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Complexity Analysis of Resting-State MEG Activity in Early-Stage Parkinson's Disease Patients

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Abstract—The aim of the present study was to analyze resting-state brain activity in patients with Parkinson's disease (PD), a degenerative disorder of the nervous system. Magnetoencephalography (MEG) signals were recorded with a 151-channel whole-head radial gradiometer MEG system in 18 early-stage untreated PD patients and 20 age-matched control subjects. Artifact-free epochs of 4 s (1250 samples) were analyzed with Lempel–Ziv complexity (*LZC*), applying two- and three-symbol sequence conversion methods. The results showed that MEG signals from PD patients are less complex than control subjects' recordings. We found significant group differences (p-values <0.01) for the 10 major cortical areas analyzed (e.g., bilateral frontal, central, temporal, parietal, and occipital regions). In addition, using receiver-operating characteristic curves with a leave-one-out cross-validation procedure, a classification accuracy of 81.58% was obtained. In order to investigate the best combination of *LZC* results for classification purposes, a forward stepwise linear discriminant analysis with leave-one out cross-validation was employed. *LZC* results (three-symbol sequence conversion) from right parietal and temporal brain regions were automatically selected by the model. With this procedure, an accuracy of 84.21% (77.78% sensitivity, 90.0% specificity) was achieved. Our findings demonstrate the usefulness of *LZC* to detect an abnormal type of dynamics associated with PD.

Keywords—Parkinson's disease, Lempel–Ziv complexity, Magnetoencephalography (MEG), ROC curves, Linear discriminant analysis.

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INTRODUCTION

Parkinson's disease (PD) is a progressive neurological disorder that can cause significant disability and a reduction in the quality of life. Neuropathologic features are the presence of Lewy bodies in the residual dopaminergic neurons and a reduction of dopaminergic neurons in the substantia nigra.[26] PD affects approximately 1% of the population over 60 years of age, becoming an important medical as well as social problem.[26] The four cardinal symptoms are resting tremor, bradykinesia, rigidity, and loss of postural reflexes.[17] A large number of patients also suffer from autonomic, cognitive, and psychiatric disturbances.[24] The gold-standard criterion for diagnosis is the pathological confirmation of the Lewy body on autopsy, but the clinical diagnosis is usually based on the patient history and physical examination. The presence of a combination of cardinal motor features and response to dopaminergic therapy are characteristic signs of PD.[17] Despite careful examination, the accuracy of clinical diagnosis is only around 80–90%.[15,16] Hence, new approaches are needed to improve PD detection.

Nowadays, magnetoencephalography (MEG) and electroencephalography (EEG) recordings are not routinely used as clinical diagnostic procedures in PD. Nevertheless, some studies have demonstrated that the analyses of brain signals could help physicians in the diagnosis of this disorder.[32] Both EEG and MEG are non-invasive techniques that record the electromagnetic fields produced by brain activity with good temporal resolution. EEG and MEG signals are generated by synchronous oscillations of pyramidal neurons.

However, they reflect slightly different characteristics, since EEG is sensitive to all primary currents and MEG is only affected by current flows oriented parallel to the scalp.[13] In addition, MEG technology offers some advantages over EEG. For instance, magnetic fields are not distorted by the resistive properties of the skull.[13] Furthermore, EEG signals are strongly influenced by a wide variety of factors, such as distance between sensors, electrode location, reference point, or conducting substance between skin and electrode. On the other hand, MEG signals are very sensitive to external artifacts. Superconducting quantum interference devices (SQUIDs) and a magnetically shielded room are necessary to detect the weak magnetic signals generated by the brain.

Several studies have focused on spectral analysis of spontaneous EEG/MEG activity in PD patients. The most common alteration in PD is generalized slowing of brain activity.[3,20,29,34,35] PD patients showed a power decrease at the EEG beta band and an increase at the theta band.[34] In another study,[29] the patients presented diffuse slowing of their quantitative EEG (qEEG) when compared with age-matched controls. Finally, MEG studies also showed that PD is associated with a slowing of resting state oscillatory brain activity.[3,20,35] Stoffers *et al.*[35] not only confirmed previously reported slowing, but for the first time made clear that these changes already occurred in the first clinical stages of PD in untreated patients. As an alternative to spectral analyses, some research studies have focused on the application of linear connectivity measures to explore the functional interactions between brain regions. Silberstein *et al.*[30] observed that EEG coherence in the beta band was correlated with the severity of parkinsonism (in the OFF state) in advanced stage PD patients considered for deep brain stimulation.

