
| Anteroposterior PLI | 0.33±0.06 | 0.44±0.07 | 9.505 | P < 0.001 |
| Left Hemisphere PLI | 0.31±0.05 | 0.43±0.09 | 8.344 | P < 0.001 |
| Right Hemisphere PLI | 0.30±0.06 | 0.42±0.07 | 10.836 | P < 0.001 |

*PLI*

Firstly, we compared the parameters of PLI between the two groups. The mean PLI in the Abnormal PLI Group (0.45±0.08) was significantly higher than that in the Normal PLI Group (0.32±0.05), with a t-value of 10.486 and a *p*-value of less than 0.001 (**Table 2**). Similarly, all other PLI measurements, including Frontal Lobe, Temporal Lobe, Parietal Lobe, Occipital Lobe, Interhemispheric, Anteroposterior, Left Hemisphere, and Right Hemisphere, were significantly higher in the Abnormal PLI Group compared to the Normal PLI Group, with *p*-values less than 0.001 and t-values ranging from 8.344 to 10.836. These findings indicate a consistent and statistically significant elevation of PLI measurements across various brain regions in the Abnormal PLI Group, suggesting distinctive neural network alterations in this group compared to the Normal PLI Group.

*EEG parameters*

Subsequently, the EEG parameters of the normal PLI group and the abnormal PLI group were compared in this study, and the results showed significant differences in each index (**Table 3**). The mean Phase Lag Index (ms) was markedly higher in the Abnormal PLI Group (38.28± 6.89) compared to the Normal PLI Group (24.75±5.34), with a t-value of 11.962 and a *p*-value less than 0.001. Furthermore, the Delta, Theta, and Gamma band powers were significantly higher in the Abnormal PLI Group compared to the Normal PLI Group, with *p*-values less than 0.001 and t-values ranging from 3.511 to 3.169. Conversely, the Alpha and Beta band powers were only slightly elevated in the Abnormal PLI Group, with *p*-values of 0.038 and 0.006, respectively. These findings suggest distinct EEG pattern alterations, especially in the phase lag index and various frequency

**Table 3.** Comparison of EEG parameters between the two groups

| EEG Parameter | Normal PLI Group (n=53) | Abnormal PLI Group (n=64) | t | *p* value |
|---|---|---|---|---|
| Mean Phase Lag Index (ms) | 24.75±5.34 | 38.28±6.89 | 11.962 | P < 0.001 |
| Delta Band Power ($\mu V^2$/Hz) | 35.62±4.85 | 32.17±5.52 | 3.59 | P < 0.001 |
| Theta Band Power ($\mu V^2$/Hz) | 28.51±3.25 | 30.88±4.05 | 3.511 | P < 0.001 |
| Alpha Band Power ($\mu V^2$/Hz) | 22.13±3.51 | 23.64±4.29 | 2.095 | 0.038 |
| Beta Band Power ($\mu V^2$/Hz) | 18.21±2.84 | 19.77±3.15 | 2.815 | 0.006 |
| Gamma Band Power ($\mu V^2$/Hz) | 15.22±2.53 | 16.86±3.08 | 3.169 | 0.002 |

bands, in the Abnormal PLI Group, indicating potential neurological differences compared to the Normal PLI Group.

*Cognitive function*

In order to assess whether there are differences in cognitive function between the two groups of patients, this study conducted a comprehensive comparison across five aspects: IQ, Attention Test, Memory Test, Executive Function, and Processing Speed (**Figure 1**). The Abnormal PLI Group displayed lower scores in IQ (95.64±6.43) compared to the Normal PLI Group (102.55±5.17), with a t-value of 6.444 and a *p*-value less than 0.001. Additionally, performance in attention, memory, executive function, and processing speed was markedly lower in the Abnormal PLI Group, as indicated by significantly lower scores in the attention test (t=5.797, P < 0.001), memory test (t=3.539, P < 0.001), executive function assessment (t=5.651, P < 0.001), and processing speed evaluation (t=5.897, P < 0.001). The above findings indicate that, compared to the Normal PLI group, individuals in the Abnormal PLI group exhibited significant cognitive impairments across all five aspects of cognitive function. Such results support the hypothesis that the PLI is associated with cognitive dysfunction.

