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RESEARCH ARTICLE

Power spectra for screening parkinsonian patients for mild cognitive impairment

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Abstract

Objective: Mild cognitive impairment in Parkinson's disease (PD-MCI) is diagnosed based on the results of a standardized set of cognitive tests. We investigate whether quantitative EEG (qEEG) measures could identify differences between cognitively normal PD (PD-CogNL) and PD-MCI patients. **Methods**: High-resolution EEG was recorded in 53 patients with Parkinson's disease (PD). Relative power in five frequency bands was calculated globally and for ten regions. Peak and median frequencies were determined. qEEG results were compared between groups. Effect sizes of all variables were calculated. The best separating variable was used to demonstrate subject-wise classification. **Results**: Lower mean values were observed in global alpha1 power and alpha1 power in five brain regions (left hemisphere: frontal, central, temporal, occipital; right hemisphere: temporal, $P < 0.05$), differentiating between PD-CogNL and PD-MCI groups. Effect sizes were high, ranging from 0.79 to 0.87. Median frequency was 8.56 $\pm$ 0.74 Hz and was not different between the groups. The variable with the best subject-wise classification was the power in the alpha1 band in the right temporal region. The area under the corresponding receiver operating characteristic (ROC) curve was 0.72. The optimal classification threshold yielded a sensitivity of 65.9% and a specificity of 66.7%. The positive and negative predictive values were 87.1% and 36.4%, respectively. **Interpretation**: Reduction in alpha1 band power in nondemented PD patients, particularly in the right temporal region, is highly indicative of MCI in PD patients. The results might be used to assist in time-efficient diagnosis of PD-MCI and avoid the drawbacks of test–retest effect in repeated neuropsychological testing.

Introduction

Cognitive and neuropsychiatric decline in patients with Parkinson's disease (PD) are key determinants of the prognosis for survival and independence.[1,2] The assessment of the cognitive status of patients is done by carrying out a battery of neuropsychological tests. Mild cognitive impairment in PD patients (PD-MCI) differs from dementia by the fact that it does not interfere with daily activities. It is diagnosed by grouping the various tests into different cognitive domains (alertness, executive functions, visuo-spatial abilities, episodic, and working memory) and applying selection criteria on the outcome.[3] This is a lengthy process that is not widely available. It incurs high costs and relatively long waiting times that hinder repetition and adequate follow-up. Moreover, test–retest effects could bias the assessment of cognitive functions in repetitive clinical examinations.

Quantitative electroencephalography (qEEG) might present itself as a potential alternative. Certain qEEG parameters were shown to be associated with dementia in patients with PD[4–9] or with Alzheimer's disease.[9,10] For instance, Caviness et al.[8] identified an association between slowing of EEG rhythms and the cognitive state of PD patients, in particular in the theta and alpha frequency bands. Babiloni et al.[6] further discussed localized associations of brain

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signals with the cognitive states in both Parkinson's disease and Alzheimer's disease patients. Moreover, most studies[4,6,8,9] agreed that alterations in signal power in the theta and lower alpha frequency bands (4–8 Hz and 8–10 Hz, respectively) are potential biomarkers of the cognitive state.

The aforementioned studies used either low-resolution standard 10-20 EEG systems,[4–6,8–10] or magnetoencephalography[5,7] for the recording of the electrical brain activity. High-resolution EEG systems are becoming widely available and have lower running costs than the standard neuropsychological assessment. They offer superior spatial resolution and allow for a better localization of the electrical activity in both signal and source spaces. Unlike cognitive tests, qEEG is immune to the test–retest effect and has high retest reliability.[11–15]

In this study, we use high-resolution EEG recordings to determine whether PD-MCI can be diagnosed with sufficient confidence using signal frequency and power content as biomarkers. We aim at identifying associations of the cognitive state with reductions in the median background frequency and in focally pronounced changes of the EEG rhythms.

Materials and Methods

Subjects

From May 2011 to January 2013, a total of 74 patients were recruited from the outpatient clinic for movement disorders of the Basel University Hospital or through advertisements in the magazine of the Swiss Parkinson's Disease Association. To be included in the study, patients had to fulfil the UK Parkinson's Disease Society Brain Bank criteria[16] and needed to have sufficient knowledge of the German language. Patients with dementia or other severe neurological conditions were excluded from the study. Anxiety, mild head injury, and drowsiness were used as additional exclusion criteria. Consequently, the final sample was reduced to 53 patients. The sample size is capable of detecting an effect size as low as 0.55 with a statistical power of 80% at a 5% significance level.

