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EEG Functional Connectivity Differences Predict Future Conversion to Dementia in Mild Cognitive Impairment With Lewy Body or Alzheimer Disease

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ABSTRACT

Background: Predicting which individuals may convert to dementia from mild cognitive impairment (MCI) remains difficult in clinical practice. Electroencephalography (EEG) is a widely available investigation but there is limited research exploring EEG connectivity differences in patients with MCI who convert to dementia.

Methods: Participants with a diagnosis of MCI due to Alzheimer's disease (MCI-AD) or Lewy body disease (MCI-LB) underwent resting state EEG recording. They were followed up annually with a review of the clinical diagnosis ($n = 66$). Participants with a diagnosis of dementia at year 1 or year 2 follow up were classed as converters ($n = 23$) and those with a diagnosis of MCI at year 2 were classed as stable ($n = 43$). We used phase lag index (PLI) to estimate functional connectivity as well as analysing dominant frequency (DF) and relative band power. The Network-based statistic (NBS) toolbox was used to assess differences in network topology.

Results: The converting group had reduced DF ($U = 285.5$, $p = 0.005$) and increased relative pre-alpha power ($U = 702$, $p = 0.005$) consistent with previous findings. PLI showed reduced average beta band synchrony in the converting group ($U = 311$, $p = 0.014$) as well as significant differences in alpha and beta network topology. Logistic regression models using regional beta PLI values revealed that right central to right lateral (Sens = 56.5%, Spec = 86.0%, −2LL = 72.48, $p = 0.017$) and left central to right lateral (Sens = 47.8%, Spec = 81.4%, −2LL = 71.37, $p = 0.012$) had the best classification accuracy and fit when adjusted for age and MMSE score.

Conclusion: Patients with MCI who convert to dementia have significant differences in EEG frequency, average connectivity and network topology prior to the onset of dementia. The MCI group is clinically heterogeneous and have underlying physiological differences that may be driving the progression of cognitive symptoms. EEG connectivity could be useful to predict which patients with MCI-AD and MCI-LB convert to dementia, regardless of the neurodegenerative aetiology.

Summary

- MCI-LB and MCI-AD patients who convert to dementia have altered EEG functional connectivity at baseline in alpha and beta frequency bands.
- EEG connectivity measures can be predict which patients with MCI will convert to dementia in future.

1 | Introduction

The prognosis of neurocognitive disorders remains challenging due to overlapping clinical symptoms and individual variability in presentation [1–3]. Further evidence to support an early biological diagnosis and inform prognosis, especially at the mild cognitive impairment (MCI) stage, is critical for current management strategies when distinguishing AD (Alzheimer's disease) from DLB (Dementia with Lewy bodies) [4]. Identifying individuals at the highest risk of progressing from MCI to dementia offers additional advantages, including their potential inclusion in interventional trials and the guidance of future disease-modifying agents.

Electroencephalography (EEG) is a non-invasive, relatively inexpensive, well-tolerated and widely available investigation that measures electrical activity in the brain using scalp electrodes. Quantitative EEG (qEEG) measures, such as band power and dominant frequency (DF), are increasingly studied and have revealed significant differences between healthy controls and patients with dementia [5–7], between types of dementia [8, 9] and between progressive and stable MCI [7, 10, 11]. One study demonstrated accurate prediction of conversion from MCI to dementia in DLB and AD using patterns of compressed spectral arrays [7]. Another study revealed low alpha-2 (10–13 Hz) power was associated with an increased risk of rapid progression from MCI with Lewy bodies (MCI-LB) to DLB [11]. EEG slowing, as demonstrated by increased theta/alpha ratio, has been associated with conversion from MCI-LB and MCI due to AD (MCI-AD) to dementia [12].

Evidence for network spread of pathology in dementia with Lewy bodies [13] and Alzheimer's disease [14] has led to studies finding altered network connectivity in these diseases [15, 16]. Phase lag index (PLI) is a measure of connectivity which quantifies nonzero phase differences between two signals and is more robust to volume conduction [17]. Reduction in PLI and differences in the topology of derived networks across multiple frequency bands have been shown when comparing DLB and AD [8, 18, 19]. Significant differences in the efficiency of connectivity networks have been revealed between AD, MCI-AD and healthy controls [20] and between MCI and healthy controls [21] suggesting pathophysiological changes can be detected by EEG in early disease and may also quantify severity. However, there exists some uncertainty over whether EEG functional connectivity may help in the prognosis of dementia at the prodromal MCI stage with limited research in this area. The aim of this study is therefore to explore the utility of EEG functional connectivity measures in delineating between stable MCI and converting MCI. Furthermore, functional connectivity between separate regions can be explored using these approaches.

We hypothesise the following:

1. Greater reduction in DF in converting MCI as compared to stable MCI.
2. Significant functional connectivity differences in converting MCI as compared to stable MCI with reduced PLI in alpha and beta band.

2 | Methods

2.1 | Participants

MCI participants were included from a prospective longitudinal study (SUPErB cohort). Recruitment, assessment and diagnosis has been described previously [12, 22] and is briefly outlined below.

