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INVESTIGATING THE VARIATIONS IN THE BRAIN ACTIVITY BETWEEN HEALTHY SUBJECTS AND MILD COGNITIVE IMPAIRMENT (MCI) PATIENTS

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Abstract

Analysis of brain activity for patients with brain disorders is an important research area. Mild cognitive impairment (MCI) is a condition in which patients have more memory or thinking problems compared to healthy people of the same age. In this work, we studied the alterations in brain activity among control subjects and patients with MCI. Three complexity techniques, namely sample entropy, approximate entropy, and fractal dimension, were employed to study electroencephalogram (EEG) signals recorded from 102 control (healthy) subjects, and seven subjects with MCI in a comfortable position, on a bed, with their eyes closed. The results showed that the EEG signals of patients with MCI show greater complexity than the EEG signals of healthy subjects. This analysis method can be applied to compare brain activity among healthy subjects and patients with other brain diseases.

Keywords: Mild Cognitive Impairment (MCI); EEG Signals; Complexity; Sample Entropy Approximate Entropy; Fractal Dimension.

1. INTRODUCTION

Many works have analyzed the brain activity of patients with various brain disorders. For example, the works that studied electroencephalogram (EEG) signals for patients with depression and schizophrenia,[1] Alzheimer's,[2] epileptic seizure,[3] Parkinson's,[4] and stroke.[5] It is known that brain disorders cause changes in the activations of the brain. Therefore, EEG signals should be changed due to different disorders. Mild cognitive impairment (MCI) is a condition in which people have more memory or thinking problems than healthy people with the same age. Searching in the literature shows many works that analyzed EEG signals to study the brain's activity of MCI patients.[6–9]

Based on the literature, researchers have used different techniques (e.g. different types of entropy,[10] feature extraction,[11] wavelet transform,[12] and machine learning[13]) to study the changes in EEG signals.

Due to the complex structure of the EEG signals,[14] we employ fractal theory. We use fractal exponent as the indicator of complexity. We can mention a wide variety of works that analyzed different biomedical signals and images, such as EMG signals,[15–17] ECG signals,[18,19] eye movements,[20–22] GSR signals,[23] stride time series,[24,25] DNA random walk,[26] and X-ray images[27] using fractal theory. Similarly, the fractal theory has been extensively used for investing EEG signals in various conditions, such as response to external stimuli,[28] body movements,[29] and specifically due to different mental disorders.[30]

Approximate entropy is a proper technique to quantify the irregularity of biomedical signals (e.g. ECG,[31] eye movement,[32] PCG signals,[33] stride time series,[34] and EMG signals[35]). It is known that its greater values indicate higher irregularity in a dataset. In other words, a bigger approximate entropy shows bigger complexity. Many works can be called that used approximate entropy to study EEG signals.[36,37]

Sample entropy is also chosen in this work to quantify the complexity of signals. Sample entropy is independent of data length. Sample entropy is used widely in studying biomedical signals such as EMG,[38,39] ECG signals,[40] stride time series,[41] GSR signals,[42] eye movements,[43] and R–R time series.[44] We can also call the applications of sample theory in investigating EEG signals in various conditions.[45,46]

We employ these complexity measures to analyze the changes in the complexity of EEG signals between control and MCI subjects.

2. METHOD

We want to compare the brain activity among control and MCI subjects. The box-counting method was chosen for the calculation of the fractal exponent. Firstly, EEG signals are covered with same-size (ε) boxes, and the number of boxes is counted by the algorithm. This process is repeated in several steps by changing ε. Finally, the fractal dimension is calculated[47]:

$$\mathrm{FD} = \frac{N(\varepsilon)}{1/\varepsilon}. \tag{1}$$

The general form of Eq. (1) for the fractal of order c is written as

$$\mathrm{FD}_c = \frac{1}{c-1}\frac{\sum_{i=1}^{N} p_i^c}{\varepsilon} \tag{2}$$

in which, p_i indicates the probability:

$$p_i = \frac{t_i}{T}, \tag{3}$$

in which, t_i and T indicates time.