Mean age of the patients was 67.2 ($\pm$8.4). The disease duration since the first symptoms was 8.6 ($\pm$4) years and patients had 14.5 ($\pm$3) years of education. Nineteen of the participants were female and 34 were male. The levodopa equivalent dose (LED) was 679 ($\pm$454) and the UPDRS III 15 ($\pm$11.3). Twelve patients were cognitively normal (PD-CogNL), whereas 41 were positively diagnosed with PD-MCI.

The study was approved by the local ethics committee (Ethikkommission beider Basel, ref. no.: 135/11). All patients gave their written informed consent.

Neuropsychological assessment of PD-MCI

PD-MCI was evaluated along the Movement Disorder Society Task Force guidelines for the diagnosis of PD-MCI.[3] In Litvan et al.[3], a separation in the diagnostic guidelines is made in which Level I is an abbreviated assessment procedure capable of identifying the possibility of PD-MCI. In contrast, Level II is a comprehensive assessment that covers more tests and cognitive domains and offers higher diagnostic certainty. In our assessment, we applied the Level II diagnostic criteria.

Test results were compared to normative data from the Memory Clinic, University Center for Medicine of Aging Basel. The normative data are based on a sample of 604 healthy subjects and are adjusted for covariates such as age, sex, and education.[17] PD-MCI in each domain was rated as positive if a patient scored below 1.28 standard deviations (representing the 10th percentile) in at least one third of the cognitive tests in that domain when compared to the normative data. A similar criterion was used elsewhere[18] in order to correct for the number of tests in each domain. A patient was rated as having global PD-MCI if there was a deficit in at least one domain. Moreover, reduced cognitive abilities in PD-MCI should not be interfering with the patient's day-to-day activities.

EEG recording

A high-resolution 256-channel DC-EEG system (Netstation 300; Electrical Geodesics, Inc., Eugene, OR) was used for recording EEG on all patients. Sampling rate was set to 1 kHz and a first high-pass filter with a cutoff frequency of 0.01 Hz was used to eliminate the direct current component. Impedance of all channels was kept below 40 kΩ. Subjects were seated comfortably in a reclining chair in a dimly lit, sound attenuated and electromagnetically shielded room. They were instructed to relax, but to stay awake while minimizing eye and body movements. A continuous EEG with closed eyes was recorded for a period of 12 min. During the data acquisition process, a subset of electrodes was monitored by a technician to check for vigilance and artifacts.

Processing pipeline

The EEG signals were treated by series of semi- and fully automatic processing steps.[14] The initial step in the processing pipeline was a visual inspection of the EEG recordings by an experienced neurologist. In this step, segments free of elevated levels of sleepiness, eye blink artifacts, and other large artifacts were marked for inclusion in subsequent processing steps. Several such segments were extracted for each subject and were required

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to fit the minimum length criterion of 35 sec. Shorter segments were stitched together using an inverse Hanning window. A high-order linear phase finite impulse response filter (Matlab®; The MathWorks, Inc., Natick, MA) was then applied to define the frequency range of interest and remove direct current and power line components from the signal (band pass: 0.5–70 Hz, notch: 50 Hz). Bad channels were automatically detected and excluded using the FASTER[19] and Fieldtrip[20] routines and the results were visually checked for plausibility. Further artifacts such as ECG and eye blinks were detected and removed by applying the independent component analysis implementation of EEGLAB[21] ("runica" with default settings) on the remaining channels followed by a visual examination of the independent activations. Bad activations were excluded and the original signal reconstructed from the cleaned activations. Channels with bad quality were replaced by spherical spline interpolations.[22] The resulting segments were subsequently stitched together in order to obtain a total cleaned recording time of at least 120 sec per subject.

The frequency spectrum was divided into five bands (delta: 1–4 Hz; theta: 4–8 Hz; alpha1: 8–10 Hz; alpha2: 10–13 Hz; beta: 13–30 Hz). Fourier transform-based frequency analysis (Welch's method,[23] Matlab®) was then applied in order to extract spectral information of the signals in each channel. Relative power was calculated as the ratio of the signal power within a frequency band to the total signal power (1–30 Hz). The results were reduced to ten predefined regions on the scalp corresponding to the anatomical brain regions – left and right frontal, central, parietal, temporal, and occipital (Fig. 1).