MCI participants aged 60 years and over were recruited from memory, geriatric medicine and neurology clinics. Potential participants were initially screened if they had symptoms which could be related to prodromal DLB. Exclusion criteria at screening included dementia diagnosis, mini-mental state examination (MMSE) score less than 20, major depression, bipolar disorder, schizophrenia and clinical cerebrovascular disease. Participants were interviewed and examined by a medical doctor at baseline and at annual reassessment. Clinical diagnosis was confirmed by a consensus clinical panel of three experienced old-age psychiatrists (A.J.T., P.C.D., J.P.T.) independently. Dopamine transporter (DaT) scan and cardiac MIBG [23, 24] were included to guide diagnostic group according to current research criteria for prodromal DLB [25]. Participants with no core clinical features of DLB, suggestive biomarkers or evidence for alternative causes of dementia were diagnosed with MCI-AD in line with NIA-AA criteria [26]. The clinical review was repeated annually, and the consensus panel diagnosis was reassessed including confirmation of ongoing MCI or conversion to dementia. Dementia was diagnosed for all groups using the NIA-AA criteria for all-cause dementia [27].

To carry out direct comparison of conversion, all MCI participants were included as a single group and subsequently classified based on year 1 and year 2 follow up diagnosis. Participants who converted to dementia in the first or second year were included in the converting group; if they maintained a diagnosis of MCI after 2 years they were included in the stable group. We also carried out subgroup analysis comparing conversion to dementia in MCI-AD and probable MCI-LB diagnostic groups separately as well as comparing year 1 and year 2 converters separately.

2.2 | EEG Acquisition and Pre-Processing

EEG used for this study has been described previously [28] and is summarised briefly here. Participants had EEG recording using a 128 electrode Waveguard cap (ANT Neuro, The Netherlands). The cap was placed according to the 10–5 system with participants seated, gel was applied to each electrode to keep impedance under 5 kΩ, the ground electrode was applied

to the right clavicle and the sampling frequency was set to 1024 Hz. Continuous recordings used for this analysis were taken at resting-state with eyes-closed for 5 min, a technician was present to supervise and confirm compliance.

Pre-processing was completed using the EEGLAB toolbox (version 14) in MATLAB (R2017a) [29]. Bandpass-filter of 0.3–54 Hz was applied and data were split in non-overlapping 2 s epochs. Noisy channels and epochs were removed by visual inspection, the first 90 s of artefact free epochs were selected with this being sufficient to perform quantitative EEG analysis [30, 31]. Independent component analysis was then applied, components were visually inspected to remove common artefacts. Finally, spherical spline interpolation was used to replace the initially excluded channels and data was average referenced.

2.3 | EEG Analysis

For each 2-s epoch, the power spectral density (PSD) was estimated with a frequency resolution of 0.5 Hz across the power spectrum from 2 to 30 Hz. The PSD was normalised to reduce the impact of inter-individual variability. The mean power in each epoch and electrode was estimated and then averaged in the delta (2–4 Hz), theta (4–5.5 Hz), pre-alpha (5.5–8 Hz), alpha (8–13 Hz), and beta (13–30 Hz) bands.

The phase lag index (PLI) was used to provide a measure of synchrony between electrodes that is robust to volume conduction [17]. The PLI accounts for the potential overestimation of functional connectivity as activity from common sources is measured without a lag or delay allowing the use of sensor space (as opposed to source space) continuous data to estimate connectivity between electrode pairs. The PLI was calculated using the filter-Hilbert method as follows. Continuous time series data from all 128 electrodes were bandpass filtered into specified frequency bands as defined previously, Hilbert transform was then applied to the filtered signal to give a phase angle time series. The difference in angles between every pair of electrodes for each time point was calculated. The mean of the sign of this difference represents the non-zero phase locking of a pair of electrodes which represents the functional connectivity between each pair. This value between 0 and 1, with 1 representing the maximum synchrony, can be used to create weighted networks or averaged across all electrode pairs to give a global measure of connectivity in each EEG frequency band. We also investigated average phase lag index between eight major electrode derivations (posterior, frontal, central and lateral on left and right side) to explore regional differences.

2.4 | Statistics

Statistical analysis was carried out with SPSS (IBM, version 29). Differences in qEEG measures between the converting and stable groups were assessed using Mann–Whitney U tests to account for expected non-normality of data, with a p-value of <0.05 considered statistically significant. Effect sizes were calculated by dividing the standardised test statistic by the square root of the number of samples. We also separately assessed differences between stable and year 1 converters, stable and year 2 converters and finally year 1 and year 2 converters. Pearson correlation between cognitive enhancer use (donepezil, rivastigmine, galantamine and memantine) and qEEG measures was used to review potential medication effects. Binary logistic regression was used to assess the classification accuracy and fit of qEEG measures. This analysis was carried out for all EEG results combined as well as separately for the MCI-AD group and the probable MCI-LB group. We also present results corrected for age and MMSE score to account for potential confounders.