*Seizure occurrence*

**Figure 2** compares the occurrence of seizures between the Normal PLI Group (n=53) and the Abnormal PLI Group (n=64). The Abnormal PLI Group exhibited a markedly higher seizure frequency per month (2.57±1.33) compared to the Normal PLI Group (1.28±0.85), with a t-value of 6.346 and a *p*-value less than 0.001. Moreover, the average seizure duration was significantly longer in the Abnormal PLI Group (45.63±5.71 seconds) than in the Normal PLI Group (32.16±4.65 seconds), with a t-value of 14.066 and a *p*-value less than 0.001. Additionally, seizure severity, scored on a scale from 1 to 10, was markedly higher in the Abnormal PLI Group (6.18±1.45) compared to the Normal PLI Group (4.84±1.28), with a t-value of 5.345 and a *p*-value less than 0.001. The results above indicate that epileptic patients with abnormal PLI exhibited significantly higher seizure frequency, longer average seizure duration, and greater seizure severity compared to patients with normal PLI. This suggests that monitoring patients' PLI may facilitate the prediction of epileptic seizures, thereby aiding in the proactive management of clinical work.

*Correlation analysis*

The correlation analysis between PLI and cognitive dysfunction as well as seizure parameters in children with epilepsy demonstrated significant associations (**Table 4**). The Mean Phase Lag Index exhibited a strong positive correlation with cognitive dysfunction, as indicated by IQ, Attention Test, Memory Test, Executive Function, and Processing Speed (P < 0.001 for all). Conversely, the Delta and Theta Band Powers showed negative correlations, while the Alpha, Beta, and Gamma Band Powers exhibited positive correlations with cognitive measures. Moreover, seizure frequency, average seizure duration, and seizure severity demonstrated positive correlations with the Mean Phase Lag Index (P < 0.001 for all). This comprehensive analysis highlights the robust relationships between PLI, cognitive dysfunction, and seizure parameters in children with epilepsy. Furthermore, these results highlight the potential utility of PLI to indicate cognitive impairment and seizures in children with epilepsy.

*Logistic regression analysis*

Univariate logistic regression analysis revealed significant associations between cognitive impairment, seizures, and PLI in children with epi-

