Evaluation of Computational Methods in EEG Signal Analysis as Biomarkers in Determination of Dementia Leve l

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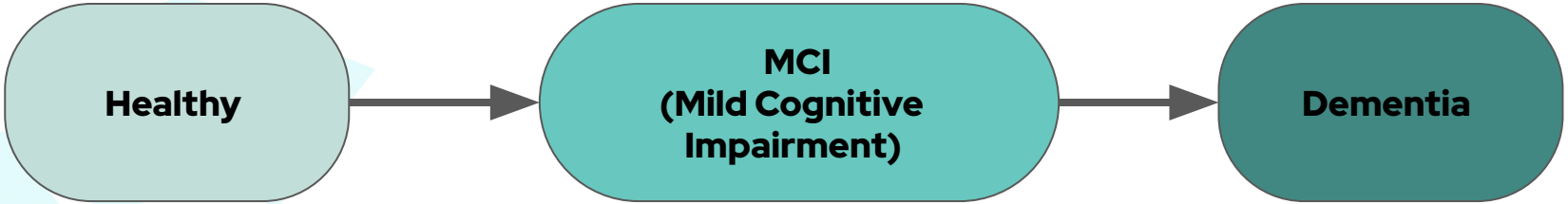
Presentation outline

- Terminology & Problem
- Study Design
- Patient Selection
- MMSE - Residential Block
- EEG Acquisition
- Preprocessing
- Computational Methods
- Results
- Acknowledgement

Terminology & Problem

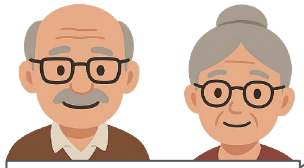


Which stage?

Limitations of psychometric assessments

Alternative Methods:
-MRI examinations
-Biological biomarkers
-EEG-based approaches focusing on frequency analysis
-Computational approaches addressing signal complexity and irregularity in EEG

Study Design



Individual group (n=38)

Mini Mental State Examination (**MMSE**)

Residential Block Classification

EEG Acquisition

Pre-processing

Feature extraction:
→FD
→QSE
→QSE
→VG

Data Triangulation

Dementia Staging

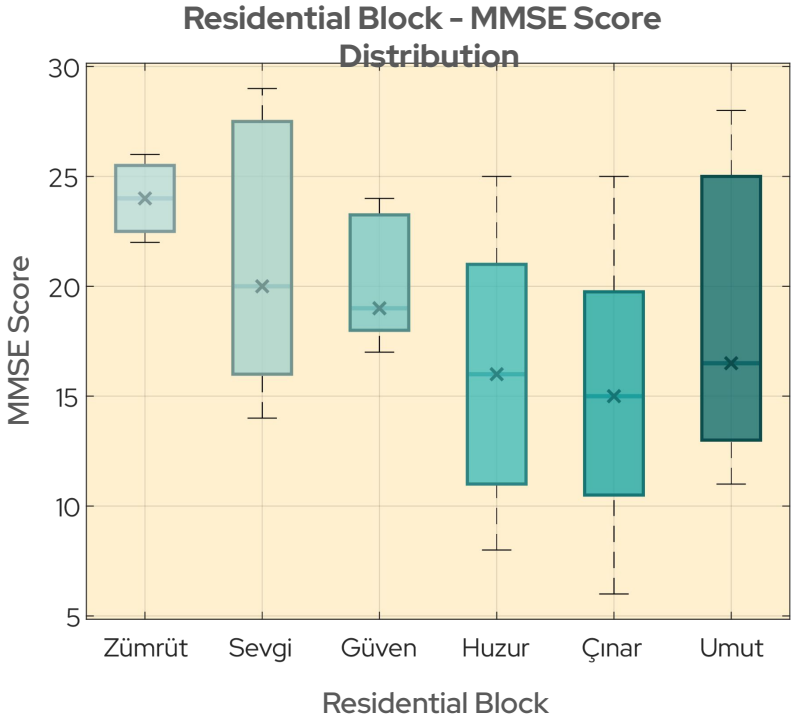
Linear Correlation (Pearson Correlation)