The Network-based statistic (NBS) toolbox was used to compare topology of the weighted networks between conversion groups; this method controls for family-wise error rate when mass-univariate testing is performed at every connection of a network [32]. We used 10 threshold values between 2.5 and 3.5 with 5000 permutations to explore networks in each frequency band with significance set at 0.05. We used cluster-based permutation testing to confirm statistical significance of multiple comparisons when analysing connectivity between major regions [33, 34].

3 | Results

3.1 | Demographics

Sixty-six participants were included in this study. Baseline demographic and diagnostic subgroups are summarised in Table 1. There were more participants in the stable group than the converting group. There was a slightly greater proportion of converters in the probable MCI-LB group than in the possible MCI-LB and MCI-AD groups. Stable and converting participants were not significantly different in age, years of education and deprivation index (a measure of relative local deprivation). However, the converting group were more likely to be prescribed cognitive enhancers ($p = 0.022$) and had a significantly lower MMSE score ($p = 0.031$) at baseline. We found no significant correlations with cognitive enhancer use and qEEG measures.

3.2 | EEG Analysis to Predict Conversion for All Diagnostic Groups

Table 2 shows the results from the frequency and averaged PLI analysis. Converters had significantly slower DF, decreased alpha power, and increased pre-alpha and theta power, compared to the stable sub-group (see Table 2). Boxplots of frequency analysis results are shown in Figure 1. The analysis of average connectivity using PLI revealed a significant difference only in the beta band with the converting group showing reduced beta PLI.

Logistic regression models using DF (Sens = 30.4%, Spec = 86.0%, −2LL = 78.04, $p = 0.013$) and beta PLI (Sens = 30.4%, Spec = 90.7%, −2LL = 79.18, $p = 0.033$) had good specificity for identifying participants in the converting group but the sensitivity remained low. Combining these two measures improved the classification accuracy and model fit (Sens = 43.5%, Spec = 86.0%, −2LL = 75.56, DF $p = 0.071$, beta

TABLE 1 | Baseline characteristics of participants.

	MCI progression group		
	Stable	**Convert**	***p*-value**
Total count ($n = 66$)	43 (65.2%)	23 (34.8%)	
Diagnosis at baseline			
MCI-AD ($n = 25$)	16 (64.0%)	9 (36.0%)	0.702
Possible MCI-LB ($n = 8$)	7 (87.5%)	1 (12.5%)	
Probable MCI-LB ($n = 33$)	20 (60.6%)	13 (39.4%)	
Sex			
Male ($n = 47$)	31 (66.0%)	16 (34.0%)	0.416
Female ($n = 19$)	12 (63.1%)	7 (36.8%)	
Mean age (SD)	73.6 (7.1)	74.6 (6.7)	0.563
Mean number of years of education (SD)	12.3 (3.0)	11.3 (2.3)	0.115
Mean MMSE score (SD)	**27.1 (2.3)**	**25.7 (2.3)**	**0.031**
Mean index of multiple deprivation decile (SD)	5.4 (2.7)	5.7 (2.8)	0.622
Prescribed cognitive enhancer	**12 (27.9%)**	**13 (56.5%)**	**0.022**

Note: Baseline characteristics of MCI cohort and diagnostic subgroups with percentages in the stable group as compared to the converting group. Cognitive enhancers are donepezil, rivastigmine, galantamine and memantine. Significance of association between conversion group and baseline characteristics displayed in right hand column. Results with significance value less than 0.05 highlighted in bold. Spearman's correlation was used to assess association of diagnosis, cognitive enhancer prescription and gender. Years of education was assessed using Mann–Whitney *U* test. Age, MMSE score and index of multiple deprivation were assessed using binary logistic regression.
Abbreviations: AD = Alzheimer's disease; LB = Lewy bodies; MCI = mild cognitive impairment; MMSE = mini-mental state examination; SD = standard deviation.

TABLE 2 | Conversion groups EEG results averaged over all electrodes.

	Stable		Convert				
EEG measure	**Mean**	**SD**	**Mean**	**SD**	***U***	**Effect**	**Sig.**
Mean DF (Hz)	**7.9**	**1.4**	**7.0**	**1.1**	**285.5**	**−0.346**	**0.005**
Delta	0.141	0.072	0.175	0.072	629.0	0.223	0.070
Theta	**0.073**	**0.042**	**0.100**	**0.045**	**673.0**	**0.296**	**0.016**
Pre-alpha	**0.200**	**0.138**	**0.275**	**0.118**	**702.0**	**0.344**	**0.005**
Alpha	**0.349**	**0.157**	**0.253**	**0.107**	**318.0**	**−0.292**	**0.018**
Beta	0.237	0.117	0.197	0.098	403.0	−0.152	0.218
Delta PLI	0.248	0.019	0.244	0.018	429.0	−0.108	0.378
Theta PLI	0.115	0.006	0.117	0.010	574.0	0.132	0.285
Pre-alpha PLI	0.272	0.050	0.275	0.037	564.0	0.115	0.350
Alpha PLI	0.272	0.067	0.246	0.050	650.0	−0.2	0.105
Beta PLI	**0.133**	**0.013**	**0.126**	**0.008**	**311.0**	**−0.304**	**0.014**

Note: Mean and standard deviation of results from the MCI progression group comparison of qEEG measures. Showing data from all diagnostic groups. Frequency specific measures are shown as relative power values ranging from 0 to 1. Mann–Whitney *U* test statistic, effect size and significance demonstrated by *p*-value are shown. Measures with $p < 0.05$ are highlighted in bold.
Abbreviations: DF = dominant frequency; PLI = phase lag index; SD = standard deviation.