Nonlinear measures have also offered valuable information to study the changes that PD produces into the patients' brains.[32] Using correlation dimension ($D2$), Stam *et al.*[33,34] suggested that PD is characterized by a complexity decrease in comparison with control subjects. In addition, demented patients had lower largest Lyapunov exponent than PD group.[33] On the other hand, PD patients showed higher dimensionality than controls during performance of complex motor tasks, indicating more complex EEG time series.[25] Finally, Anninos *et al.*[2] studied the MEG activity in PD, concluding that external magnetic stimulation might help in the management of idiopathic PD. In sum, $D2$ is the nonlinear measure most widely used for characterizing EEG/MEG recordings in PD, in spite of its drawbacks from a signal-processing point of view. First, $D2$ requires the signals to be stationary and noise free, something that cannot be achieved for physiological data. Moreover, long time series are necessary to obtain meaningful results.[6] Therefore, there is a need for other nonlinear methods to enable a proper analysis of the electromagnetic brain activity in PD. For instance, synchronization likelihood, a nonlinear measure of functional connectivity, revealed significant differences in the MEG background activity between demented and non-demented PD patients.[4] Using the same measure, Stoffers *et al.*[36] concluded that increased resting-state cortico-cortical functional connectivity in the 8–10 Hz alpha range is a feature of PD from the earliest clinical stages. Finally, Pezard *et al.*[27] described higher localized entropy in the EEG of L-Dopa naive PD patients.

The present study is a new approach to explore the potential of nonlinear methods to characterize MEG rhythms in PD. Particularly, the so-called Lempel–Ziv complexity (LZC) was used.[22] LZC is a complexity measure for finite sequences related to the number of distinct substrings and the rate of their occurrence along the sequence.[22] LZC has been previously applied to MEG recordings to evaluate the complexity alterations produced by different pathological states, such as mild cognitive impairment,[8] Alzheimer's disease,[10,11,14] major depressive disorder,[23] and attention-deficit/hyperactivity disorder.[9] To our knowledge, this is the first time that this method is applied to study the brain activity in PD. The objective of the present study was to analyze the MEG background activity in PD patients to detect the presence of abnormal brain dynamics associated with this disorder. Based on the above-mentioned EEG studies,[33,34] we hypothesized that there would be a pattern of reduced LZC values in PD patients, in comparison with control subjects.

MATERIALS AND METHODS

MEG Recording

The signals were acquired with a 151-channel whole-head radial gradiometer MEG system (CTF Systems Inc., Port Coquitlam, BC, Canada) placed in a magnetically shielded room. The subjects were seated in a chair, in a relaxed state and with their eyes closed. They were asked to stay awake and to avoid making movements. For each subject, MEG registration was performed with a 312.5 Hz sampling frequency, using a hardware band-pass filter of 0.25–125 Hz. For each subject, 12 artifact-free epochs of 4 s (1250 data points) were selected by an experienced technician who was blind to the patients' diagnosis. Subsequently, these epochs were filtered using a Finite Impulse Response (FIR) band-pass filter with a Hamming window and cut-off frequencies at 0.5 and 45 Hz.

Subjects

For the present study, we analyzed MEG signals obtained in 18 recently diagnosed PD patients (12 men and 6 women) with a mean age of 59.67 ± 7.99 years (mean ± SD), never treated with anti-Parkinson medication and with a subjective disease duration of less than 2 years. They were recruited from the outpatient clinic for movement disorders at the VU University Medical Center (Amsterdam, the Netherlands). The control group consisted of 20 age-matched control subjects without past or present neurological disorders (11 men and 9 women; mean age = 59.40 ± 7.46). This group was composed of spouses of the patients as well as other healthy volunteers. The difference in the mean age of both populations was not statistically significant (p-value = 0.91). Cognitive status was screened in both groups using six tasks from the Cambridge Neuropsychological Test Automated Battery (CANTAB Eclipse 2.0, Cambridge Cognition, Cambridge, UK) and two tasks from the Vienna Test System version 6.0 (Dr. G. Shuhfried GmbH, Mödling, Austria). Before the MEG recording, all subjects gave written informed consent for the participation in this research study. The medical ethical committee of the VU University Medical Center approved the study protocol.

Lempel–Ziv Complexity

LZC is a measure for sequences of finite length suggested by Lempel and Ziv[22] in 1976. Later, Kaspar and Schuster[19] presented a computer program that determined the *LZC* using only two simple operations: to copy and to insert. This program is an appropriate measure of complexity in Kolmogorov sense as well as in a statistical sense.[39] *LZC* assigns higher values to more complex data. Previous studies have shown that this measure mainly depends on the bandwidth of the signal spectrum, although a slight dependence on the sequence probability density function was also found.[1,7] In addition, *LZC* could be interpreted as a harmonic variability metric.[1] This measure has already been applied in many different areas, including the analysis of biomedical signals, such as EEG recordings,[38] MEG signals,[10] or DNA sequences.[12]