Patient Selection

Darülaceze Senior Center, operated by the Istanbul Metropolitan Municipality (Istanbul, Turkiye)

Nişantaşı University Ethics Committee (2023/42-2023)

Characteristics	Informations
Subject Number	38
Laterality	%95 right-handed
Age (Mean ± SD)	83.5 ± 9.6
Gender	%37 women
Literacy rate	%63
MMSE (Mean ± SD)	19.1 ± 5.9
Time since Diagnosis (Mean ± SD)	3.8 ± 3.2



MMSE - Mini Mental State Examination

- Taken by Physician
- Score range: 0 - 30
- Limitations of MMSE

Residential Block Name	n	*p*-value
Zümrüt	3	0.688
Sevgi	7	0.205
Güven	9	0.405
Huzur	6	0.246
Çınar	5	0.235
Umut	9	0.039

Shapiro-Wilks Normality Test Results

Residential Block Classification (Supportive info)

- Classifying the patient according to severity by physicians and caregiver opinions
- Against the MMSE limitations **Data Triangulation**

EEG Acquiring

Resting state - Eye closed - 25 min

Patients' rooms or in the nearest suitable location (Dimly and free from electrical devices as much as possible)

- PSD for noise assessment

10-20 Electrode mapping

Monopolar Montage (M2)

500 Hz

FIR band-pass filter (1 to 45 Hz)

Preprocessing

- Artifact Subspace Reconstruction (ASR)
- wavelet enhanced Independent Component Analysis (wICA)
- Common average referencing (CAR)
- Frequency Separation
  - Entire Spectrum (1-45 Hz)
  - Delta (1-3 Hz)
  - Theta (3-7 Hz)
  - Alpha (7-12 Hz)
  - Beta I (12-18 Hz)
  - Beta II (18-24 Hz)
  - Beta III (24-30 Hz)
  - Gamma (30-45 Hz)

Computational Methods

-Fractal Dimension (FD)

-Quadratic Sample Entropy (QSE)

-Quantile Graph (QG)

-Visibility Graph (VG)

Assumption

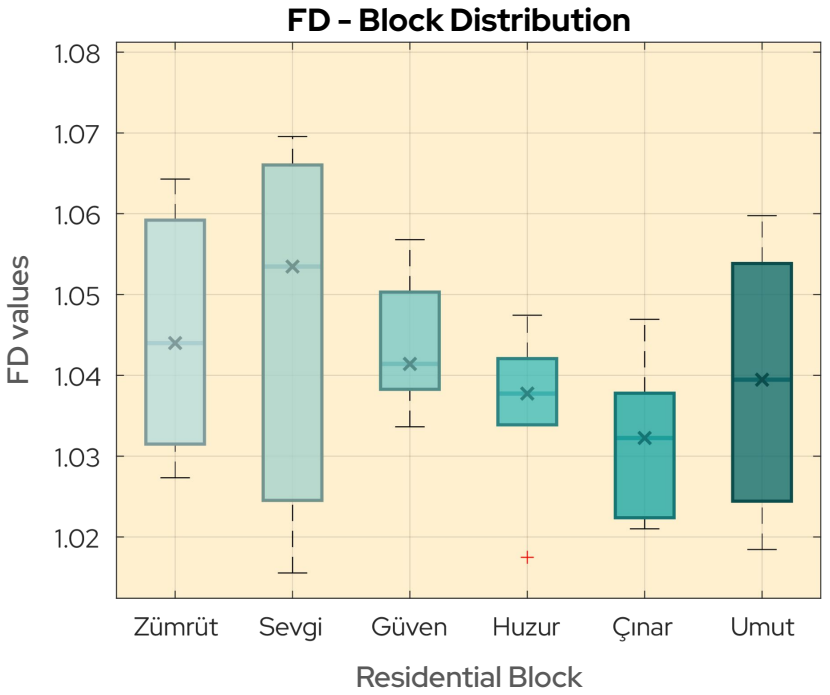
FD - Fractal Dimension

A derived quantity that measures the **self-similarity** and **complexity** of a signal.

$$FD = \frac{\log(n)}{\log(n) + \log(d/L)}$$

Here:

- n: Total number of data points in the time series,
- xi: The i-th data point in the time series,
- L: Total waveform length of the time series,
- d: Maximum waveform diameter.