PLI $p = 0.146$) but neither variable remained significant. When adjusted for age and MMSE score DF remained significant (Sens = 81.4%, Spec = 39.1%, −2LL = 75.41, $p = 0.038$) but beta PLI was no longer significant (Sens = 86.0%, Spec = 47.8%, −2LL = 75.95, $p = 0.066$).

Analysis with NBS revealed no significant connection differences in the delta, theta or pre-alpha networks. The alpha networks showed significant differences between a threshold of 2.5 (n connections = 171, $p = 0.039$) and 3.2 (n connections = 3, $p = 0.043$). The beta networks had significant connections at all thresholds between 2.5 (n connections = 512, $p = 0.006$) and 3.5 (n connections = 5, $p = 0.041$). There was a recurring pattern of right sided connectivity changes in both significant frequency bands which is illustrated in Figure 2 showing beta networks and Figure 3 showing alpha networks alongside a boxplot of the respective average PLI values.

Regional beta PLI values are displayed in Figure 4. Right central to right lateral (Sens = 56.5%, Spec = 86.0%, −2LL = 72.48, $p = 0.017$) and left central to right lateral (Sens = 47.8%, Spec = 81.4%, −2LL = 71.37, $p = 0.012$) beta PLI had better classification

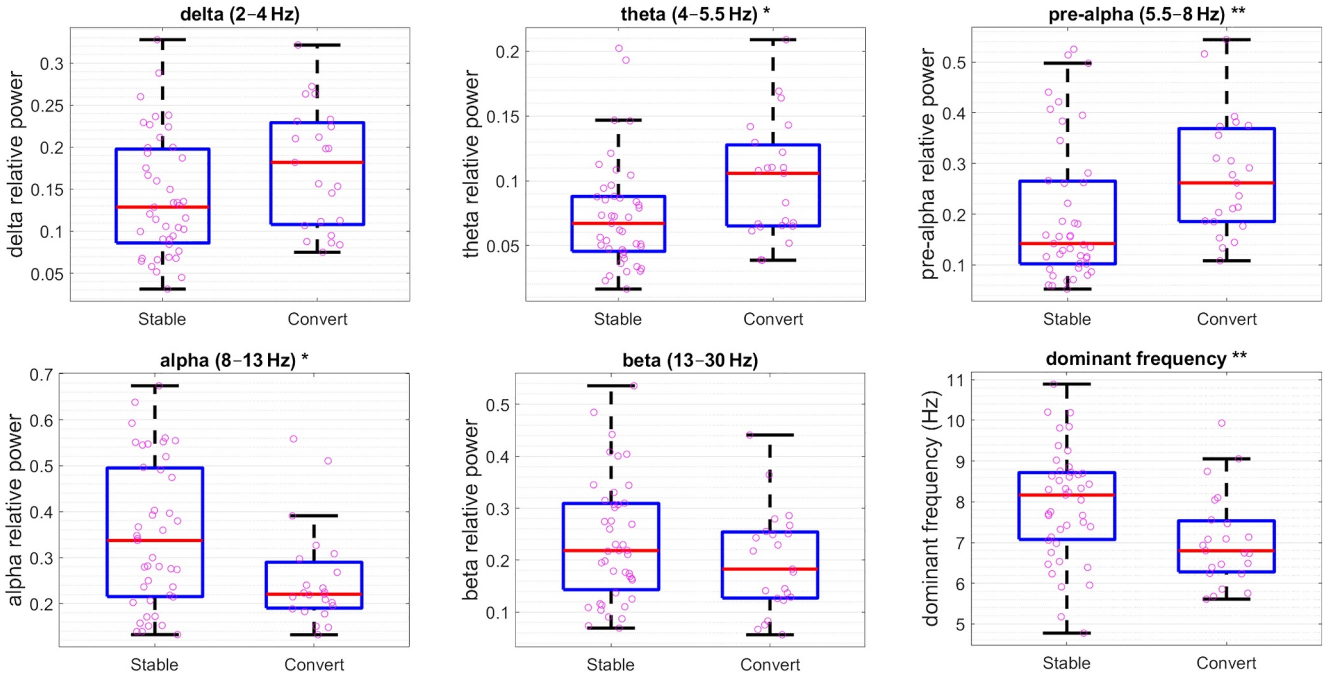

FIGURE 1 | Boxplots showing group comparison of EEG frequency analysis of relative power in each frequency band as well as dominant frequency across all electrodes, $*p < 0.05$, $**p < 0.01$.