Irregularity of EEG signals is also considered and quantified by calculating the approximate entropy.[48] A bigger approximate entropy indicates higher randomness or greater complexity in the signal. For a time series, a vector is formulated:

$$a(i) = [x(i), x(i+1), \ldots, x(i+m-1)], \tag{4}$$

in which, m and r, respectively, indicate the embedding dimension and the tolerance. $C_i^m(r)$ is written as

$$C_i^m(r) = \frac{\begin{array}{c}\text{number of } a(j) \text{ such that}\\ d[a(i), a(j) \leq r]\end{array}}{N-m+1}. \tag{5}$$

The difference is written as

$$d[a, a] = \max_c |x(c) - x^*(c)|, \tag{6}$$

$x(c)$ is m scalar component of x. By averaging $C_i^m(r)$ using Eq. (7), ApEn (approximate entropy) is defined (Eq. (8)).

$$\phi^m(r) = \frac{\sum_{i=1}^{N-m+1} \log(C_i^m(r))}{N-m+1}, \tag{7}$$

$$\mathrm{ApEn} = \phi^m(r) - \phi^{m+1}(r). \tag{8}$$

Sample entropy is also chosen to quantify the complexity of EEG signals. Considering $(x(1), x(2), \ldots, x(n))$ as a time series, the sample entropy is calculated using Eq. (9).[49]

$$\mathrm{SampleEntropy}(h, r, n) = -\log\frac{X}{Y}, \tag{9}$$

h and r, respectively, indicate the embedding dimension and tolerance.

X and Y are the number of template vector pairs that satisfy Eqs. (10) and (11)

$$d[f_{h+1}(i), f_{h+1}(j)] < r \tag{10}$$

$$d[f_h(i), f_h(j)] < r, \tag{11}$$

in which $f_h(i)$ is written as

$$f_h(i) = \{x(i), x(i+1), \ldots, x(i+h-1)\}. \tag{12}$$

We quantify the complexity of EEG signals and then discuss their variations between different conditions.

3. DATABASE AND ANALYSIS

We employed the dataset by Cejnek *et al.*[50] This dataset includes the EEG data recorded from 59 patients with Alzheimer's disease, 102 control (healthy) subjects, and seven subjects with MCI while they were in a comfortable position, on a bed, with their eyes closed. Since, according to the literature, several works have been focused on the analysis of the variations of EEG signals between control subjects and patients with Alzheimer's disease,[51–53] in this research, we only focus on analyzing the change in the EEG signals among control and MCI subjects. Cejnek *et al.*[54] recorded EEG data from subjects using a 21-channel digital EEG setup (Walter EEG PL-231, Germany) with a sampling frequency of 256 Hz and TruScan 32 (Alien Technik Ltd., Czech Republic) with a frequency of 128 Hz and 21-channel setup. Then, they downsampled the recorded data to 128 Hz. After detrending the data, they used a notch filter, which filtered the data out of 50 Hz. They also manually removed artifacts (e.g. eye movements, ECG artifacts) from data. More information can be found in Ref. 54.

We quantified the complexity using the equations in the method section. Boxes with the size of $\frac{1}{2}, \frac{1}{4}, \frac{1}{16}, \ldots, \frac{1}{n}$ were chosen. The calculation of parameters was performed in MATLAB 2022a. After that, we compared the significance of the difference in the complexity of EEG signals between control and MCI subjects using a one-way ANOVA test. 0.05 was considered as the significance level.

4. RESULTS

The fractal dimensions of EEG signals are shown in Fig. 1. This figure shows that the FD of EEG signals has a smaller value for control subjects than for MCI subjects. Since the FD indicates the complexity, the EEG signals' complexity for MCI

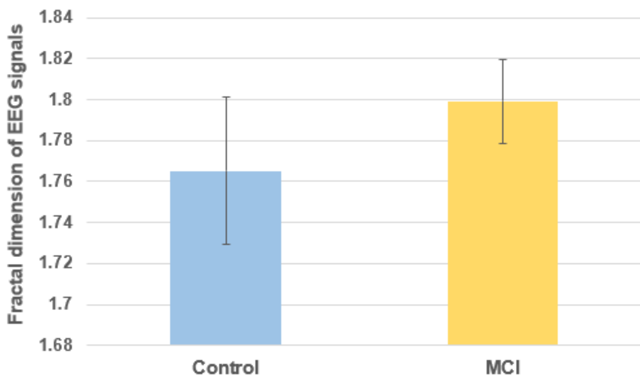

Fig. 1 FD of EEG signals in healthy and MCI subjects. Error bars indicate standard deviation.