LZC analysis is based on a coarse-graining of the measurements, and so the MEG time series must be transformed into a finite symbol sequence before estimating its complexity. In this study, we have used two different sequence conversion methods:

- 0–1 sequence conversion. The median value is estimated as a threshold T_d, as partitioning about this value is robust to outliers.[28] By comparison with the threshold, the original time series $X = x(1), x(2),\ldots,x(N)$ is converted into a 0–1 sequence $P = s(1), s(2),\ldots,s(N)$, where $s(i) = 0$ if $x(i) < T_d$ and $s(i) = 1$ if $x(i) \geq T_d$.[38]
- 0–1–2 sequence conversion. For each of the MEG epochs, the median x_m, maximum x_{max}, and minimum x_{min} are calculated. Two thresholds are obtained: $T_{d1} = x_m - |x_{min}|/16$ and $T_{d2} = x_m + |x_{max}|/16$. Then, the original time series X is converted into a 0–1–2 sequence $P = s(1), s(2),\ldots,s(N)$, where $s(i) = 0$ if $x(i) \leq T_{d1}$, $s(i) = 1$ if $T_{d1} < x(i) < T_{d2}$ and $s(i) = 2$ if $x(i) \geq T_{d2}$.[38]

Afterward, the new string P is scanned from left to right, and a complexity counter $c(N)$ is increased by one unit every time a new subsequence of consecutive characters is encountered in the scanning process. The detailed algorithm for the measure of the *LZC* is the following[38]:

- Let S and Q denote two sub-sequences of the original sequence P, and SQ be the concatenation of S and Q, while $SQ\pi$ is a string derived from SQ after its last character is deleted (π means the operation to delete the last character).
- Let $v(SQ\pi)$ denote the vocabulary of all different substrings of $SQ\pi$.
- At the beginning, the complexity counter $c(N) = 1$, $S = s(1)$, $Q = s(2)$, $SQ = s(1), s(2)$, and $SQ\pi = s(1)$.
- In general, suppose that $S = s(1), s(2),\ldots,s(r)$, $Q = s(r + 1)$ and, therefore, $SQ\pi = s(1), s(2),\ldots,s(r)$. If $Q \in v(SQ\pi)$, then Q is a subsequence of $SQ\pi$, not a new sequence.
- If S does not change and renew Q to be $s(r + 1)$, $s(r + 2)$, then judge if Q belongs to $v(SQ\pi)$ or not.
- The previous two steps are repeated until Q does not belong to $v(SQ\pi)$. Now $Q = s(r + 1), s(r + 2),\ldots,s(r + i)$ is not a subsequence of $SQ\pi = s(1), s(2),\ldots,s(r + i - 1)$, and so increase the counter by one.
- Thereafter, S and Q are combined and renewed to be $s(1), s(2),\ldots,s(r + i)$, and $s(r + i + 1)$, respectively.
- Repeat the previous steps until Q is the last character. At this time, the number of different substrings is $c(N)$, the measure of complexity.

In order to obtain a complexity measure which is independent of the sequence length, $c(N)$ should be normalized. The upper limit of $c(n)$ is given by $b(n) = N/\log_\alpha(N)$, and $c(N)$ can be normalized via $b(N)$: $C(N) = c(N)/b(N)$.[22] The normalized *LZC*,

$C(N)$, reflects the emerging rate of new patterns along with the sequence.[38] To ensure that defect-related features will be included for the complexity calculation, a minimum data length needs to be considered.[37] Therefore, the effect of the data length on *LZC* was analyzed for the MEG epochs. These analyses showed that the complexity values decline quickly at the beginning and become stable from 1000 data points. For this reason, $C(n)$ can be viewed as independent of number of samples for epoch lengths higher than 1000 data points. As an example, Fig. 1 illustrates one curve of the complexity values versus the data length for a MEG recording. Thus, an epoch length of 1250 (4 s of recording) was used in our study for the complexity measure.

Statistical Analysis

Initially, a descriptive analysis was performed to explore the distribution for the *LZC* values. Mann–Whitney *U*-tests were used to evaluate the differences between PD patients and controls. In order to address the problem of multiple comparisons, a Bonferroni correction was applied to *p*-values. Bonferroni-adjusted *p*-values are just the normal *p*-values multiplied by the number of outcomes being tested.