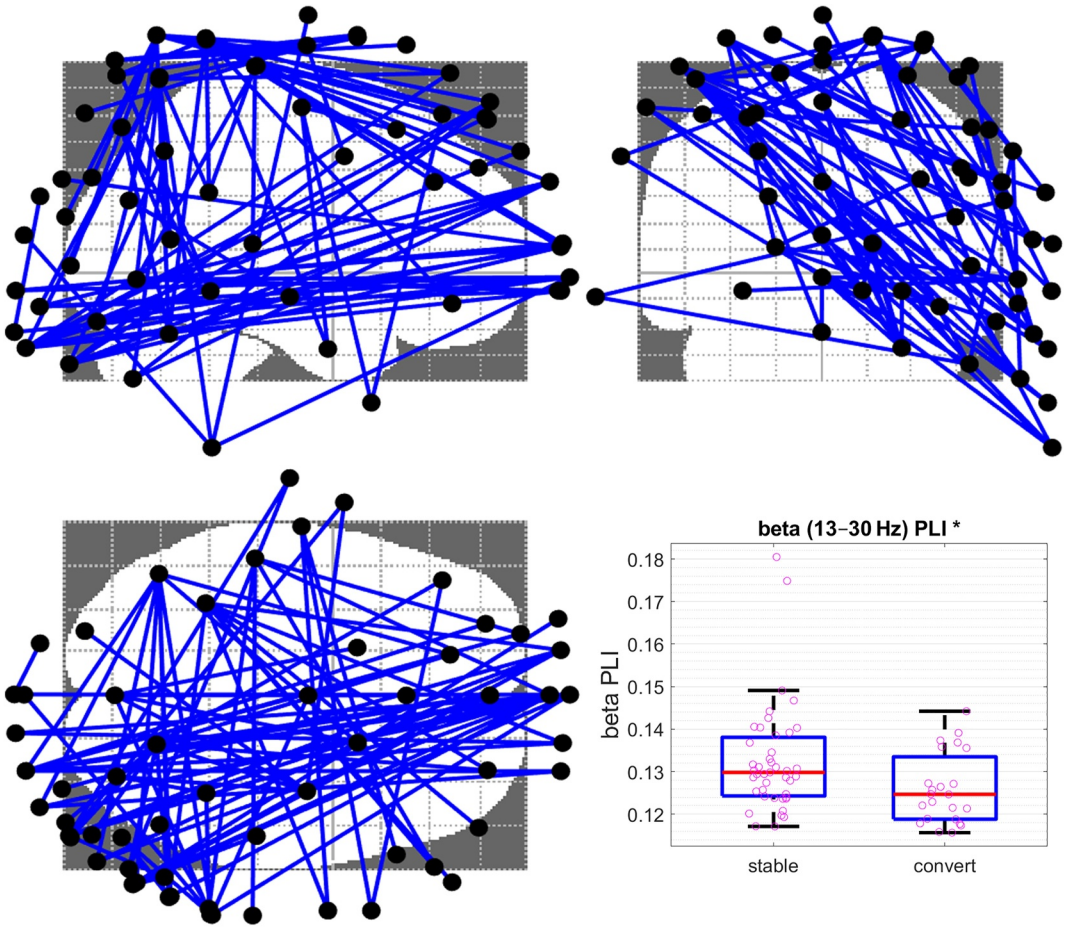

FIGURE 2 | Results from Network-based statistic toolbox analysis of beta frequency band networks derived phase lag index in the axial, coronal and sagittal plane. Networks which showed a significant effect when comparing groups are displayed, EEG electrodes (black dots) with significant connections (blue lines) using a threshold of 3.1 with 5000 permutations which revealed 86 connections and 59 nodes with p-value = 0.008. Boxplot showing average beta phase lag index value comparing the two groups ($p = 0.015$).