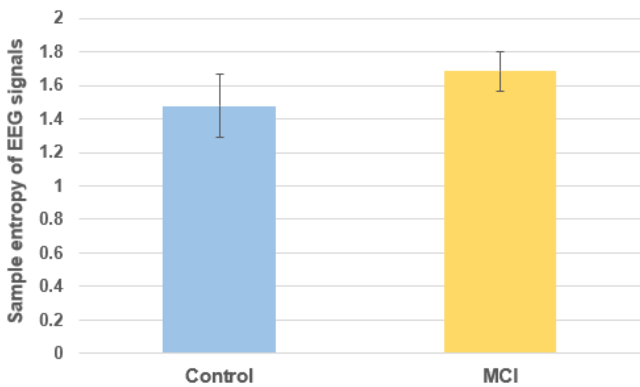

Fig. 2 EEG signals' sample entropy in healthy and MCI subjects. Error bars indicate standard deviation.

patients is greater than for control subjects. The p-value $= 0.0151$ states that the difference in the fractal dimension of EEG signals among healthy and MCI subjects is significant.

The signals' sample entropy for control and MCI subjects are presented in Fig. 2. The sample entropy has a smaller value for control subjects than for MCI subjects. Therefore, EEG signals of MCI subjects are more complex than the EEG signals of control ones. Furthermore, p-value $= 0.0052$ indicates that the change in the sample entropy between healthy and MCI subjects is significant.

The approximate entropy of signals for control and MCI subjects is presented in Fig. 3.

The approximate entropy of EEG signals has a smaller value for control subjects than for MCI subjects. Therefore, it can be stated that the EEG signals of MCI subjects are more random than the EEG signals of control subjects. In other words, the EEG signals of MCI subjects are more complex than those of control subjects. Furthermore, p-value $= 0.0217$ indicates that the change in the

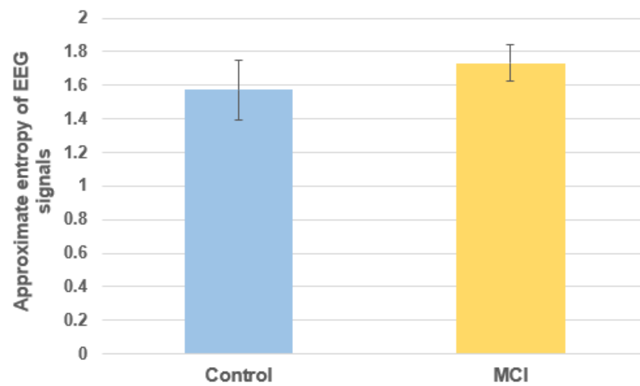

Fig. 3 Approximate entropy of EEG signals in healthy and MCI subjects. Error bars indicate standard deviation.

approximate entropy of EEG signals between control and MCI subjects is significant. Therefore, the approximate entropy changes are similar to the fractal dimension and sample entropy.

5. DISCUSSION AND CONCLUSION

We investigated the changes in brain activity among healthy and MCI subjects. We utilized complexity methods to analyze the EEG signals. Based on the results, the EEG signals of MCI patients show greater complexity than the healthy subjects. Therefore, EEG signals of MCI subjects are more complex than EEG signals of healthy ones. The results of ANOVA tests stated that the change in the complexity of signals among healthy and MCI subjects is significant. The obtained results can be concluded from the fact that MCI patients have more memory or thinking problems than healthy people of the same age. Accordingly, higher activity in the brain leads to greater complexity in the EEG signals[55] for these patients than healthy people.