In addition to these statistical analyses, notched boxplots were used for visualizing the distributions of the *LZC* values averaged over the major cortical areas (frontal, central, temporal, parietal, and occipital) on the left and right sides of the brain. A boxplot is a graphical representation that provides a visual summary of several characteristics of a data distribution. Moreover, receiver operating characteristic (ROC) curves were used to assess the ability of *LZC* to discriminate PD patients from control subjects in the 10 aforementioned brain regions. A ROC curve summarizes the performance of a two-class classifier across the range of possible thresholds. It is a graphical representation of the trade-offs between sensitivity and specificity. Sensitivity is the true positive rate whereas specificity is equal to the true negative rate. Accuracy is the percentage of subjects (PD patients and controls) correctly recognized. A leave-one-out cross-validation procedure was used to calculate sensitivity, specificity, and accuracy values. In the leave-one-out method, the data from one subject are excluded from the training set one at a time and then classified on the basis of the threshold calculated with the data from the remaining subjects. The leave-one-out cross-validation procedure provides a nearly unbiased estimate of the true error rate of the classification procedure.[31]

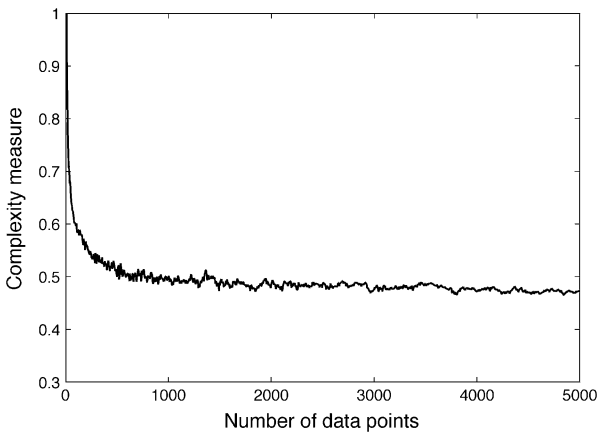

FIGURE 1. Effect of the epoch length on the *C*(*n*) value.

Finally, a forward stepwise linear discriminant analysis (LDA) with a leave-one-out cross-validation scheme was performed to investigate group classification combining *LZC* results across the 10 brain regions. This forward stepwise LDA starts with a model that does not include any variable. Then, a forward selection procedure is applied to automatically select the first independent variable that will be introduced into the model. This variable is characterized by its ability to separate the categories as much as possible. Then, the stepwise LDA chooses the variable that provides a greater discriminatory ability than others when used in conjunction with the previous one. This procedure is repeated until either the measure is (locally) maximized or the improvement due to the addition of other independent variable falls below some critical value. Results were shown in terms of sensitivity (i.e., proportion of PD patients correctly classified), specificity (i.e., percentage of healthy subjects properly identified), and accuracy (i.e., total fraction of subjects well classified). This statistical analysis was performed using SPSS software (version 15.0; SPSS Inc, Chicago, IL).

RESULTS

Channel-By-Channel Analysis

In a first stage, complexity analyses were carried out separately for each MEG channel. We have used *LZC* algorithm to quantify the complexity in MEG time series of 1250 samples. Lempel–Ziv algorithm was applied to each epoch. Then, the 12 epochs corresponding to each channel were averaged, obtaining a complexity value per channel and subject. Figures 2 and 3 summarize the average *LZC* values estimated for PD patients and control subjects at all MEG channels for 0–1 and 0–1–2 sequence conversions, respectively. PD patients displayed lower *LZC* values than control subjects for all the MEG channels both with the binary as well as the three-symbol sequence conversion. With the binary conversion, mean values obtained were

0.4809 ± 0.0269 for controls and 0.4326 ± 0.0299 (mean $\pm$ SD) for PD patients. Using three-symbol sequence conversion, we obtained mean values of 0.4572 ± 0.0228 for the control group, and 0.4162 ± 0.0245 for the PD group. These results suggest that the complexity, in the sense of a number of new subsequences in the data, is lower in PD patients' MEGs than in control subjects. Moreover, differences were statistically significant for several channels placed at parietal, occipital, and temporal regions (Bonferroni-adjusted p-values <0.05).

Regional Analysis

In a second stage, we grouped the MEG channels into 10 cortical regions (frontal, central, temporal, parietal, and occipital areas at the right and left sides of the brain) to explore the differences between PD patients and controls. Graphical summaries of the distributions are depicted in Figs. 4 and 5, which show the corresponding boxplots at each brain region for sequence conversions of two and three symbols. From visual inspection of the plot, it becomes evident that differences in regional *LZC* values between PD patients and controls subjects were statistically significant, as boxplot notches do not overlap. Numerical testing confirmed PD patients having lower *LZC* values than controls for all brain areas examined for both sequence conversions. Bonferroni-adjusted p-values are displayed in corresponding figures.

ROC curves with a leave-one-out cross-validation procedure were used for evaluating the ability of *LZC* to distinguish PD patients from the control subjects in the aforementioned brain regions. The area under the ROC curve (AUC) indicates the probability that a randomly selected PD patient has a *LZC* value lower than a randomly chosen control subject. Sensitivity, specificity, accuracy, and AUC values obtained with both sequence conversions at each region are displayed in Tables 1 and 2.