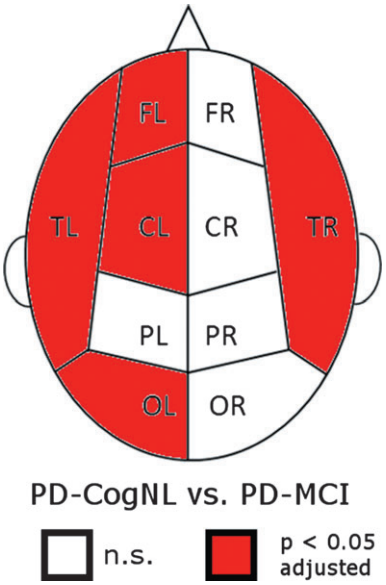

Figure 1. Head plot showing the ten regions corresponding to the anatomical regions of the brain. Highlighted in red are the regions where alpha1 power showed statistically significant differences between the PD-MCI and PD-CogNL after correction for multiple testing. PD, Parkinson's disease; MCI, mild cognitive impairment; CogNL, cognitively normal.

Extracted measures

Following the frequency analysis, a total of 57 different measures could be derived. These are the median and peak frequencies recorded on the occipital electrodes, global power, and power in every region in all five frequency bands. These measures are carried forward to the next steps of our analysis.

Statistical analysis

Potential confounding by factors, such as age, gender, and education of the patients was accounted for by calculating linear regression models. Various variable combinations and interactions were tested and a stepwise backward elimination process was applied.

For every qEEG measure, group differences between the PD-MCI and the PD-CogNL patients were assessed. Permutation tests on *t*-statistics with 10,000 permutations were used to correct for multiple testing within the frequency bands. The effect size associated with PD-MCI classification was calculated for every variable (ratio of the difference between means to the pooled standard deviation). The confidence intervals around the differences between the means of the two groups were calculated using standard errors multiplied by *t*-quantiles for 97.5% cumulative probability and degrees of freedom generated using the Welch–Satterthwaite equation. This approach was chosen due to the relatively small sample size and potentially unequal variances between the groups.

Toward subject-wise classification

Up to this point, attempts to identify group-wise differences were carried out. However, the ultimate goal is to set a basis for automatic subject-wise classification methods. To this purpose, the receiver operating characteristic (ROC) curve for the strongest marker identified through the exploratory statistics described above was generated. The strongest marker was chosen so that it has a high effect size, a low *P*-value, a tight confidence interval around the difference of means, and the highest area under the ROC curve (AUC). The ROC curve was smoothed by fitting a cubic spline. Youden's index[24] (J = sensitivity + specificity − 1) was used to calculate the optimal point on the ROC curve and subsequently the classification threshold. Bootstrapping with 10,000

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samples was performed in order to calculate the 95% confidence interval around the ROC curve as well as around the classification threshold. Additionally, the positive and negative predictive values (PPV/NPV) were calculated for the classification threshold.

Results

The linear regression models revealed that the effect of the potential confounding factors was negligible. Age, gender, and education were not associated with PD-MCI ($P > 0.05$).

Global power and power in five out of ten regions showed differences in the alpha1 frequency band between PD-MCI patients and cognitively normal PD patients. The effect size of the differences in alpha1 power between the two groups ranged from 0.79 to 0.87. The overall background median frequency was 8.56 ± 0.74 (mean $\pm$ SD) and was not different between the two groups. The detailed results are listed in (Table 1). In (Fig. 1), the regions that showed group differences are highlighted in red. Figure 2 shows a side-by-side comparison of the variable that presented statistically significant differences.

The variable that matched the criteria of the strongest marker was the alpha1 power in the right temporal region. The AUC under its ROC curve was 0.72. The classification threshold was calculated to be 0.178 (95% CI: 0.172–0.187). The ROC curve and its corresponding boxplot showing the classification threshold and the confidence interval around it are presented in Figure 3. Using the calculated optimal classification threshold on one variable, the test was able to achieve a sensitivity of 65.9% (CI: 63.4–70.7) and a specificity of 66.7% (CI: 58.3–66.7). The PPV and NPV of the binary classification using the same threshold were 87.1% and 36.4%, respectively.

Table 1. Summary statistics of main variables.