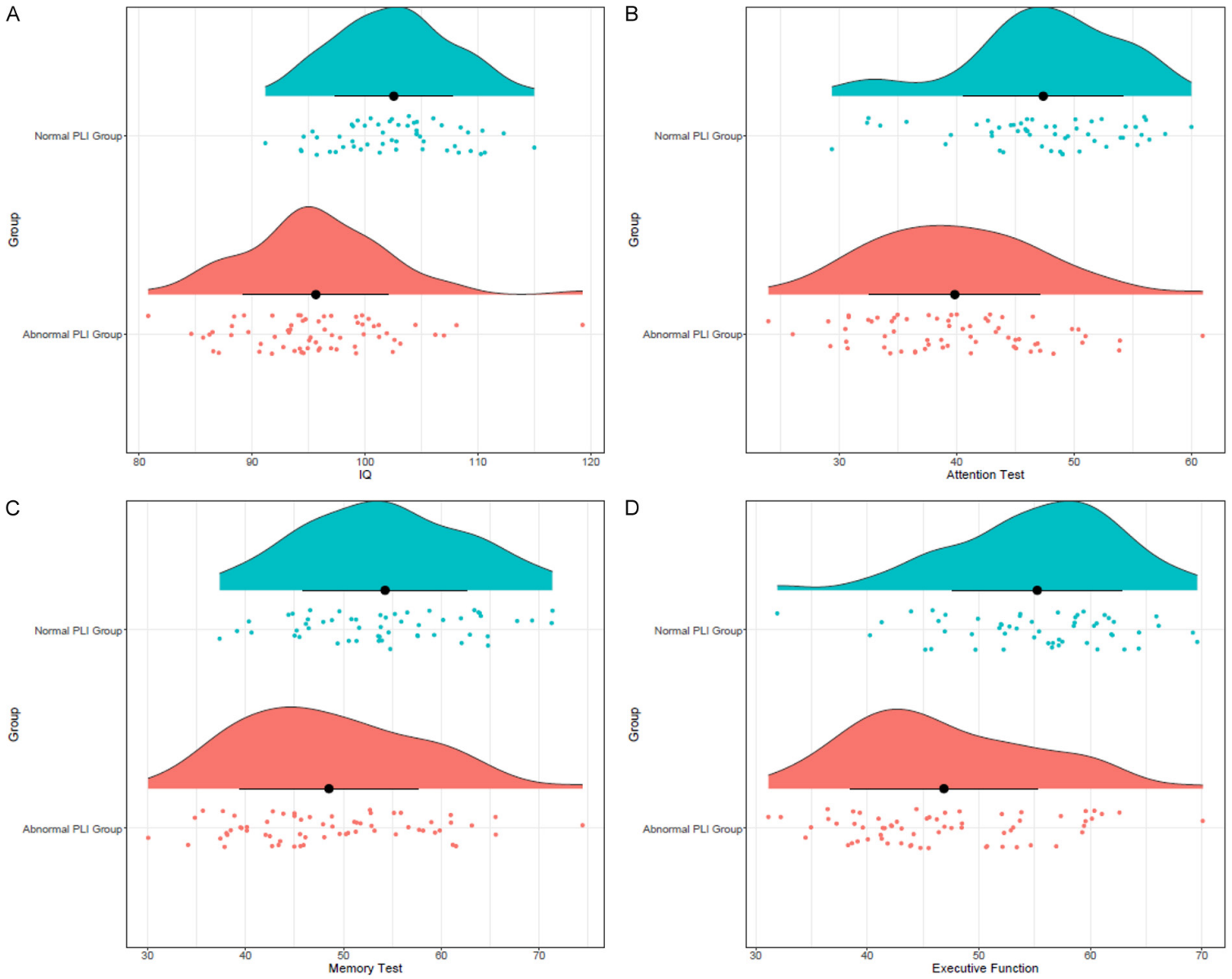


**Figure 1.** Comparison of cognitive function scores between the two groups. A. IQ. B. Attention test. C. Memory test. D. Executive function.