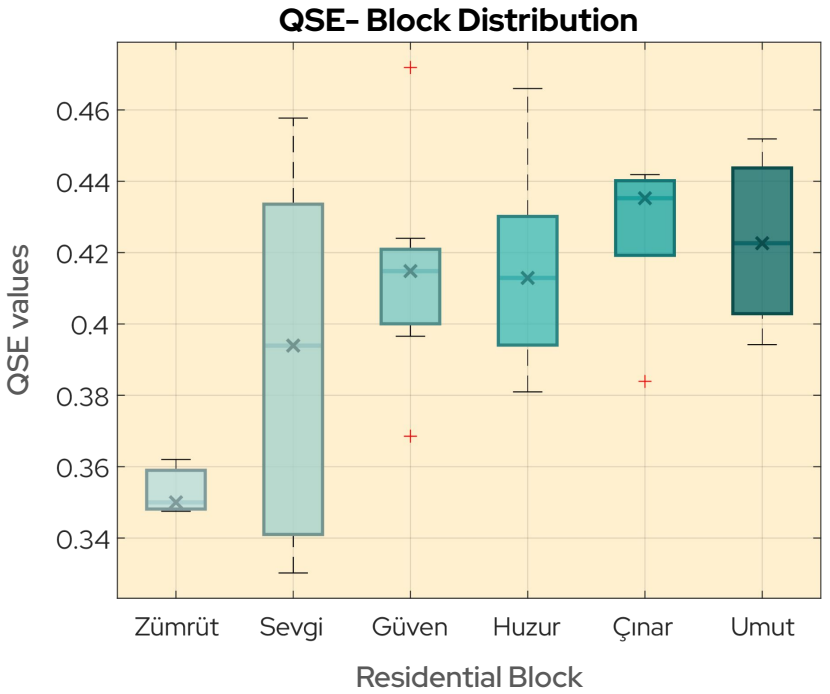
QSE - Quadratic Sample Entropy

Entropy-based methods are used to quantify the **randomness** and **uncertainty** of signals.

$$\text{SampEn} = -\ln\left(\frac{A^m(r)}{B^m(r)}\right)$$

Here:
- m: Signal segment length,
- r: Tolerance,
- Bi: Count of matches at a distance of m for each segment,
- Ai: Count of matches at a distance of m + 1.