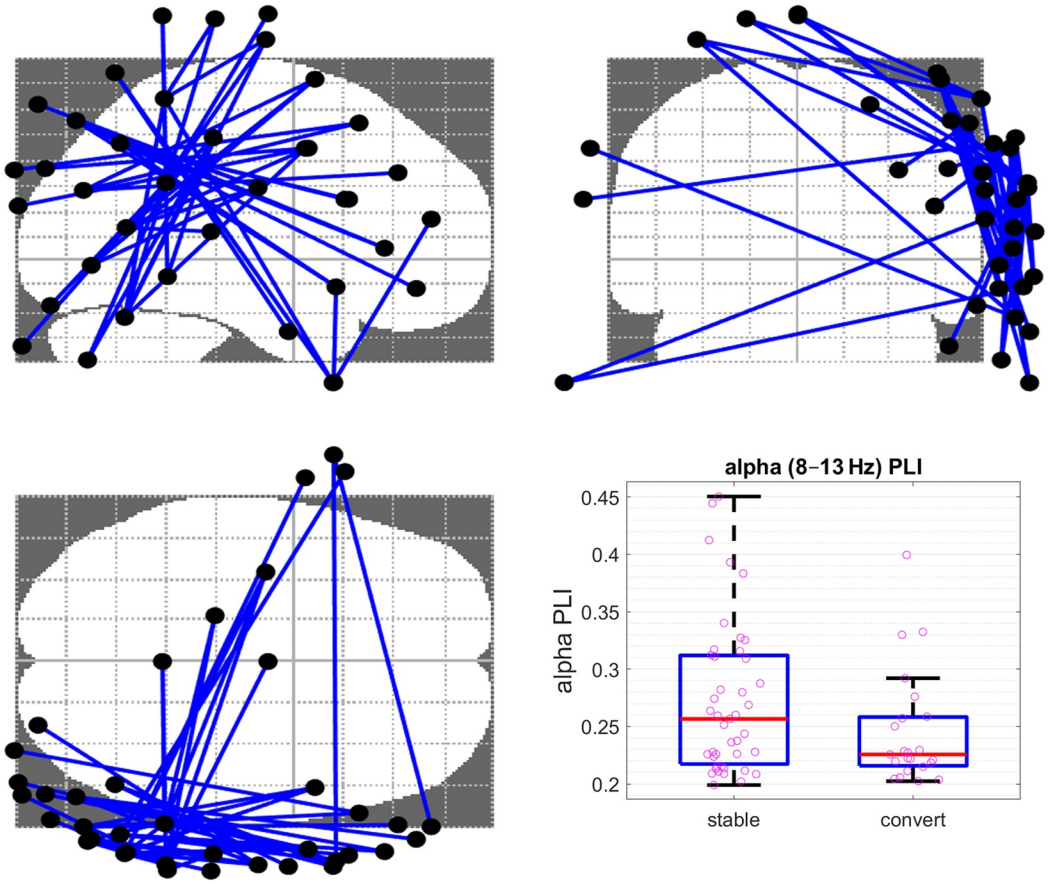

FIGURE 3 | Results from Network-based statistic toolbox analysis of alpha frequency band networks derived from phase lag index values in the axial, coronal and sagittal plane. Networks which show a significant effect when comparing conversion group are displayed, EEG electrodes (black dots) with significant connections (blue lines) using a threshold of 2.8 which revealed 48 connections and 38 nodes with *p*-value of 0.031. Boxplot showing average alpha phase lag index values comparing the two groups ($p = 0.105$).

accuracy and model fit compared to other between-region beta connectivity values when adjusted for age and MMSE score. These regional measures were also confirmed as significantly different between groups on cluster-based permutation testing.

Analysis of conversion year showed significant differences between year 1 converters ($n = 16$) and stable group ($n = 43$) with reduced DF ($U = 381$, $p = 0.045$), increased relative theta ($U = 465$, $p = 0.039$), reduced relative pre-alpha ($U = 468$, $p = 0.034$) and reduced global beta PLI ($U = 188$, $p = 0.008$). When comparing the stable group with participants who converted to dementia in year 2 ($n = 7$), DF was significantly reduced ($U = 59$, $p = 0.009$) and relative pre-alpha power was significantly increased ($U = 234$, $p = 0.018$), however there were no statistically significant differences in average PLI measures between the stable group and year 1 converters. There were also no statistically significant differences between year 1 and year 2 converters, however this analysis may be limited by the smaller sample sizes.

3.3 | Conversion in MCI-AD Subgroup

Mann–Whitney *U* tests revealed the most significant differences across all electrodes were relative theta power and beta PLI. The converting MCI-AD subgroup had statistically significant reduction in beta PLI (mean = 0.123, SD = 0.007) compared to the stable MCI-AD subgroup (mean = 0.132, SD = 0.014, $U = 33$, effect = −0.442, $p = 0.027$). The converting MCI-AD subgroup also had increased relative theta power (mean = 0.087, SD = 0.032) as compared to the stable MCI-AD subgroup (mean = 0.057, SD = 0.030, $U = 113$, effect = 0.464, $p = 0.020$).

Logistic regression analysis in this subgroup revealed that average beta PLI had similar classification accuracy and model fit (Sens = 55.6%, Spec = 93.8%, −2LL = 26.34, $p = 0.047$) compared to relative theta power (Sens = 33.3%, Spec = 93.8%, −2LL = 27.86, $p = 0.055$). However, beta PLI ($p = 0.056$) and relative theta power ($p = 0.076$) did not remain significant when adjusted for age and MMSE score.

Analysis of between-region beta PLI values revealed that right central to right lateral beta PLI had a better fitting model of conversion compared to other between-region beta connectivity values when adjusted for age and MMSE score (Sens = 87.5%, Spec = 88.9%, −2LL = 18.72, $p = 0.016$). This measure was also confirmed with cluster-based permutation testing.