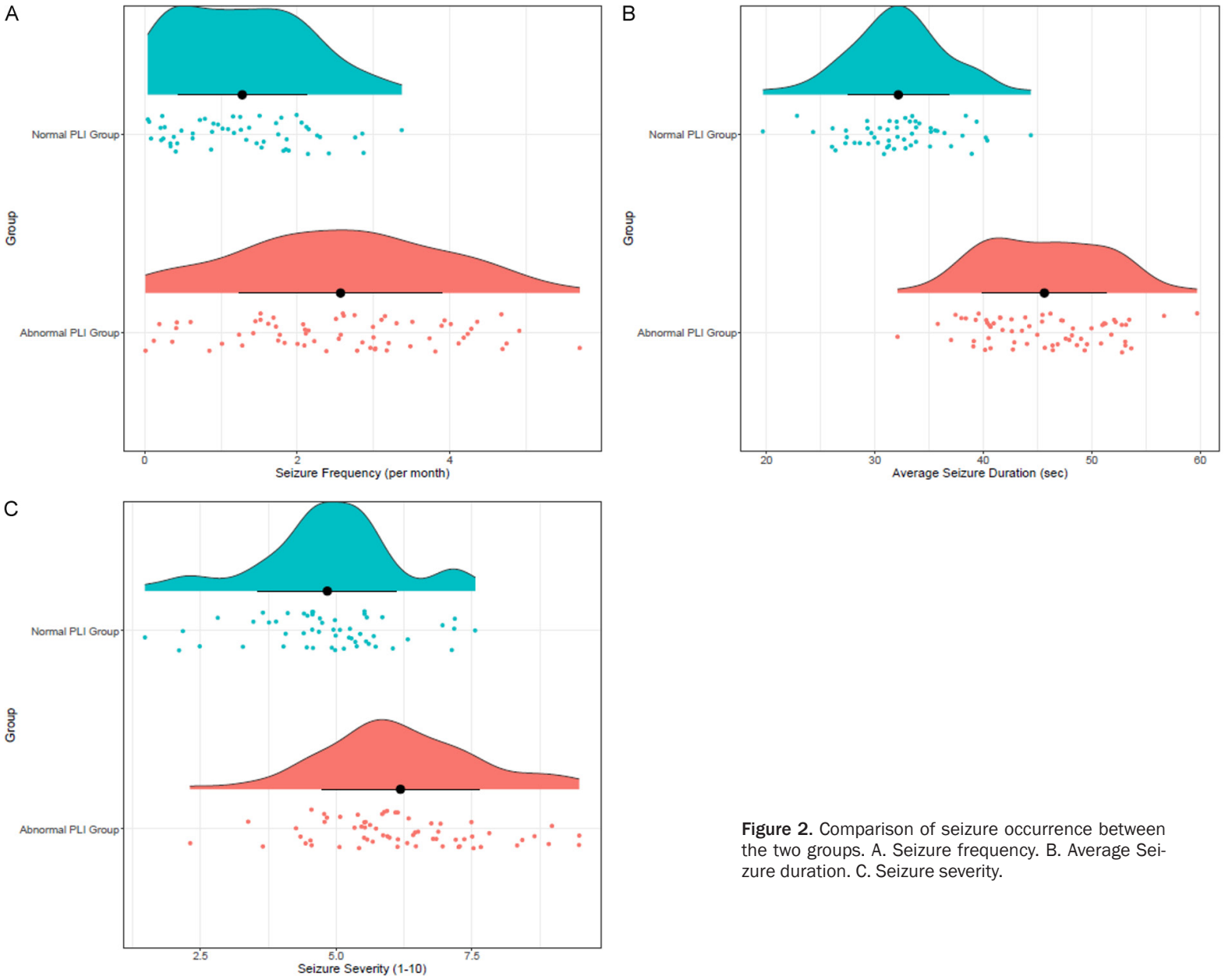


**Figure 2.** Comparison of seizure occurrence between the two groups. A. Seizure frequency. B. Average Seizure duration. C. Seizure severity.

**Table 4.** The correlation between PLI and cognitive dysfunction and seizures in children with epilepsy

| Parameters | r | *p* value |
|---|---|---|
| Mean Phase Lag Index | 0.737 | P < 0.001 |
| Delta Band Power | -0.314 | P < 0.001 |
| Theta Band Power | 0.305 | P < 0.001 |
| Alpha Band Power | 0.188 | 0.042 |
| Beta Band Power | 0.252 | 0.006 |
| Gamma Band Power | 0.279 | 0.002 |
| IQ | -0.507 | P < 0.001 |
| Attention Test | -0.473 | P < 0.001 |
| Memory Test | -0.311 | P < 0.001 |
| Executive Function | -0.463 | P < 0.001 |

**Table 5.** Univariate logistic regression analysis was used to analyze the relationship between cognitive impairment, seizures and PLI

| Parameters | coef | OR | B | Beta | P |
|---|---|---|---|---|---|
| Mean Phase Lag Index | 0.358 | 1.431 | 5.61 | 0.358 | P < 0.001 |
| Delta Band Power | 0.125 | 0.882 | 3.266 | -0.125 | 0.001 |
| Theta Band Power | 0.175 | 1.191 | 3.152 | 0.175 | 0.002 |
| Alpha Band Power | 0.1 | 1.105 | 1.997 | 0.1 | 0.046 |
| Beta Band Power | 0.177 | 1.194 | 2.633 | 0.177 | 0.008 |
| Gamma Band Power | 0.206 | 1.229 | 2.91 | 0.206 | 0.004 |
| IQ | 0.208 | 0.812 | 4.786 | -0.208 | P < 0.001 |
| Attention Test | 0.149 | 0.861 | 4.608 | -0.149 | P < 0.001 |
| Memory Test | 0.074 | 0.929 | 3.228 | -0.074 | 0.001 |
| Executive Function | 0.124 | 0.883 | 4.585 | -0.124 | P < 0.001 |
| Processing Speed | 0.151 | 0.86 | 4.679 | -0.151 | P < 0.001 |
| Seizure Frequency | 1.02 | 2.773 | 4.75 | 1.02 | P < 0.001 |
| Average Seizure Duration | 0.556 | 1.743 | 4.98 | 0.556 | P < 0.001 |
| Seizure Severity | 0.771 | 2.162 | 4.236 | 0.771 | P < 0.001 |