	Variable	*P*-value	Effect size	95% confidence interval (around difference of means)
Alpha1 – 8–10 Hz	Frontal left	0.033	0.82	0.01–0.133
	Central left	0.044	0.79	0.006–0.109
	Temporal left	0.046	0.79	0.006–0.106
	Temporal right	0.025	0.86	0.012–0.122
	Occipital left	0.022	0.87	0.016–0.161
	Global power	0.034	0.82	0.01–0.131
	Median Frequency	n.s.	0.44	−0.78 to 0.238

Discussion

Patients with PD-MCI display a decrease in the alpha1 power (8–10 Hz) when compared to the PD-CogNL group, particularly in the right temporal region. The median frequency does not show significant differences between the groups. This finding is in line with the literature where changes in alpha1 power have been shown to be associated with the cognitive state.[6,8,10] One study[8] indicated an association between the increase in signal power in the theta range and PD-MCI. In our analysis, theta power shows a nonsignificant association trend with PD-MCI ($P = 0.078$), but does not necessarily contradict the findings of Caviness et al.[8] The lack of association might be due to the limited sample size and to differences in diagnosing and assessing MCI.

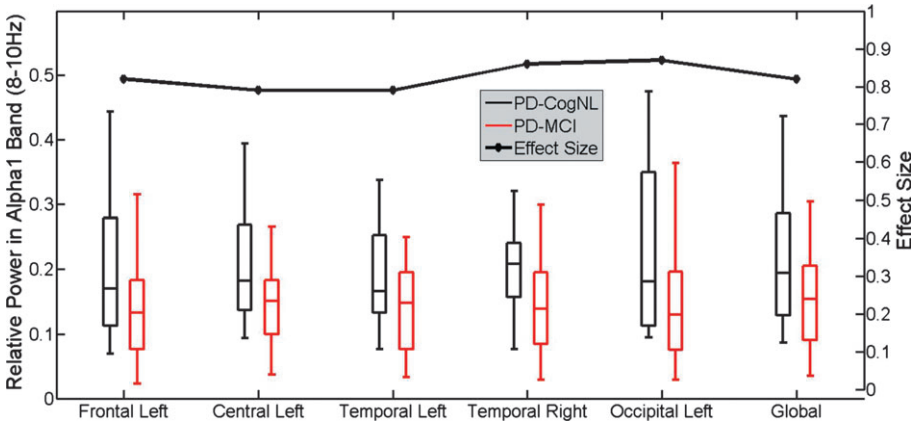

Figure 2. Boxplots of the power variables in the alpha1 range (8–10 Hz) that presented statistically significant differences between the two groups. The effect size for every variable is also shown.

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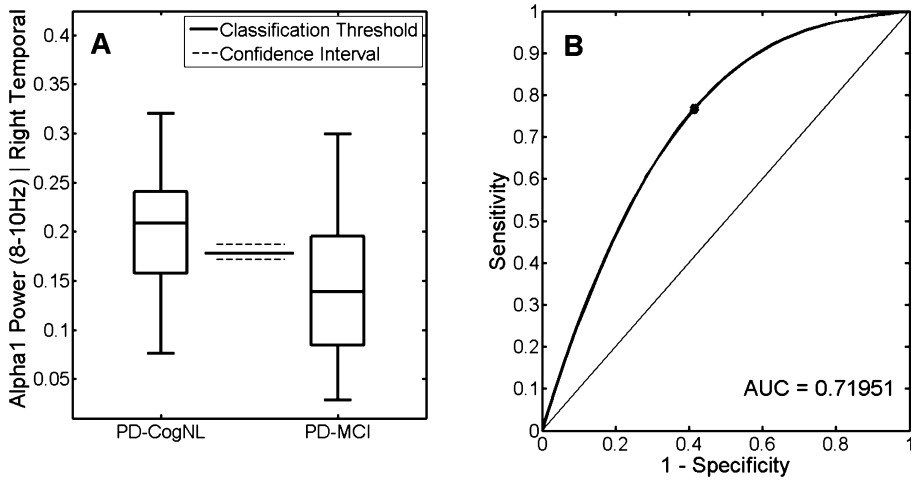

Figure 3. (A) Boxplot comparing the PD-MCI and PD-CogNL patient groups. (B) ROC curve showing the predictive performance of the subject-wise classification using the best separating variable, i.e., alpha1 power in the right temporal region. The optimal point on the ROC curve and its corresponding classification threshold are derived using Youden's index. PD, Parkinson's disease; MCI, mild cognitive impairment; CogNL, cognitively normal; ROC, receiver operating characteristic.

Alpha1 power extracted from EEG recordings may serve as a surrogate marker for cognitive mild impairment. Therefore, the shortcomings associated with repeated neuropsychological assessment, such as availability, cost, test–retest reliability, and learning effects might be circumvented.