Stepwise LDA

A forward, stepwise LDA with a leave-one-out cross-validation procedure was used for investigating the best combination of *LZC* results to classify PD patients and healthy controls. The first variable to enter the model was *LZC* with three-symbol conversion at the right parietal brain region. In the next step, *LZC* with 0–1–2 sequence conversion at the right temporal area was added to the model used by the stepwise LDA to classify the subjects. The remaining *LZC* results were left out of the model, since they were linearly related to the variables that had already been included into the model and provided no additional information. This LDA model achieved an accuracy of 84.21% (77.78% sensitivity; 90.0% specificity).

DISCUSSION AND CONCLUSIONS

In this study, we analyzed the MEG resting-state activity of 18 early-stage, drug-naive PD patients and 20 controls by means of *LZC*. It was revealed that early-stage PD patients have lower complexity values than controls for all MEG channels. Moreover, significant statistical group differences were found for the 10 major cortical areas (p-values <0.05, Mann–Whitney U-test with Bonferroni correction). Our findings support the notion that brains affected by PD show less complex activity.

Previous studies have documented that PD involves an overall loss of complexity in the electromagnetic background activity.[33,34] In the first study mentioned, $D2$ values in PD patients' EEGs were lower than in controls, but higher than in demented patients.[34]

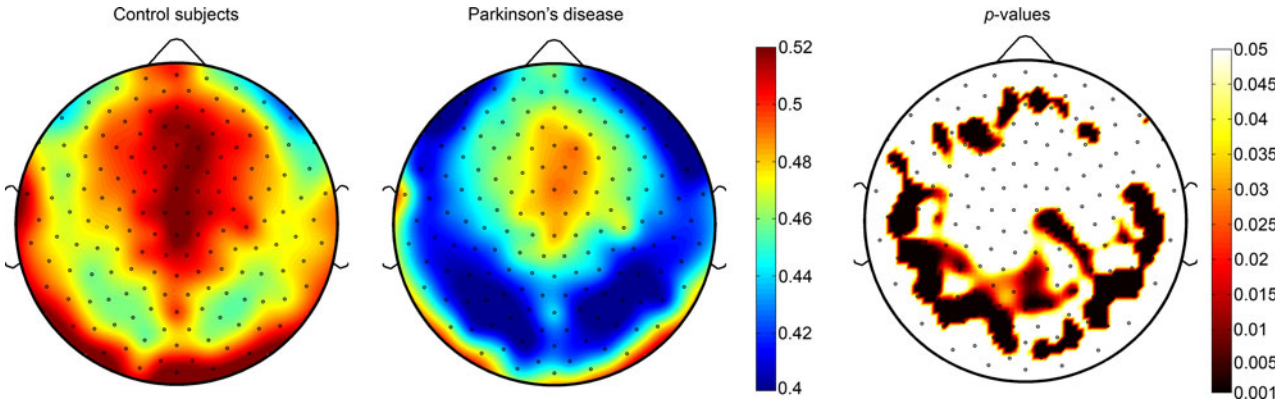

FIGURE 2. Sensor layouts showing the distribution of the *LZC* values (0–1 sequence conversion) at both groups and the corresponding Bonferroni-adjusted *p*-values.

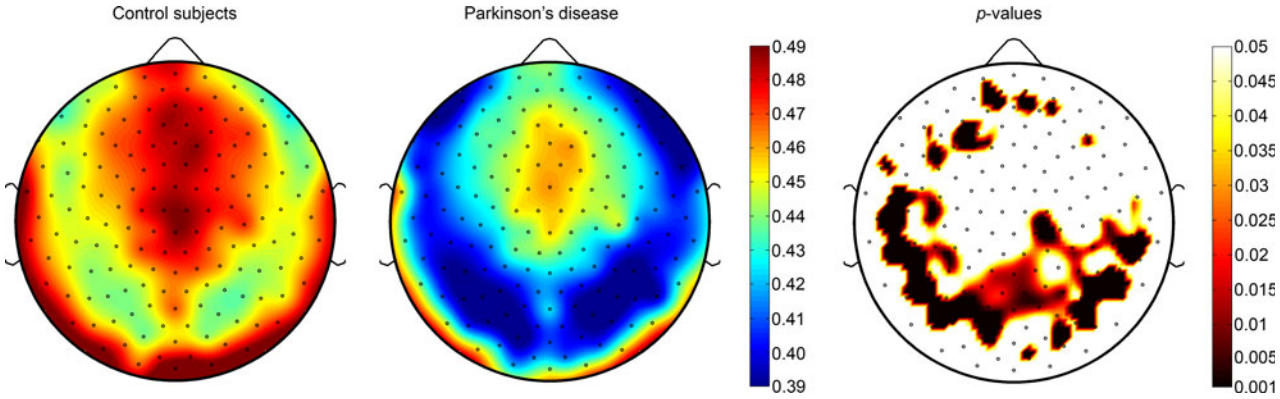

FIGURE 3. Sensor layouts showing the distribution of the *LZC* values (0–1–2 sequence conversion) at both groups and the corresponding Bonferroni-adjusted *p*-values.