3.4 | Conversion in Probable MCI-LB Subgroup

The only significant difference in the qEEG measures averaged across all electrodes was reduced DF in the converting MCI-LB

subgroup (mean = 6.697, SD = 0.821) compared to the stable MCI-LB subgroup (mean = 7.631, SD = 1.179, $U = 66$, effect = −0.410, $p = 0.018$). Logistic regression in this subgroup showed that DF remained significant when adjusted for age and MMSE score (Sens = 53.8%, Spec = 75.0%, −2LL = 35.60, $p = 0.045$).

Mann–Whitney U tests of between-region beta PLI values did not show any statistically significant differences, with the right posterior to right central having the most marked association with conversion groups in the probable MCI-LB subgroup ($U = 83$, $p = 0.087$).

4 | Discussion

We hypothesised that MCI converters would have reduced dominant frequency and reduced functional connectivity in the higher frequency alpha and beta bands at baseline. We found significant reductions in overall beta frequency connectivity in the converting group compared to the stable group although this was not significant in the alpha band. We also found a significant reduction in dominant frequency at baseline in the converting group compared to the stable group. Further network analysis revealed a regional pattern of changes with right lateral to right central beta hypoconnectivity showing the most marked difference between stable and converting MCI. There were also reductions in alpha network connectivity when assessing the entire network although these changes were less significant than those found in beta functional connectivity networks.

Analysis of the smaller diagnostic subgroups revealed connectivity differences were statistically significant between stable and converting MCI-AD patients. The probable MCI-LB patients did not show statistically significant connectivity differences, but they did show significant differences in the frequency analysis between conversion groups.

These findings show that pathophysiological changes detected by EEG functional connectivity measures predate the conversion of MCI-AD and MCI-LB to dementia. These results also suggest that qEEG measures provide further prognostic information in these patients beyond cognitive testing.

There is previous research comparing EEG connectivity differences in stable MCI and MCI patients who convert to AD, they have regularly shown differences between groups but with varying methods and results. Imaginary part of coherency, a different method for measuring EEG functional connectivity, was increased in low frequency bands (delta and theta) in converting MCI patients [35]. Another study showed lower gamma and higher alpha2 small world index of lagged linear connectivity networks to be most statistically significant differences between conversion groups [36]. This study also revealed connectivity measures outperformed power density spectrum analysis. Reduced beta frequency amplitude correlations across channels was shown in converting MCI-AD compared to stable MCI [37]. This study identified the best EEG biomarkers for prediction which also revealed 5 other non-connectivity measures related to power spectral density (PSD): three involving beta frequency, relative alpha power and alpha/theta ratio. Reduced posterior alpha power has also been associated with conversion to dementia [38]. Absent beta network modulation during memory tasks compared to reduced alpha network modulation at high load memory tasks has been previously shown [39], and this may explain the greater changes in beta networks compared to alpha networks that we observed in the converting group.

We are not aware of any studies reviewing EEG connectivity differences in stable and converting MCI-LB patients, although quantitative measures of PSD have been investigated. Low alpha-2 power was related to time to conversion to DLB in MCI-LB [11]. Reduced dominant frequency was found at baseline in MCI patients who went on to develop DLB [10]. EEG slowing, as demonstrated by increased theta/alpha ratio, was found to significantly increase risk of transition to dementia per year in MCI-AD and MCI-LB patients [12]. Our findings confirm this by demonstration of slowing with reduced dominant frequency in converting MCI-LB.

Previous studies have explored a range of other biomarkers to predict conversion to both AD and DLB. Lower cognitive scores, clinical symptoms and cortical thinning are associated with risk of progression [40–44]. Clinical phenotype Genotyping (apolipoprotein) and fluid (plasma and cerebrospinal) biomarkers have also been explored [45]. The emergence of a range of biomarkers will likely lend the most benefit to patients. Common contraindications to certain tests such as magnetic resonance imaging or lumbar punctures combined with the relative tolerability and non-invasive nature EEG make it a useful biomarker to research in this area.

The availability of baseline, 1-year and 2-year follow up diagnosis made by a panel of three experienced old-age psychiatrist is a major strength of this study. The lack of randomisation for cognitive enhancer use is a limitation of this study. Participants were prescribed these medications by their regular practitioners prior to entering the study and therefore the specific effect of these medications on qEEG measures cannot be interpreted directly from these results. However, there were no significant correlations between cognitive enhancer use and qEEG measures. Another limitation of this study is the lack of cerebrospinal fluid analysis to inform diagnosis which may have improved discrimination between AD and LB patients; however pathological heterogeneity and co-pathology, particularly Alzheimer's within the Lewy body diseases [46] present further challenges to understanding neurophysiological changes in the LB group. A simple clinical test with EEG that can provide prognostic information across these two groups may therefore still have value in clinical practice. A potential limitation is the difference in baseline cognitive scores between the two analysed groups although this was corrected in the statistical analysis, however these results suggest prediction accuracy can be improved when combining EEG with cognitive tests. The use of sensor space analysis limits the interpretation of the results as we are unable to determine the intracortical source of any changes, however sensor space analysis using PLI provides useful neurophysiological information about functional connectivity [17–19] with fewer computational and methodological steps [47].