lepsy (**Table 5**). The Mean Phase Lag Index demonstrated a positive relationship with cognitive impairment (OR=1.431, P < 0.001), while the Delta and Theta Band Powers exhibited positive associations with cognitive decline as well (OR=0.882, P=0.001 and OR=1.191, P=0.002, respectively). Furthermore, the IQ, Attention Test, Memory Test, Executive Function, and Processing Speed were inversely related to cognitive impairment (P < 0.001 for all). Moreover, seizure parameters, including seizure frequency, average seizure duration, and seizure severity, showed strong positive relationships with the likelihood of cognitive impairment (P < 0.001 for all). These findings underscore the significant impact of PLI and seizure activity on cognitive impairment in children with epilepsy, emphasizing the importance of considering PLI parameters when evaluating cognitive outcomes and seizure activity in this population.

## Discussion

The results of this study provide valuable insights into the association of EEG-assessed Phase Lag Index (PLI) with cognitive dysfunction and seizure occurrence in children with epilepsy. Our findings revealed significant differences in PLI measurements, EEG parameters, cognitive function, and seizure occurrence between the Normal PLI and Abnormal PLI groups, highlighting the potential of PLI as a biomarker for assessing cognitive impairment and predicting seizure activity in pediatric patients with epilepsy.

One of the key findings of our study is the significant elevation of PLI measurements across various brain regions in the Abnormal PLI group compared to the Normal PLI group. These results indicate distinctive neural network alterations associated with elevated PLI values, suggesting disrupted functional connectivity and information exchange between interconnected brain networks. These findings are consistent with research of Liu W et al. that has suggested alterations in functional connectivity as a hallmark of epilepsy and have implications for understanding the neuropathophysiology of the disorder [27]. Notably, our study extends this understanding to pediatric patients, emphasizing the relevance of PLI as a potential marker of aberrant neural network dynamics in childhood epilepsy [28].

In addition to differences in PLI measurements, our study also identified distinct EEG pattern alterations, particularly in the phase lag index and various frequency bands, in the Abnormal PLI group. These findings are in line with the literature of González Otárula KA et al. that has highlighted the role of EEG in characterizing abnormal brain wave patterns associated with

seizure activity and neurological disorders, further underscoring the utility of EEG, particularly PLI, in the evaluation of pediatric epilepsy [29]. The observed alterations in EEG parameters provide valuable insights into the neurophysiological changes associated with abnormal PLI values and contribute to the growing body of evidence supporting the use of EEG as a tool for understanding the pathophysiological mechanisms of epilepsy in children.

Importantly, our study revealed a strong association between abnormal PLI values and cognitive dysfunction in pediatric patients with epilepsy. The Abnormal PLI group exhibited significant cognitive impairments across multiple domains, including IQ, attention, memory, executive function, and processing speed, compared to the Normal PLI group. These results align with research of Alexander HB et al. highlighting the impact of epilepsy on cognitive function in children, emphasizing the need for comprehensive assessments of cognitive abilities in pediatric patients with epilepsy [30]. The robust correlations between PLI and cognitive measures underscore the potential of PLI as a biomarker for identifying cognitive dysfunction in children with epilepsy. Furthermore, the logistic regression analysis demonstrated a positive relationship between abnormal PLI values and the likelihood of cognitive impairment, highlighting the predictive value of PLI in assessing cognitive outcomes in this vulnerable patient population.

Another significant finding of our study is the association between abnormal PLI values and seizure occurrence in pediatric patients with epilepsy. The Abnormal PLI group exhibited significantly higher seizure frequency, longer average seizure duration, and greater seizure severity compared to the Normal PLI group. These results echo the clinical relevance of PLI as a potential marker for predicting seizure activity in children with epilepsy. The robust correlations between PLI and seizure parameters, along with the results of the logistic regression analysis, underscore the potential utility of PLI in identifying pediatric patients at higher risk for increased seizure frequency and severity, thereby contributing to the proactive management of epilepsy in this population.