We can expand the analysis by considering different types of brain disorders. For instance, we can study how EEG signals' complexity is different among healthy subjects and patients with Alzheimer's or Schizophrenia diseases.[56]

Since the brain controls different organs of the human body,[57] in further research, we can compare the correlation of the brain and different organ activities among healthy subjects and patients with other disorders. For example, we can compare the brain–heart correlation in healthy subjects with the brain–heart correlation in MCI patients to investigate how the disorder affects the brain on controlling the activation of different organs. For this purpose, we analyze the complexity of an organ's physiological signal (e.g. ECG signals in the case of the heart) versus the complexity of EEG signals.

All these analyses help scientists decode the changes in the brain activity of patients in comparison with healthy subjects.

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REFERENCES

1. B. Thirioux *et al.*, *Eur. Arch. Psychiatry Clin. Neurosci.* (2023), doi:10.1007/s00406-023-01642-6.
2. P. Prado *et al.*, *Alzheimers Dement.* (*Amst*) (2023), doi:10.1002/dad2.12455.
3. B. Kapoor *et al.*, Epileptic seizure prediction based on hybrid seek optimization tuned ensemble classifier using EEG signals, *Sensors* (*Basel*) **23**(1) (2022) 423.
4. R. Pezzetta *et al.*, Combined EEG and immersive virtual reality unveil dopaminergic modulation of error monitoring in Parkinson's disease, *NPJ Parkinsons Dis.* **9** (2023) 3.
5. F. Pichiorri *et al.*, Exploring high-density corticomuscular networks after stroke to enable a hybrid brain–computer interface for hand motor rehabilitation, *J. Neuroeng. Rehabil.* **20**(1) (2023) 5.
6. H. Azami *et al.*, Beta to theta power ratio in EEG periodic components as a potential biomarker in mild cognitive impairment and Alzheimer's dementia, *Alzheimer's Res. Ther.* **15** (2023) 133.
7. R. Wu *et al.*, Screening for mild cognitive impairment with speech interaction based on virtual reality and wearable devices, *Brain Sci.* **13** (2023) 1222.
8. W. S. Kumar and S. Ray, Healthy ageing and cognitive impairment alter EEG functional connectivity in distinct frequency bands, *Eur. J. Neurosci.* **58**(6) (2023) 3432–3449, doi:10.1111/ejn.16114.
9. A. M. Alvi, S. Siuly and H. Wang, A long short-term memory based framework for early detection of mild cognitive impairment from EEG signals, *IEEE Trans. Emerg. Top. Comput. Intell.* **7**(2) (2023) 375–388.
10. S. Mujib Kamal, N. Mat Dawi and H. Namazi, Information-based decoding of the coupling among human brain activity and movement paths, *Technol. Health Care* **29**(6) (2021) 1109–1118.
11. T. Avdeenko *et al.*, Comparative analysis of feature extraction methods for intelligence estimation based on resting state EEG data, *Eng. Proc.* **33** (2023) 25.
12. V. Tolmanova and D. Andrikov, A review of engineering techniques for EEG processing, *Eng. Proc.* **33** (2023) 46.
13. K. M. Hossain *et al.*, Status of deep learning for EEG-based brain–computer interface applications, *Front Comput. Neurosci.* **16** (2023) 1006763.
14. M. H. Babini *et al.*, Decoding of heart–brain relation by complexity-based analysis of heart rate variability (HRV) and electroencephalogram (EEG) signals, *Fractals* **30**(7) (2022) 2250190.
15. A. A. Navish *et al.*, *Comput. Methods Biomech. Biomed. Eng. Imaging Vis.* (2022), doi:10.1080/21681163.2022.2092035.
16. J. Ramadoss *et al.*, Decoding the correlation among leg muscle and brain activations in different body movements, *Fractals* **30**(4) (2022) 2250120.
17. N. Pakniyat *et al.*, Age-based analysis of the brain activity during sleep induced by medication, *Fractals Fract.* **31**(1) (2023) 2350011.
18. N. Mat Dawi, P. Maresova and H. Namazi, Complexity-based analysis of heart rate variability during aging, *Fractals* **30**(9), (2022) 2250198, doi:10.1142/S0218348X22501985 (2022).
19. H. Namazi, Complexity and information-based analysis of the heart rate variability (HRV) while sitting, hand biking, walking, and running, *Fractals* **29**(5) (2021) 2150201.
20. R. Ramamoorthy *et al.*, *Fractals* **29**(8) (2021) 2150274.
21. H. Alipour, H. Namazi, H. Azarnoush and S. Jafari, Fractal-based analysis of the influence of color tonality on human eye movements, *Fractals* **27**(3) (2019) 1950040.
22. H. Alipour *et al.*, Complexity-based analysis of the relation between fractal visual stimuli and fractal eye movements, *Fluct. Noise Lett.* **18**(3) (2019) 1950012.
23. H. Namazi, D. Baleanu, S. Omam and O. Krejcar, Analysis of the correlation between brain and skin