$$\text{QSE} = \text{SampEn} + \ln(2r)$$

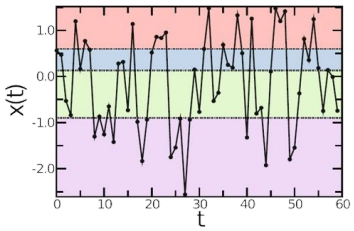


QG - Quantile Graph

Average Jump Length

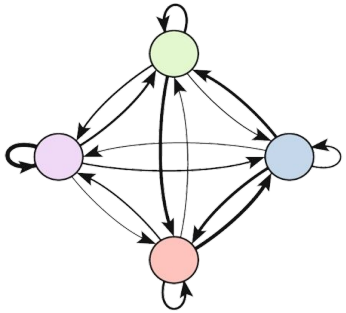
$$\Delta(k) = \frac{1}{Q} tr(PW_k^T)$$

Time series, X



k=1

Network, g

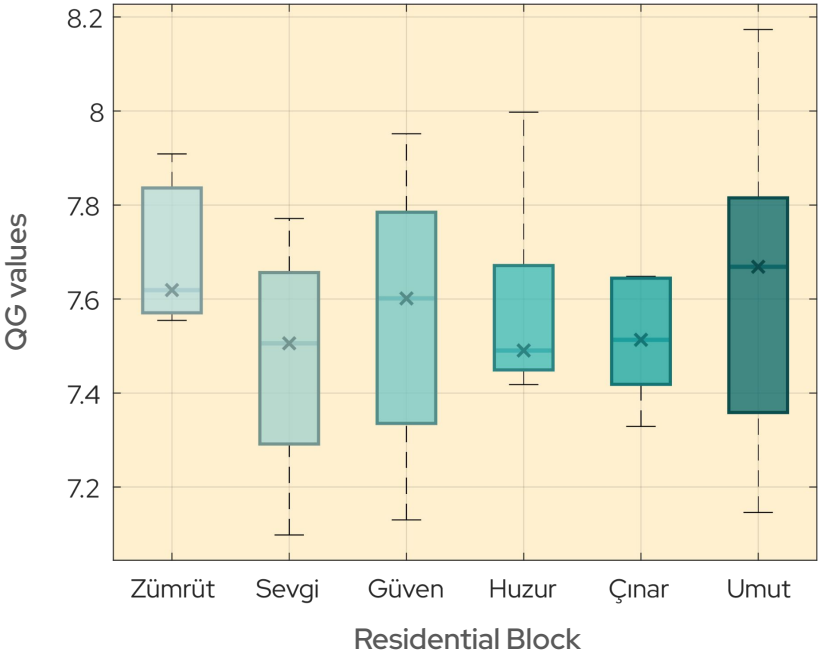


Transition matrix

	0.47	0.27	0.20	0.07
	0.21	0.29	0.14	0.36
	0.13	0.33	0.20	0.33
	0.20	0.13	0.40	0.27

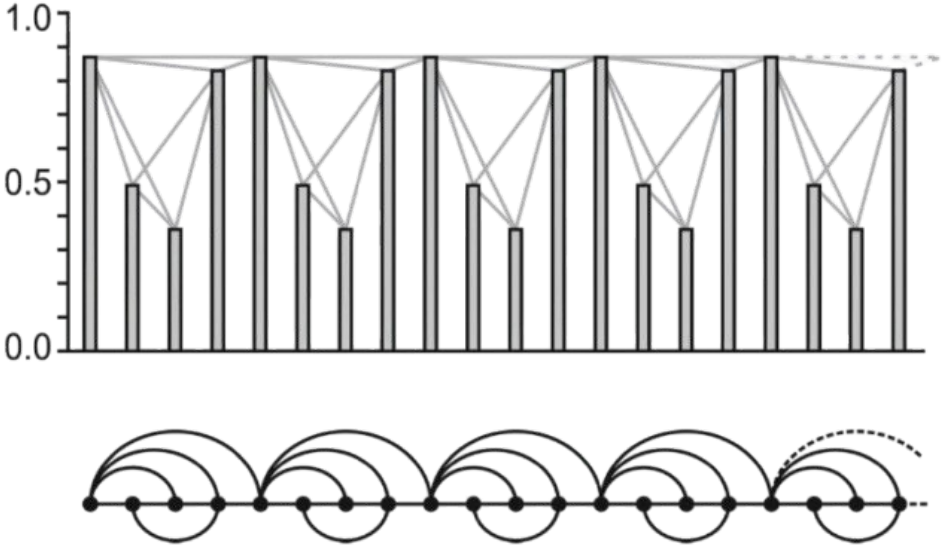
Campanharo et al., 2017, Lecture Notes in Computer Science