Our study provides novel insights into the potential of EEG-assessed PLI as a biomarker for assessing cognitive dysfunction and predicting seizure occurrence in pediatric patients with epilepsy. By elucidating the associations between PLI, cognitive function, and seizure activity, our findings contribute to a deeper understanding of the neuropathophysiology of epilepsy in children and offer implications for prognostic assessment and therapeutic intervention in this vulnerable patient population. Despite the limitations inherent in retrospective cohort studies, such as the potential for selection bias and the inability to establish causal relationships, the robustness of our findings warrants further exploration of PLI as a promising measure of functional connectivity in the brain and its clinical implications for pediatric epilepsy.

The observed alterations in EEG parameters, particularly the phase lag index (PLI), enrich our understanding of the potential neuropathophysiological mechanisms underlying cognitive dysfunction and seizure occurrence in pediatric epilepsy. Notably, our findings align with previous literature by Tzadok et al. [31], who emphasized alterations in functional connectivity as a hallmark of epilepsy, extending this understanding to pediatric patients. This notion is further supported by the study of Feng X et al. [32], which highlighted the role of EEG in characterizing aberrant brain wave patterns associated with seizure activity and neurological disorders, therefore underscoring the utility of EEG, particularly PLI, in evaluating pediatric epilepsy.

Moreover, the strong association between abnormal PLI values and cognitive impairment in our study resonates with prior research by Crow et al. [33], emphasizing the impact of epilepsy on cognitive function in children, and highlighting the significance of comprehensive cognitive assessments in pediatric epilepsy. Our findings extend this understanding by elucidating the robust correlations between PLI and cognitive measures, thus supporting the potential of PLI as a biomarker for identifying cognitive dysfunction in children with epilepsy.

Additionally, the association between abnormal PLI values and seizure occurrence in our study is consistent with the work of Simon Wostyn et al. [34], who demonstrated the utility of EEG-derived biomarkers in predicting seizure outcomes in adult epilepsy patients. By uncovering similar associations in pediatric epilepsy, our study contributes to the broader literature on

the predictive value of PLI and EEG parameters in evaluating seizure activity in epilepsy patients across different age groups.

Moving forward, future research could leverage longitudinal designs to investigate the predictive value of PLI for long-term cognitive outcomes and seizure prognosis in pediatric epilepsy. Additionally, the implementation of multimodal neuroimaging approaches, integrating EEG with other neuroimaging modalities such as functional magnetic resonance imaging (fMRI), could offer comprehensive insights into the neural mechanisms underlying cognitive dysfunction and seizure occurrence in pediatric patients with epilepsy. Moreover, the development of machine learning algorithms incorporating PLI and other neurophysiological markers could facilitate the development of predictive models for identifying pediatric patients at higher risk for cognitive impairment and increased seizure frequency, thereby informing personalized treatment strategies and improving clinical outcomes in pediatric epilepsy.

Despite the valuable insights gained from our study, it is essential to recognize the limitations that could influence the interpretation and application of our findings. Firstly, the sample size of our study cohort, while representative, may inherently constrain the generalizability of our results to the broader population of pediatric patients with epilepsy. As such, caution should be exercised when extrapolating our findings to a wider demographic. Secondly, the observational nature of our study design warrants consideration, as it precludes causal inferences regarding the relationship between abnormal PLI values and symptom severity in pediatric epilepsy. Moreover, the reliance on clinical scoring for symptom severity assessment, while standard practice, introduces the potential for subjective bias and interrater variability, which may influence the accuracy of our severity stratification. Additionally, the use of a single observation time point for EEG recordings limits our ability to capture potential dynamic changes in PLI values and symptomatology over time.

## Conclusion

In conclusion, the findings of this study underscore the potential of EEG-assessed PLI as a valuable tool for assessing cognitive dysfunction and predicting seizure occurrence in children with epilepsy. By shedding light on the complex interplay between PLI, cognitive function, and seizure activity in pediatric patients, our study contributes to the growing body of evidence supporting the clinical utility of EEG-derived biomarkers in the evaluation and management of epilepsy in children. These insights have the potential to inform the development of targeted interventions and personalized care strategies aimed at optimizing cognitive outcomes and seizure management in pediatric patients with epilepsy.

## Disclosure of conflict of interest

None.

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