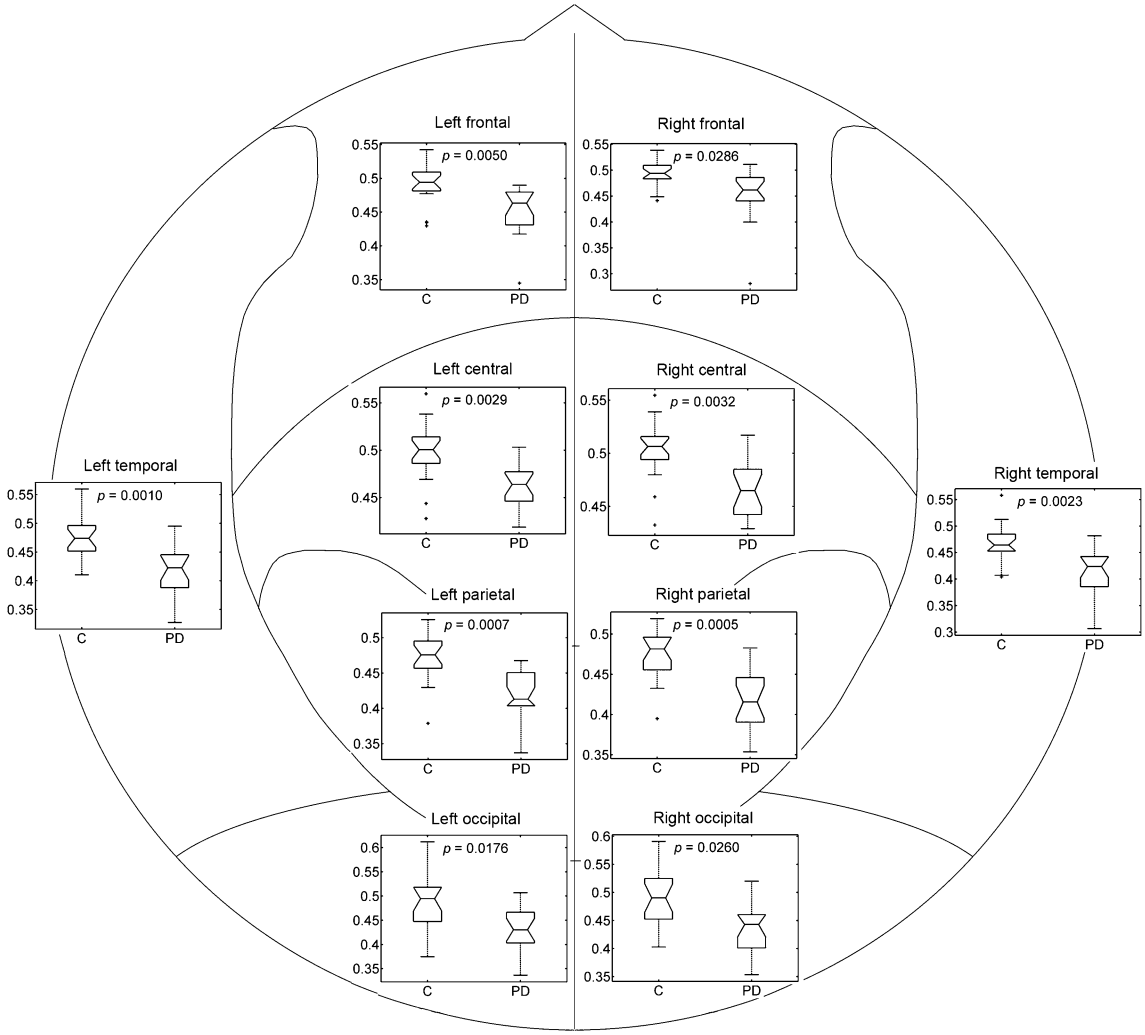

FIGURE 4. Notched boxplots displaying the distribution of *LZC* values (0–1 sequence conversion) for each brain area.

The second one explored nonlinearity of EEG signals from the same three subjects groups.[33] Demented patients had significantly lower $D2$ and lower largest Lyapunov exponent compared to controls, whereas largest Lyapunov was higher in PD patients than in demented ones.[33] These studies are in agreement with our results, supporting the notion that PD is characterized by a EEG/MEG complexity decrease.