QG- Block Distribution



VG - Visibility Graph

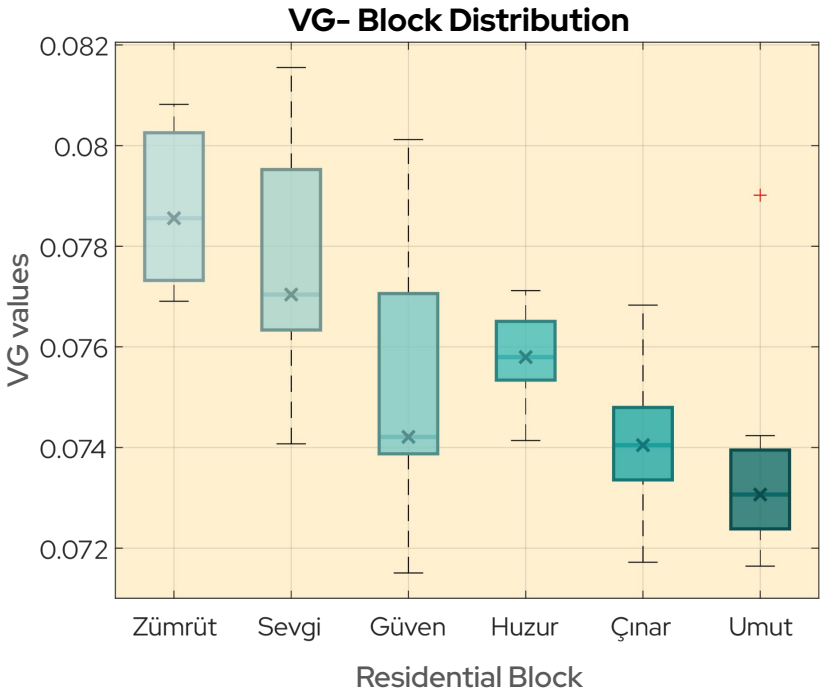
Time Series → Complex Network

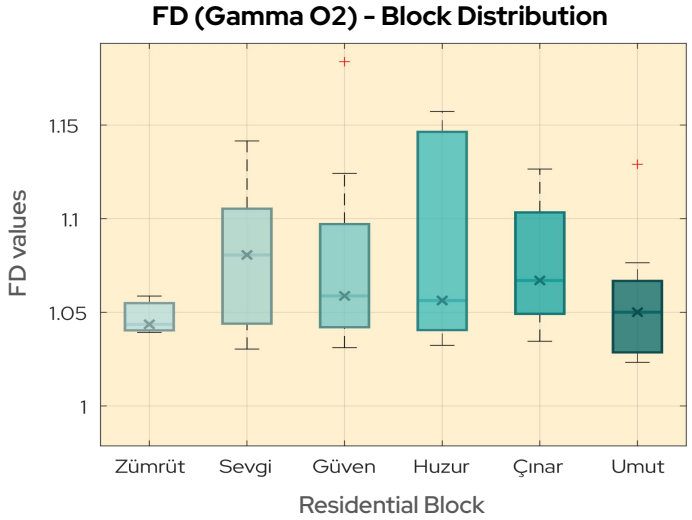


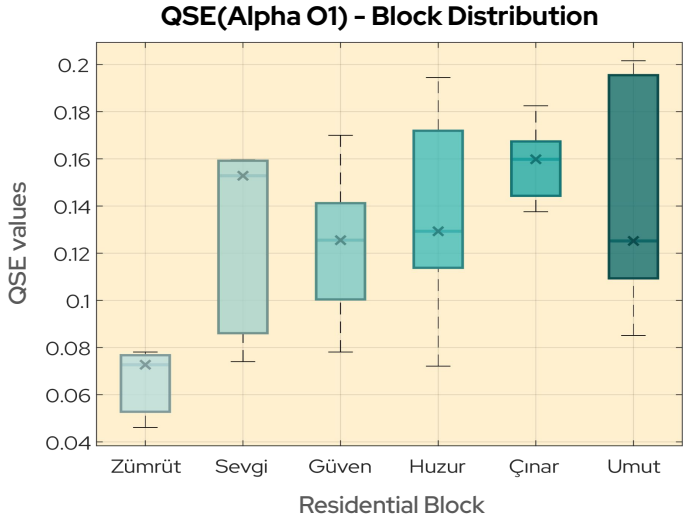
Kaynak: Lacasa et al., 2008, PNAS

Graph Index Complexity

