Development of EEG metrics predictive of cognitive decline in Parkinson’s Disease
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Introduction

- Parkinson’s Disease (PD) is the second-most common degenerative disorder of the central nervous system. PD causes motor dysfunction and often some degree of impairment in cognitive function, particularly as age and disease severity progress. Those with PD are at a much higher risk for developing dementia, approximately four to six times that of the general population.

- Treatment involves taking a number of factors into consideration; the non-motor symptoms of the disease significantly impact quality of life, so a focus on treatment to improve cognitive function is often just as important as physical therapy.

- Mild Cognitive Impairment (MCI) has been linked to Alzheimer’s Disease. A similar disease state has been identified, known as PD Impaired (PDI), which is associated with PD dementia.

- In this study, we investigated the relatedness of MCI to PDI, as well as to other disease states, in order to explore potential biomarkers that could aid in predicting the likelihood of progression to dementia. We hypothesized that the brain would show region-specific as well as frequency-specific differences in activity among subjects.

Methods

- hdEEG was recorded in four groups of 36 total subjects (21 M) were analyzed: PD (Parkinson’s Disease, n = 10), PDI (Parkinson’s Disease Impaired, n = 8), MCI (Mild Cognitive Impairment, n = 7), and healthy control subjects (n = 11).

- Evaluations were performed by experienced neurologists (NYU Langone Medical Center) with expertise in neurodegenerative diseases. The Clinical Dementia Rating (CDR) was used to determine the presence or absence of dementia and, if present, to stage its severity. The CDR is derived from a semi-structured interview with the participant and a knowledgeable informant.

- hdEEG data were recorded using a 256-channel HydroCel Geodesic Sensor Net (HCGSN) for approximately eight minutes total, in four two-minute intervals, in eyes-closed resting state. This yielded four runs, or segments, of EEG data per subject.

- hdEEG data were processed with EEGLAB (version 12.0.2.4b), a program extension of MATLAB (version R2013a). Channels with corrupted signals and showing substantial noise were removed, and the data was filtered to remove physiological artifact.

- The data were analyzed by examining Power Spectral Density plots and calculating the normalized power over the classical frequency ranges: delta (1-4 Hz), theta (4-7 Hz), alpha (7-12 Hz), and beta (12-40 Hz).

- Total power was calculated by summing the squares of all time samples for each channel. For each channel, the normalized power in each band was calculated by summing the squares after band pass filtering and dividing by the total power.

- The normalized power was analyzed for regional differences in the anterior and remaining areas (Fig. 1). All statistical analyses were performed using JMP Pro 11. A significance level of 0.05 was applied using a nonparametric method Kruskal-Wallis Test; the significance of the differences was found in spectral content across the four groups.

Acknowledgements

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Table 1

<table>
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<th>MCI</th>
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<td>60 - 78</td>
<td>61 - 85</td>
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</table>

Results

- Differences in the power distribution by frequency were seen in anterior/frontal regions relative to central and posterior (Fig. 2 & 3).

- No statistically significant differences were seen across the study populations in any of the analyzed frequency bands.

- PD patients have been reported to show generalized cortical slowing characterized by an increase in theta power relative to healthy controls. Although it did not achieve statistical significance, theta spectral power was greater in PD and PDI subjects relative to controls.

- Alpha spectral power was increased posteriorly in all patient groups relative to controls. Careful regional analysis of shifts in spectral content may reveal more significant differences between groups.

Figure 1

Sensor array of an HCGSN 256-electrode cap with the first 30 channels in red.

Figure 2

Regional analysis of spectral content: Anterior and Posterior

Conclusions

- Although the results show no indication of statistically significant differences among the four subject groups of interest, it is not conclusive evidence that differences to differentiate these disease states are nonexistent. The large p values obtained may have been due to small sample size and quality of data.

- Biomarkers are defined as having sensitivity and specificity. While spectral content alone is not sufficient to constitute a biomarker, analyzing its degree of variation among subjects could be useful in determining one component of a potential biomarker.

- Further analyses are to be done for more conclusive results. Microstate analysis could potentially yield informative results that may allow for differentiation between the disease states.

References