In clinical routine, subject-wise classification using qEEG markers would be desirable. Although sensitivity and specificity are relatively modest, PPV and NPV help the clinician to decide whether an individual patient is affected by PD-MCI. Using the classification threshold that simultaneously optimizes specificity and sensitivity, a high PPV along with a low NPV was obtained. Therefore, and if corroborated in additional studies, these results imply that PD-MCI could be screened for with an acceptable level of certainty using the alpha1 power in the right temporal region. However, lack of a decrease in alpha1 power in the right temporal region is without diagnostic significance.

This study was based on a relatively limited sample size in which a large number of variables were examined. Nevertheless, the statistical analysis methods were chosen in way to address the known limitations and minimize the risk of spurious findings. More specifically, permutation tests and the Welch–Satterthwaite equation are particularly suitable for multiple testing scenarios, small sample sizes, and uneven group distributions.

Moreover, variations in the alpha power could be linked to factors other than MCI. For instance, drowsiness, anxiety, or mild head injury could be reflected by changes in the signal amplitude in the alpha range. Similarly, the patient's age, gender, level of education, and medication play a further confounding role. In our approach, we came around the problem of confounding factors by either excluding from the analysis patients with known status, or by numerically affirming the nonsignificant effect of certain factors using linear regression analysis.

The results, if corroborated by prospective confirmatory studies, can be used as a foundation for further development of automated diagnostic methods. Various variables could be combined and presented to computerized classification algorithms. Moreover, the potential predictive variables underlined in this work might serve as a screening tool for beginning cognitive decline in PD patients.

Acknowledgment

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Author Contribution

Dr. Bousleiman conceived and designed the study and was responsible for its execution. Wrote the first draft, developed the preprocessing pipeline, and performed

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statistical data analysis and interpretation. Contributed core ideas and was involved in critically revising the paper for important intellectual content. Dr. Zimmermann conceived and designed the study and supervised the neuropsychological evaluations. Contributed core ideas and was involved in critically revising the paper for important intellectual content. Dr. Ahmed carried out the visual inspection of EEG, the manual selection of clean segments, and the automatic preprocessing. Contributed core ideas and was involved in critically revising the paper for important intellectual content. Dr. Hardmeier developed the preprocessing pipeline and contributed core ideas and was involved in critically revising the paper for important intellectual content. Dr. Hatz performed the neurological assessments, developed the preprocessing pipeline, and managed the database infrastructure. Contributed core ideas and was involved in critically revising the paper for important intellectual content. Dr. Schindler gave statistical advice for the study design and data evaluation. Contributed core ideas and was involved in critically revising the paper for important intellectual content. Dr. Roth gave statistical advice for the study design and data evaluation. Contributed core ideas and was involved in critically revising the paper for important intellectual content. Dr. Gschwandtner conceived and designed the study, supervised the neuropsychological assessments, and carried out the visual inspection and manual selection of EEG. Contributed core ideas and was involved in critically revising the paper for important intellectual content. Dr. Fuhr conceived and designed the study and was responsible for its execution. Performed and supervised neurological assessments and was principal investigator and will act as guarantor for the paper. Contributed core ideas and was involved in critically revising the paper for important intellectual content.

Conflict of Interest

Dr. Schindler, Dr. Hatz, Dr. Bousleiman, Dr. Hardmeier, Dr. Zimmermann, Dr. Ahmed, Dr. Gschwandtner reports grants from Swiss National Science Foundation, Parkinson Schweiz, Gossweiler Foundation, Freiwillige Akademische Gesellschaft Basel. Dr. Fuhr reports grants from Swiss National Science Foundation, Parkinson Schweiz, Gossweiler Foundation, Freiwillige Akademische Gesellschaft Basel, Roche, GE Healthcare, UCB Pharma, Abbvie, Bortnar Foundation, Mach-Gaensslen Foundation. Dr. Roth reports grants from Swiss National Science Foundation, Parkinson Schweiz, Gossweiler Foundation, Freiwillige Akademische Gesellschaft Basel, Swiss National Science Foundation.