$$\mathrm{GIC} = 4c(1-c)$$

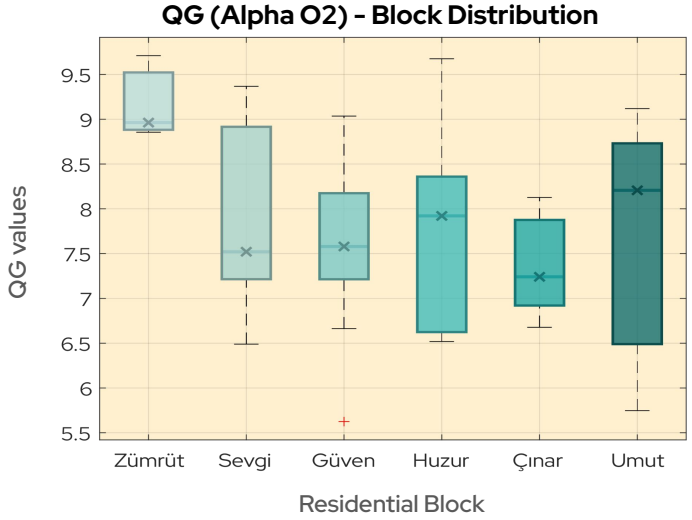


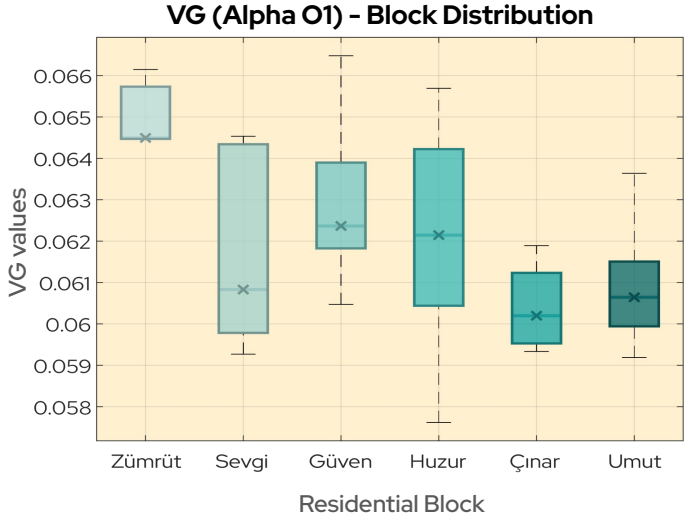




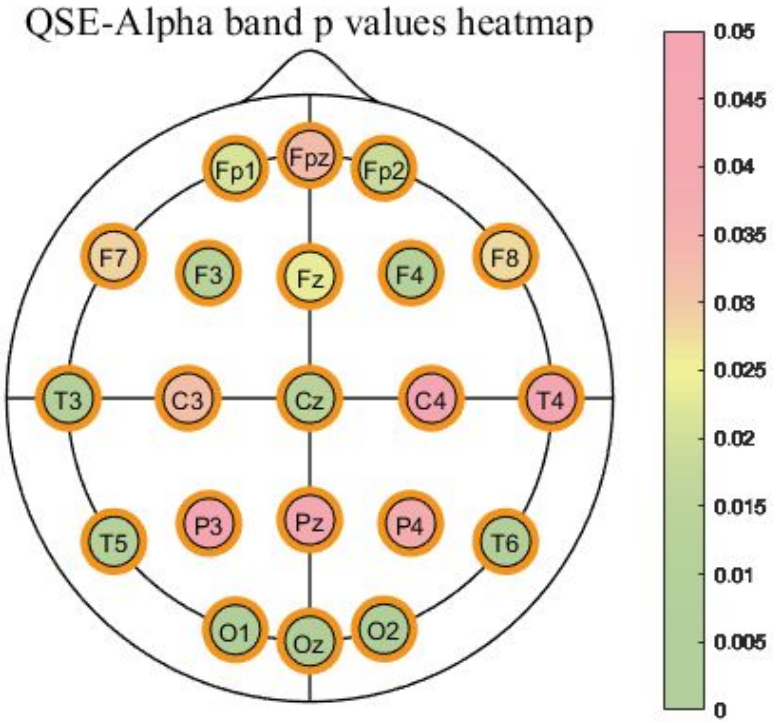
Results

- Total 90 significant features combination,
- 3 from FD
- 48 from QSE
- 4 from QG
- 35 from VG





