Differences in nonlinear correlations between brain regions for patients with multiple sclerosis

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Multiple sclerosis (MS) is a chronic immune-mediated disease, the most common non-traumatic disorder of the central nervous system (CNS) [1]. The pathological hallmark of MS is demyelination and subsequent axonal degeneration that results in CNS lesions [2]. These neural alterations are present even in patients with early-stage MS [3]. Electroencephalography (EEG) can be used as a method to study secondary disease-induced changes in MS, such as cognitive impairment and other functional declines [4].

The multiscale methodology is one of the primary methods for studying complex systems and analyzing complex time series, which are undoubtedly EEG signals from the human brain [5].

In the investigation, a statistical analysis of the EEG data recorded during the resting state was performed for patients of the same age 30-40 with multiple sclerosis and the corresponding control group. The idea of the research was to examine differences in nonlinear cross-correlations, measured by the q-dependent detrended cross-correlation coefficient $\rho_q(s)$ [6], between brain regions represented by electrodes for various factors such as the duration of the disease, the stage of the disease, which is measured by the Expanded Disability Status Scale (EDSS), and medications administered during treatment. The results presented in Fig. 1 contain only the connection between two electrodes that exists, when the difference between two groups, for these electrodes, is statistically significant. The most significant differences are observed in case (b) - for group 1 patients who were being treated with Tecfidera®, and group 2 patients who were being treated with Interferon®. Differences between groups are also visible in case (c), where correlation matrices for patients in different stages of the disease (quantified by EDSS) from group 1 with EDSS > 1 and patients from group 1 with EDSS ≤ 1 are compared.

Furthermore, the fractal and multifractal properties of the EEG time series for 20 representative electrodes were also studied by using a multifractal detrended fluctuation analysis [7]. These measures can quantitatively describe the persistence and complexity of the considered time series [8, 9]. Looking at the differences in the width of the multifractal spectrum $\Delta\alpha$ - Fig. 2, it was possible to distinguish between the stage of the disease (quantified by EDSS -c) and the type of drug (b). There was almost no difference when the duration of the disease was taken into account. All observed differences were stronger in the phase of the experiment with closed eyes, which may be related to the delta waveform. It is also worth noting that the highest differences were observed in the time scale range $s = 200ms - 2500ms(5Hz - 0.4Hz)$, which corresponds to the delta wave.

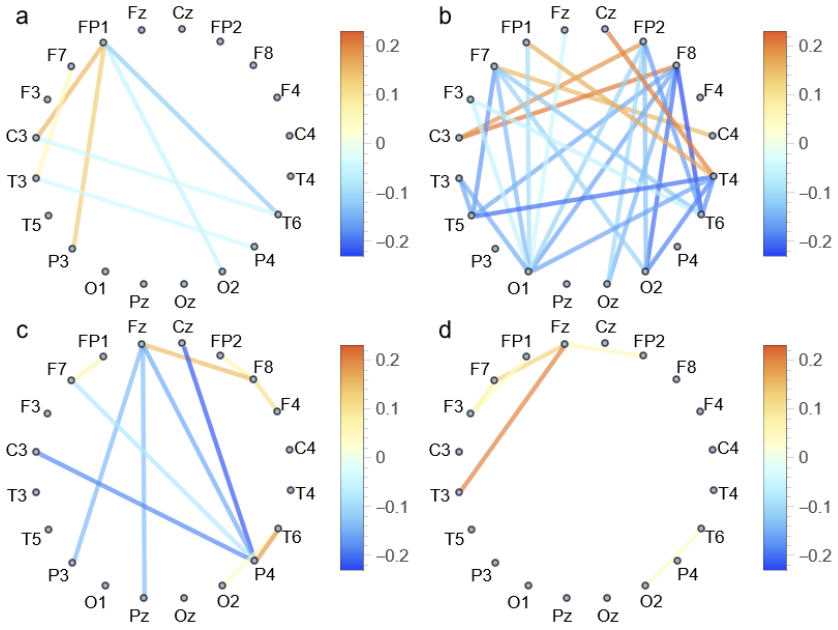

Fig. 1. Connections between 20 electrodes representing statistically significant differences between average correlation matrices ($\rho(q = 1, s = 200\,\text{ms}$) for various cases: (a) control and patients group, (b) patients 1 - Tecfidera® and patients 2 - Interferon® (c) patients 1 with EDSS > 1 and patients 1 with EDSS ≤ 1 (d) patients 1 with the time of disease longer than 7.5 years and patients 1 shorter than 7.5 years. In all cases, people between the ages of 30-40 and with closed eyes are considered.

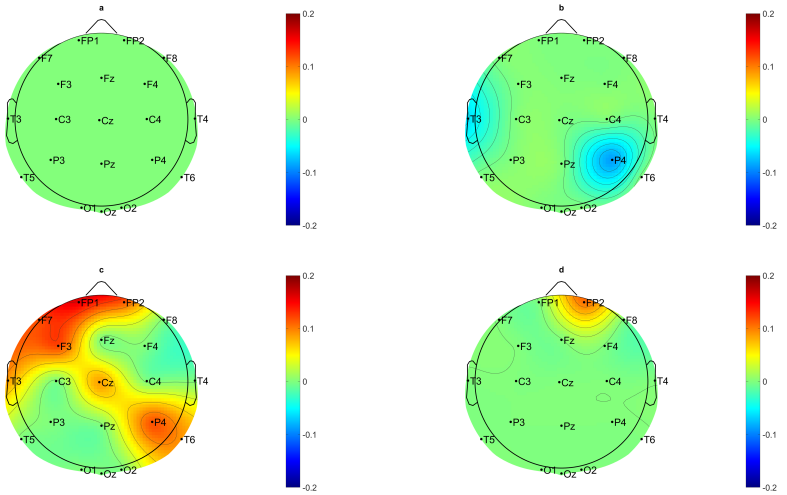

Fig. 2. Statistically significant differences between average multifractal spectra width $\Delta\alpha$ over 20 electrode areas for various cases: (a) control and patients group, (b) patients 1 - Tecfidera® and patients 2 - Interferon® (c) patients 1 with EDSS > 1 and patients 1 with EDSS ≤ 1 (d) patients 1 with time of disease longer than 7.5 years and patients 1 shorter than 7.5 years. In all cases people in the age 30-40 and with closed eyes are considered.

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