reactions to different types of music, *Fractals* **29**(2) (2021) 2150124.
24. T. Azizi, On the fractal geometry of gait dynamics in different neuro-degenerative diseases, *Phys. Med.* **14** (2022) 100050.
25. A. Phinyomark, R. Larracy and E. Scheme, Fractal analysis of human gait variability via stride interval time series, *Front. Physiol.* **11** (2020) 333.
26. H. Namazi and N. Mat Dawi, Information and complexity-based analysis of the variations of the coronavirus genome between different countries, *Fractals* **28**(7) (2020) 2050134.
27. H. Namazi and V. V. Kulish, Complexity-based classification of the coronavirus disease (COVID-19), *Fractals* **28**(5) (2020) 2050114.
28. M. Soundirarajan, O. Krejcar and H. Namazi, Analysis of the coupling between the brain and facial muscle responses to auditory stimulation, *Fractals* **30**(6) (2022) 2250132.
29. J. Ramadoss, N. Mat Dawi, K. Rajagopal and H. Namazi, Complexity and information-based analysis of the electroencephalogram (EEG) signals in standing, walking, and walking with a brain–computer interface, *Fractals* **30**(1) (2022) 2250041.
30. O. E. Dick, S. V. Murav'eva, V. S. Lebedev and Y. E. Shelepin, Fractal structure of brain electrical activity of patients with mental disorders, *Front. Physiol.* **13** (2022) 905318.
31. E. E. Solís-Montufar, G. Gálvez-Coyt and A. Muñoz-Diosdado, Entropy analysis of RR-time series from stress tests, *Front. Physiol.* **11** (2020) 981.
32. K. Harezlak, D. R. Augustyn and P. Kasprowski, An analysis of entropy-based eye movement events detection, *Entropy* **21**(2) (2019) 107.
33. H. Namazi and O. Krejcar, Analysis of pregnancy development by complexity and information-based analysis of fetal phonocardiogram (PCG) signals, *Fluct. Noise Lett.* **20**(4) (2021) 2150028.
34. N. Mat Dawi *et al.*, Analysis of the correlation between muscle reaction and stride interval variability in single-task and dual-task walking, *Fractals* **29**(7) (2021) 2150272.
35. R. Sun, R. Song and K.-Y. Tong, Complexity analysis of EMG signals for patients after stroke during robot-aided rehabilitation training using fuzzy approximate entropy, *IEEE Trans. Neural Syst. Rehabil. Eng.* **22**(5) (2014) 1013–1019.
36. D. M. Zolezzi, L. M. Alonso-Valerdi and D. I. Ibarra-Zarate, EEG frequency band analysis in chronic neuropathic pain: A linear and nonlinear approach to classify pain severity, *Comput Methods Programs Biomed.* **230** (2023) 107349.
37. C. Pappalettera, F. Miraglia, M. Cotelli, P. M. Rossini and F. Vecchio, Analysis of complexity in the EEG activity of Parkinson's disease patients by means of approximate entropy, *Geroscience* **44**(3) (2022) 1599–1607.
38. N. Babault, M. Hitier, C. Cometti, Usefulness of surface electromyography complexity analyses to assess the effects of warm-up and stretching during maximal and sub-maximal hamstring contractions: A cross-over, randomized, single-blind trial, *Biology* **11** (2022) 1337.
39. S. Sriram *et al.*, Complexity-based analysis of muscle activation during walking at different speeds, *Fractals* **31**(3) (2023) 2350032.
40. T. Kumarasinghe *et al.*, Complexity-based evaluation of the correlation between heart and brain responses to music, *Fractals* **29**(6) (2021) 2150238.
41. H. Namazi, Complexity-based analysis of the correlation between stride interval variability and muscle reaction at different walking speeds, *Biomed. Signal Process.* **69** (2021) 102956.
42. H. Namazi, S. Omam, K. Kuca and O. Krejcar, Evaluation of the coupling between electroencephalogram (EEG) and galvanic skin response (GSR) signals versus the complex structure of music, *Fractals* **29**(4) (2021) 2150175.
43. A. Menon, O. Krejcar and H. Namazi, Evaluation of the coupling among visual stimuli, eye fluctuations, and brain signals, *Chaos Soliton Fractals* **153**(1) (2021) 111492.
44. J. Ramadoss, N. Pakniyat, K. Rajagopal and H. Namazi, Decoding the correlation between brain and heart activations in the combination of mental workload and physical activity, *Fract. Complex Geom. Patterns Scal. Nat. Soc.* **30**(4) (2022) 2250119, doi:10.1142/S0218348X22501195.
45. P. Ramanand, V. P. N. Nampoori and R. Sreenivasan, Complexity quantification of dense array EEG using sample entropy analysis, *J. Integr. Neurosci.* **3**(3) (2004) 343–358.
46. N. Pakniyat *et al.*, Complexity-based analysis of the variations of the brain's reactions in different types of locomotions, *Fractals* **31**(3) (2023) 2350031.
47. H. Namazi, Fractal-based classification of electromyography (EMG) signal between fingers and hand's basic movements, functional movements, and force patterns, *Fractals* **27**(4) (2019) 1950050.
48. H. Namazi, Complexity-based classification of the coronavirus genome versus genomes of the human immunodeficiency virus (HIV) and dengue virus, **28**(7) (2020) 2050129.
49. H. Namazi, A. Selamat and O. Krejcar, Complexity-based analysis of the alterations in the structure of coronaviruses, *Fractals* **29**(2) (2021) 2150123.
50. M. Cejnek, (2017): Dataset.zip. figshare. Dataset (2017), doi:10.6084/m9.figshare.5450293.v1.
51. W. Xia, R. Zhang, X. Zhang and M. Usman, A novel method for diagnosing Alzheimer's disease using