Heatmaps of Frequency–Feature Pairs with Highest Correlations



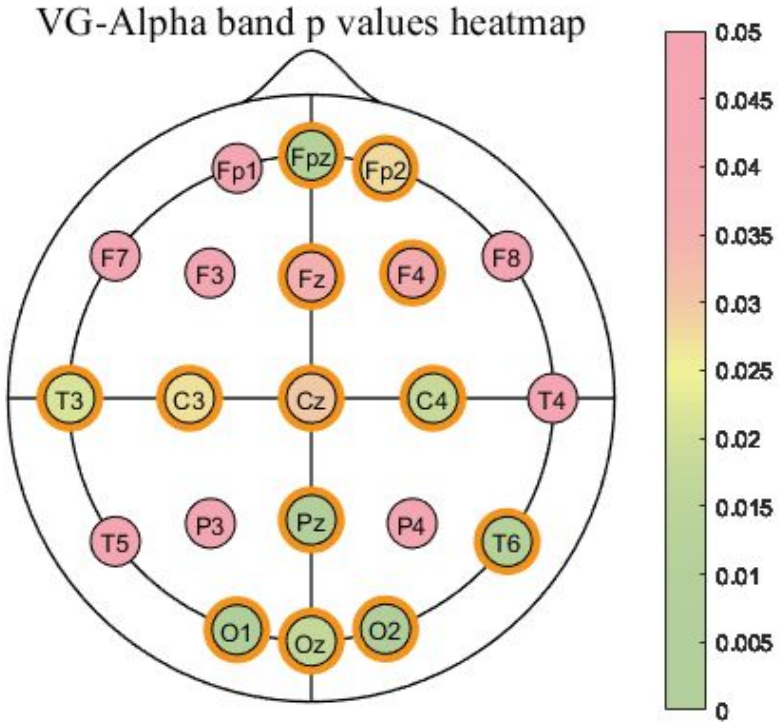


Table of Significant Correlations Between Frequency Bands and Electrode Locations

	Fp1	Fpz	Fp2	F7	F3	Fz	F4	F8	T3	C3	Cz	C4	T4	T5	P3	Pz	P4	T6	O1	Oz	O2	SUM
Entire Spectrum	0	1	1	0	1	0	0	0	1	0	0	0	0	0	0	0	1	2	2	2	2	13
Delta	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6
Theta	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Alpha	1	2	2	1	1	2	2	1	2	2	2	2	1	1	1	2	1	2	3	2	3	36
Betal	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
BetaII	0	0	0	0	0	0	1	0	1	0	1	0	0	0	0	0	0	2	2	1	2	10
BetaIII	0	0	0	0	0	0	2	0	2	0	2	0	0	0	0	0	0	2	1	1	2	12
Gamma	0	0	0	0	0	2	1	0	2	0	0	0	0	0	0	0	0	2	2	2	2	13
SUM	3	5	5	1	2	4	6	1	8	2	5	2	1	1	1	2	2	10	10	8	11	90

Acknowledgement

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Nişantaşı University Ethics Committee (2023/42-2023)

Istanbul Darülaceze Branch Directorate, Health Department of the Istanbul Metropolitan Municipality (1534/ 13.12.2022)

İhsan Kara

Anısına...

In the Electrophysiology aspect:

- Neurodejenerative Disorders
- Autism SD. and Epileptic Syndrome in Children
- Functional food and effect

3100 m2
Araştırma ve Üretim Alanı

5
Merkez Araştırma Laboratuvarı

Moleküler Biyoloji ve Hücre Kültürü

Enstrümental Analiz

Model Organizma

Mikrobiyal Biyoteknoloji

Hesaplamalı Nörobilim

Publications and ongoings

2025
Is Neurodegeneration Accelerated? Investigating Covid-19's Impact on Dementia via Functional Connectivity
Authors: Aynur Muduroglu-Kirmizibekmez, Alparslan Önder, Mustafa Yasir Ozdemir, Onder Yuksel Eryigit & Ertan Yurdakos
Journal: Archives of Neuropsychiatry (accepted)