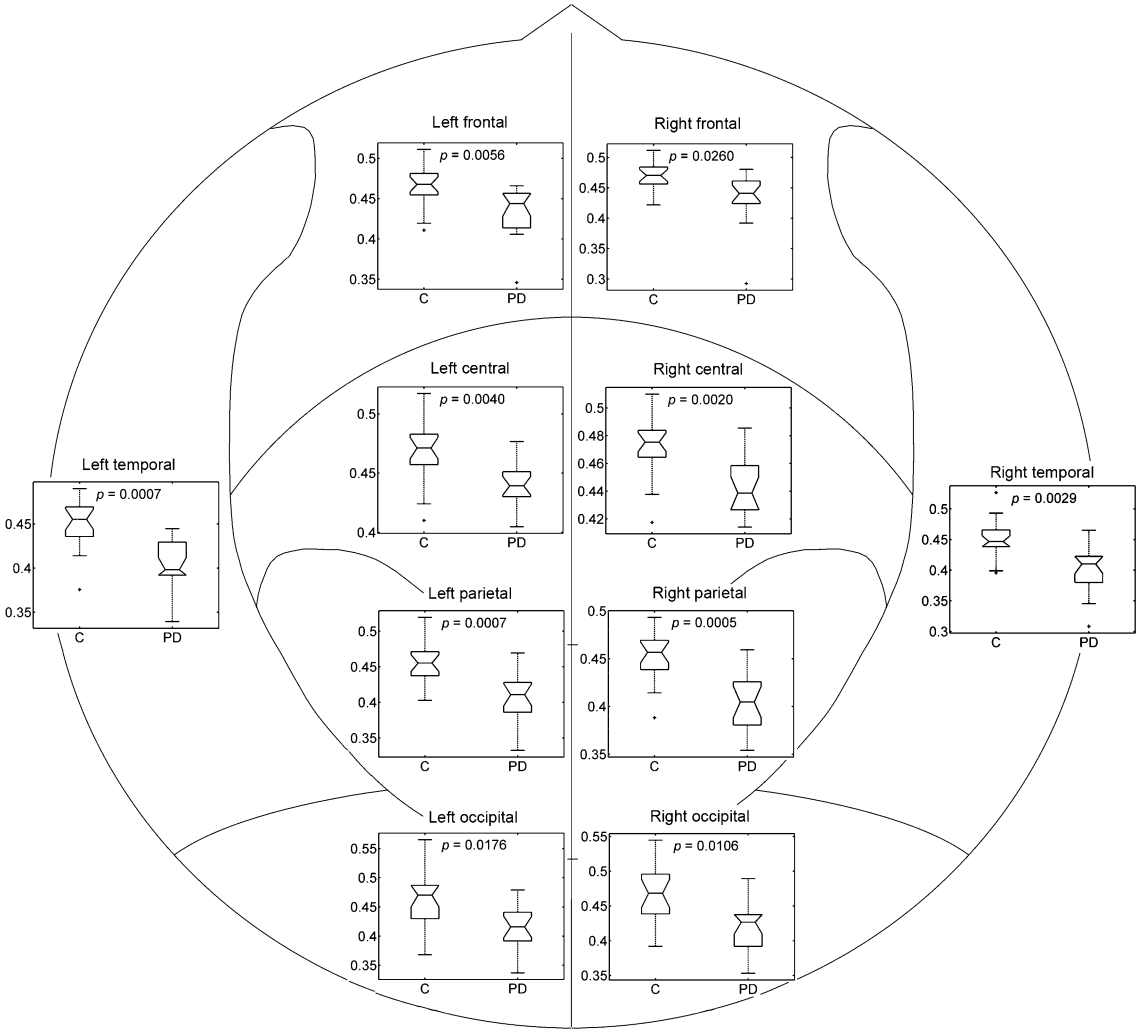

FIGURE 5. Notched boxplots displaying the distribution of *LZC* values (0–1–2 sequence conversion) for each brain area.

TABLE 1. Sensitivity, specificity, accuracy, and AUC values obtained with *LZC* (0–1 sequence conversion) for each region.

Cortical area	Sensitivity (%)	Specificity (%)	Accuracy (%)	AUC
Left central	83.33	75.00	78.95	0.8444
Left frontal	72.22	55.00	63.16	0.8306
Left occipital	61.11	65.00	63.16	0.7972
Left parietal	77.78	75.00	76.32	0.8778
Left temporal	77.78	80.00	78.95	0.8694
Right central	77.78	75.00	76.32	0.8417
Right frontal	72.22	70.00	71.05	0.7833
Right occipital	77.78	65.00	71.05	0.7861
Right parietal	66.67	80.00	73.68	0.8861
Right temporal	72.22	80.00	76.32	0.8500

More recent studies have applied other measures to study PD-related changes in the MEG background activity. Stoffers *et al.*[35] showed extensive changes in oscillatory brain activity in PD patients relative to controls, which included widespread increases in theta and alpha power as well as overall decreases in beta and gamma power. In a subsequent study assessing functional connectivity, a global increase in alpha1 synchronization was found in untreated PD patients compared with control subjects.[36] In line with our

TABLE 2. Sensitivity, specificity, accuracy, and AUC values obtained with *LZC* (0–1–2 sequence conversion) for each region.