deep pyramid CNN based on EEG signals, *Heliyon* **9**(4) (2023) e14858.
52. H. K. Park *et al.*, Functional brain changes using electroencephalography after a 24-week multidomain intervention program to prevent dementia, *Front. Aging Neurosci.* **14** (2022) 892590.
53. A. Flores-Sandoval *et al.*, Spectral power ratio as a measure of EEG changes in mild cognitive impairment due to Alzheimer's disease: A case-control study, *Neurobiol. Aging* **130** (2023) 50–60.
54. M. Cejnek, O. Vysata, M. Valis and I. Bukovsky, Novelty detection-based approach for Alzheimer's disease and mild cognitive impairment diagnosis from EEG, *Med. Biol. Eng. Comput.* **59**(11–12) (2021) 2287–2296.
55. M. Soudirarajan *et al.*, Evaluation of the correlation between facial muscle and brain activities in auditory stimulation, *Fractals* **29**(1) (2021) 2150100.
56. H. Namazi, Information-based classification of electroencephalography (EEG) signals for healthy adolescents and adolescents with symptoms of Schizophrenia, *Fluct. Noise Lett.* **19**(4) (2020) 2050033.
57. H. Namazi, T. Kumarasinghe and O. Krejcar, Information-based analysis of the coupling between the alterations of heart and brain activities in response to auditory stimuli, *Fluct. Noise Lett.* **20**(6) (2021) 2150049.