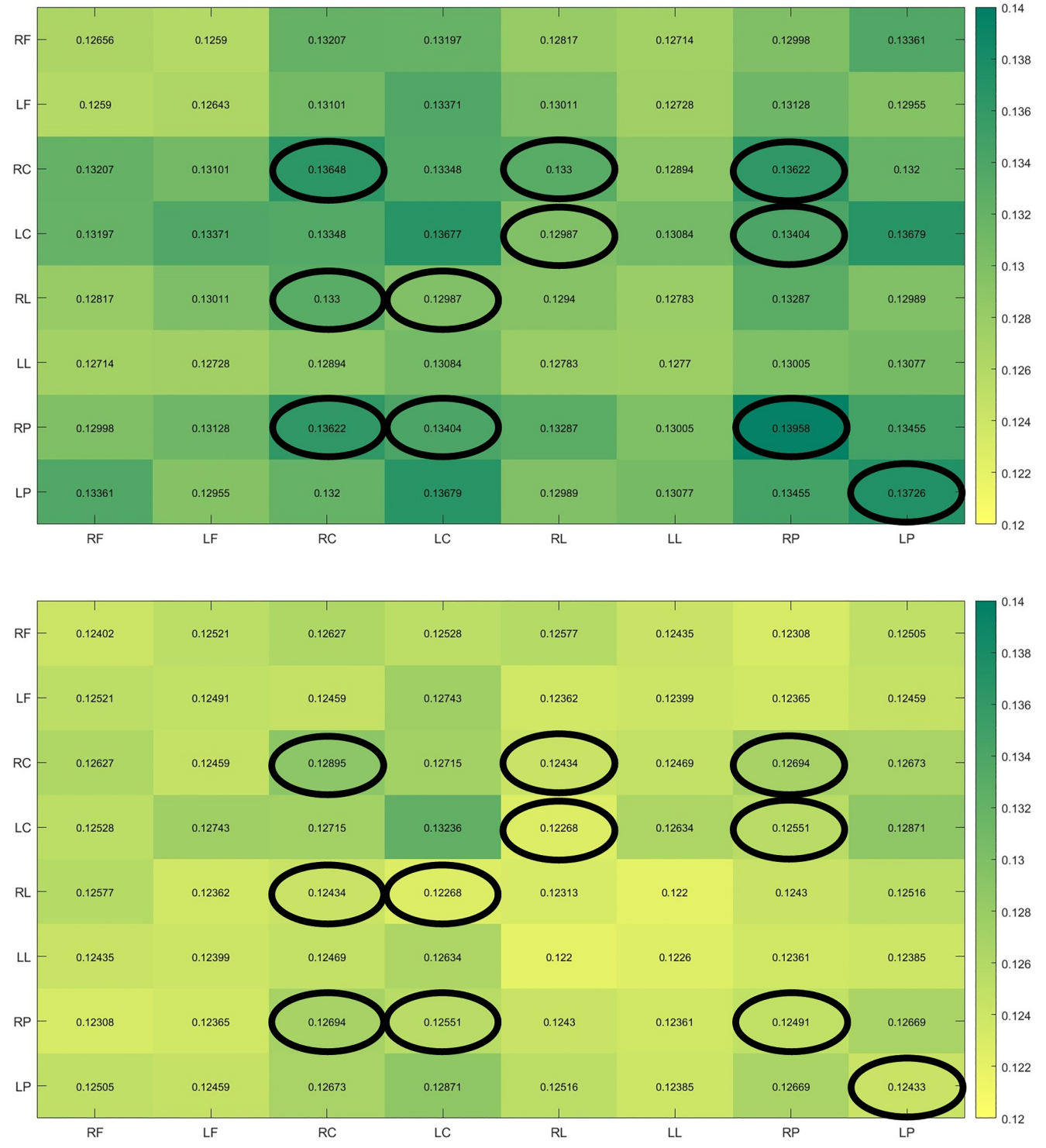

FIGURE 4 | Adjacency matrix displaying the conversion group average values for within and between region phase lag index (PLI) with higher values representing increased functional connectivity. LC = left central, LF = left frontal, LL = left lateral, LP = left posterior, RC = right central, RF = right frontal, RL = right lateral, RP = right posterior. $p < 0.01$ highlighted with black circle.

Further research is required to confirm differences in a larger sample size. This would also allow for a better comparison between frequency and connectivity measures, the statistical significance of differences in prediction using connectivity measures needs to be quantified. Assessing correlates with imaging and pathology data is also needed to provide further insight into the potential drivers of the observed neurophysiological changes. Multimodal investigation of progression in MCI-LB patients may also be beneficial to identify predictive biomarkers in this patient group.

5 | Conclusion

Patients with MCI-LB and MCI-AD who convert to dementia have altered EEG functional connectivity at baseline in the higher frequency alpha and beta bands. EEG connectivity measures can be useful for predicting which patients with MCI will convert to dementia.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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