Cortical area	Sensitivity (%)	Specificity (%)	Accuracy (%)	AUC
Left central	77.78	75.00	76.32	0.8361
Left frontal	72.22	60.00	65.79	0.8279
Left occipital	61.11	65.00	63.16	0.7972
Left parietal	77.78	70.00	73.68	0.8778
Left temporal	77.78	70.00	73.68	0.8778
Right central	72.22	75.00	73.68	0.8528
Right frontal	66.67	65.00	65.79	0.7861
Right occipital	72.22	70.00	71.05	0.8111
Right parietal	77.78	80.00	78.95	0.8833
Right temporal	77.78	85.00	81.58	0.8444

current study, both studies demonstrate that PD-related changes are quite diffuse rather than limited to specific brain regions.[35,36]

The methodology applied in this study is a novel approach to analyze the changes in brain activity caused by PD. *LZC* offers some distinct advantages over classical complexity measures. First of all, *LZC* is an easy and fast method to estimate the time series complexity, as only two simple mathematical operations are needed for its calculation: sequence comparison and number accumulation. Moreover, the median value used as threshold is robust to outliers.[28] In addition, it can be applied to any time series, irrespective of whether their origin is stochastic or deterministic.[38] Therefore, only those differences between activity patterns that are found to discriminate between PD and control conditions are considered. Nevertheless, the limitations of this measure should also be taken into consideration. Most importantly, *LZC* is based on a coarse-grained measure of the recordings.[38] The MEG data were transformed into a pattern of a few symbols, only two (0–1) and three (0–1–2) in our study. Thus, it is possible that some information from the signal that might have been lost with these symbol conversions could have been retained using more symbols.

ROC curves were used for assessing the potential of using *LZC* values at different brain regions to classify PD patients and age-matched control subjects. Our study shows that *LZC* may be a suitable method to differentiate the MEG activity from PD patients and control subjects. The highest accuracy (81.57%) was obtained at the right temporal area using *LZC* with a sequence conversion of three symbols. In addition, we wanted to assess whether *LZC* values from different brain areas could provide complementary information. We applied a forward stepwise LDA with a leave-one-out cross-validation procedure, which automatically selected *LZC* results (0–1–2 conversion) from right parietal and temporal areas. With this LDA model, an accuracy of 84.21% (77.78% sensitivity, 90.0% specificity) was reached. The accuracy increase is quite low (only 2.64%) compared to values obtained with ROC curves at individual brain regions. This is because *LZC* results from different brain areas are highly correlated. For this reason, LDA modeling does not provide a significant advantage over ROC curves. Although it would be great to compare these values with others obtained in previous studies, this research study is, to our knowledge, the first that uses brain signals for classification purposes between controls and PD patients. Nevertheless, the obtained accuracy suggests that nonlinear analyses of the brain activity might be a useful tool to aid physicians in the diagnosis of PD. On the other hand, the decreased complexity is not specific of PD, and it also appears in other neurodegenerative diseases, such as vascular dementia,[18] mild cognitive impairment,[8] and Alzheimer's disease.[10,11,14] Thus, the findings of this study should be regarded as preliminary and require replication in a larger patient population, including patients with other diagnoses, before any conclusion can be made about the clinical diagnostic value of this measure.

Some potential confounding factors have to be considered. First, a loss of physiological complexity often accompanies aging.[21] However, in the present study, the groups were matched for age, and so the significantly reduced complexity is likely to be a disease-related phenomenon. Second, the current study was carried out during a resting-state eyes-closed condition. In a previous study, Cassidy and Brown[5] suggested that a visuomotor tracking task might increase the discrimination between controls and PD patients. Another study revealed that a central reduction of EEG complexity during motor tasks, which is normally present in healthy individuals, is absent in PD.[25] In any case, our results suggest that MEG resting-state background activity could be useful in differentiating PD patients from elderly controls.

In summary, this research work presents the *LZC* as a novel method to study MEG background activity in PD patients. It was demonstrated that PD patients

show widespread decreases in *LZC* compared with control subjects. Moreover, an accuracy of 84.21% was achieved in the classification between the two groups using a LDA model with a leave-one-out cross-validation procedure. Our findings show the usefulness of *LZC* to detect changes in the dynamic behavior of brains injured by PD. The complexity changes in PD could be related to the presence of early, subtle cognitive deficits.

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