References

1. Goetz CG, Stebbins GT. Risk factors for nursing home placement in advanced Parkinson's disease. Neurology 1993;43:2227–2229.
2. Forsaa EB, Larsen JP, Wentzel-Larsen T, Alves G. What predicts mortality in Parkinson disease?: a prospective population-based long-term study. Neurology 2010;75:1270–1276.
3. Litvan I, Goldman JG, Tröster AI, Schmand BA, et al. Diagnostic criteria for mild cognitive impairment in Parkinson's disease: Movement Disorder Society Task Force guidelines. Mov Disord 2012;27:349–356.
4. Klassen BT, Hentz JG, Schill HA, Driver-Dunckley E, et al. Quantitative EEG as a predictive biomarker for Parkinson disease dementia. Neurology 2011;77:118–124.
5. Stoffers D, Bosboom JLW, Deijen JB, Wolters EC, et al. Slowing of oscillatory brain activity is a stable characteristic of Parkinson's disease without dementia. Brain 2007;130(Pt 7):1847–1860.
6. Babiloni C, De Pandis MF, Vecchio F, Buffo P, et al. Cortical sources of resting state electroencephalographic rhythms in Parkinson's disease related dementia and Alzheimer's disease. J Clin Neurophysiol 2011;122:2355–2364.
7. Olde Dubbelink KT, Stoffers D, Deijen JB, Twisk JW, et al. Cognitive decline in Parkinson's disease is associated with slowing of resting-state brain activity: a longitudinal study. Neurobiol Aging 2013;34:408–418.
8. Caviness JN, Hentz JG, Evidente VG, Driver-Dunckley E, et al. Both early and late cognitive dysfunction affects the electroencephalogram in Parkinson's disease. Parkinsonism Relat Disord 2007;13:348–354.
9. Fonseca L, Tedrus GM, Carvas PN, Machado EC. Comparison of quantitative EEG between patients with Alzheimer's disease and those with Parkinson's disease dementia. Clin Neurophysiol 2013;124:1970–1974.
10. Schmidt MT, Kanda PAM, Basile LFH, da Silva Lopes HF, et al. Index of alpha/theta ratio of the electroencephalogram: a new marker for Alzheimer's disease. Front Aging Neurosci 2013;5:60.
11. Näpflin M, Wildi M, Sarnthein J. Test–retest reliability of resting EEG spectra validates a statistical signature of persons. Clin Neurophysiol 2007;118:2519–2524.
12. Fingelkurts AA, Fingelkurts AA, Ermolaev VA, Kaplan AY. Stability, reliability and consistency of the compositions of brain oscillations. Int J Psychophysiol 2006;59:116–126.
13. Grandy TH, Werkle-Bergner M, Chicherio C, Schmiedek F, et al. Peak individual alpha frequency qualifies as a stable neurophysiological trait marker in healthy younger and older adults. Psychophysiology 2013;50:570–582.
14. Hatz F, Hardmeier M, Bousleiman H, Rüegg S, Schindler C, Fuhr P. Clin Neurophysiol. 2014; Jun 2. pii: S1388-2457(14)00289-2. doi: 10.1016/j.clinph.2014.05.014. [Epub ahead of print]

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15. Hardmeier M, Hatz F, Bousleiman H, Schindler C, Stam CJ, Fuhr P. Reproducibility of functional connectivity and graph measures based on the phase lag index (PLI) and weighted phase lag index (wPLI) derived from high resolution EEG. PLoS ONE 2014. In press.
16. Hughes AJ, Daniel SE, Kilford L, Lees AJ. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. J Neurol Neurosurg Psychiatry 1992;55:181–184.
17. Berres M, Zehnder A, Bläsi S, Monsch AU. Evaluation of diagnostic scores with adjustment for covariates. Stat Med 2008;27:1777–1790.
18. Aarsland D, Bronnick K, Williams-Gray C, Weintraub D, et al. Mild cognitive impairment in Parkinson disease: a multicenter pooled analysis. Neurology 2010;75:1062–1069.
19. Nolan H, Whelan R, Reilly RB. FASTER: Fully Automated Statistical Thresholding for EEG artifact Rejection. J Neurosci Methods 2010;192:152–162.
20. Oostenveld R, Fries P, Maris E, Schoffelen JM. FieldTrip: Open source software for advanced analysis of MEG, EEG, and invasive electrophysiological data. Comput Intell Neurosci 2011;2011:156869.
21. Delorme A, Makeig S. EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. J Neurosci Methods 2004;134:9–21.
22. Perrin F, Pernier J, Bertnard O, Giard MH, et al. Mapping of scalp potentials by surface spline interpolation. Electroencephalogr Clin Neurophysiol 1987;66:75–81.
23. Welch PD. The use of fast Fourier transform for the estimation of power spectra: a method based on bime averaging over short, modified periodograms. IEEE Trans Audio Electroacoust 1967;AU-15:70–73.
24. Youden WJ. Index for rating diagnostic tests. Cancer 1950;3:32–35.

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