Aronia Melanocarpa Extract May Modulate Brain Oscillations and Functional Connectivity: Evidence from EEG Analysis
Authors: Aynur Muduroglu Kirmizibekmez, Alparslan Önder, Mustafa Yasir Ozdemir & Ihsan Kara
Journal: Namik Kemal Medical Journal (accepted)

Efficacy of ACTH Therapy in Children with Landau-Kleffner Syndrome and Autism Spectrum Disorder: A Retrospective Analysis
Authors: Atilla Altunel, Aynur Muduroglu-Kirmizibekmez, Alparslan Önder, Ozlem Altunel, Ali Sever & Ihsan Kara
Journal: Epilepsy & Behavior Journal

2024
Investigation of the Acute Impact of Rosemary Consumption on Brain Activity in Healthy Volunteers
Authors: Aynur Muduroglu-Kirmizibekmez, Ceren Cati, Alparslan Önder, Sevcan Aydin & Ihsan Kara
Journal: Nutritional Neuroscience Journal

Ongoing

Investigation of Autism Diagnostic Biomarkers in Children with Developmental Disorders (2024–Present)
Team: Alparslan Önder, Mustafa Yasir Ozdemir, Aynur Muduroglu-Kirmizibekmez & Ihsan Kara

Effects of the Traditional Herb Astragaloside IV on Human Brain Waves (2024–Present)
Team: Aynur Muduroglu Kirmizibekmez, Alparslan Önder, Mustafa Yasir Ozdemir, Sevcan Aydin, Ceren Cati & İhsan Kara

A Longitudinal Investigation of Anthocyanin's Impact on EEG Abnormalities and Gut Microbiota in Children with Autism Spe
Disorder (2024–Present)
Team: Aynur Muduroglu-Kirmizibekmez, Alparslan Önder, Mustafa Yasir Ozdemir, Sevcan Aydın & Ihsan Kara

Feeding the Mind: How Anthocyanins Shape Brain Activity and Gut Microbiota in Cognitive Impairments (2023–Present)
Team: Aynur Muduroglu-Kirmizibekmez, Alparslan Önder, Mustafa Yasir Ozdemir,Sevcan Aydın, Gamze Gurerk, Onder Yukse
Mehmet Oktar Guloglu & Ihsan Kara

The Effects of Anthocyanin Consumption on Functional Connectivity in Dementia and Type 2 Diabetes Mellitus (2023–Pre
Team: Aynur Muduroglu-Kirmizibekmez, Alparslan Önder, Mustafa Yasir Ozdemir, Onder Yuksel Eryigit & Ihsan Kara






Questions

References

- Katz MJ. Fractals and the analysis of waveforms. *Comput Biol Med.* 1988;18(3):145–56. doi:10.1016/0010-4825(88)90041-8.
- Simons S, Abasolo D, Escudero J. Classification of Alzheimer's disease from quadratic sample entropy of electroencephalogram. *Healthc Technol Lett*. 2015;2(3):70-73. Published 2015 May 21. doi:10.1049/htl.2014.0106
- Campanharo ASLO, Doescher E, Ramos FM. Automated EEG signals analysis using quantile graphs. In: Rojas I, Joya G, Catala A, editors. Advances in Computational Intelligence. Cham: Springer International Publishing; 2017. p. 95–103.
- Ahmadlou M, Adeli H. Visibility graph similarity: A new measure of EEG-seizure similarity. *Clin Neurophysiol*. 2012;123(10):1922–31. doi.10.1016/j.physd.2011.09.008
- Lacasa L, Luque B, Ballesteros F, Luque J, Nuño JC. From time series to complex networks: The visibility graph. *Proc Natl Acad Sci U S A*. 2008;105(13):4972–5. doi:10.1073/pnas.0709247105.
- Vicchietti M, Ramos F, Betting L, Campanharo A. Computational methods of EEG signals analysis for Alzheimer’s disease classification. Sci Rep. 2023 May;13. doi:10.1038/s41598-023-32664-8.