

Brain function and connectivity extracted from EEG recordings

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Outline



- EEG recordings
- Event Related Potentials (ERPs)
- Brain Connectivity
 - ✓ What is brain connectivity?
 - ✓ EG connectivity
 - ✓ Case studies on EEG connectivity
 - ✓ Graph Theory
 - ✓ Examples

Outline



EEG recordings

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EEG recordings



- Our brains are continuously working
- Biochemistry exchanges between cells produce small electrical activity when the neurons communicate among them.
- A single electric signal from neuron to neuron is not recordable but when millions of neurons synchronize, the electric field generated can be measured from the scalp
- These electroencephalographic (EEG) signals are transmitted through tissue, bone, and hair before they are recorded, and by then its amplitude is very attenuated (easily corrupted by artifacts)
- Characteristic frequency ranges and spatial distributions (correlated with functional states of the brain)

Delta, theta, alpha (mu), beta, gamma



EEG TECHNICAL FEATURES



✓ NUMBER OF ELECTRODES

- Will determine the amount of information that we can measure from the brain
- Commonly, the number of "recording" electrodes ranges between 8 and 128
- EEG systems used in research typically have 64 electrodes or more
- In addition to these electrodes, we usually need to add:
 - One reference: an electrode that is used to subtract the common mode noise from the recording electrodes
 - One ground electrode
- A higher number of electrodes will allow more detailed measurements from different brain areas
- High-density EEG are required for ICA or inverse modelling
- However, the increase in the number of electrodes comes with an increase in the cost and the complexity of both the experimental set-up and the data analysis





EEG TECHNICAL FEATURES



✓ EEG AMPLIFIER

- Responsible for accommodating, amplifying and converting the analog electrical signals captured by the scalp
 electrodes into digital signals that can be processed by a computer
- EEG sampling rate (a common sampling rate is 256Hz)
 - □ EEG bandwidth: 0.5 80 Hz
 - According to the Nyquist theorem, the minimum sampling rate to measure activity at 80Hz will be 160Hz
- **Resolution:** Number of bits used to encode the analog EEG signal voltage values into discrete numbers
- Input rage
 - □ Maximum amplitude that can be recorded before saturation
 - □ The input-referred noise is the noise generated by the circuitry of the amplifier even in the absence of input signal and should be as low as possible to avoid contaminating the signal
- Power supply: cable-powered or battery-powered (duration and mobility)
- Connectivity: Wired or wireless-communication (mobility)

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EEG recordings

Event Related Potentials (ERPs)

- Brain Connectivity
 - ✓ What is brain connectivity?
 - ✓ EG connectivity
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 - ✓ Examples

ERP



- EEG records the electrical activity of the cortex. Event-related potentials (ERP) are specific periods of the EEG that reflect the cortex's response to different stimuli:
 - Cognitive events (visual, auditory ..)
 - Motor response/intention (MRCP)
 - Electrical or magnetic (somatosensory evoked potentials, SEP)
- They can be described as scalp-recorded voltage fluctuations that are time-locked to an event
- Each stimulus produces an evoked potential embedded in the EEG





NOMENCLATURE



There are different ERPs associated with different local peaks, which are named using a **letter and a number**

- The **letter** indicates the **polarity** of the potential:
 - P: positive peak
 - N: negative peak
- The number represents the time (in ms) after the stimulus when the ERP appears (latency).
 For instance, the N100 is a negative potential that appears 100 ms after the event.



• In some cases, they can be named differently depending on their function, such as error-related negativity (ERN) (when the subject makes an error and she/he corrects) or the no-go N2 (in a go/no-go task)

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TYPES OF ERPs



EXOGENOUS: early waves (<100 ms of the stimulus onset) that depend largely on the **physical properties** of the stimulus. Related to **sensory processing** and they are considered obligatory, thus they have clinical value as a **test of the integrity of the subcortical sensory pathways** ex: N100 that appears when a stimulus is presented

ENDOGENOUS: late waves (>100 ms of the stimulus onset) that reflect the **manner** in which the **subject evaluates the stimulus** (psychological effects of the stimulus). Therefore, it is considered a form of **controlled brain processing**

ex: P300 visual/auditory stimulus involved in processing information

IMPORTANT!! an ERP component does not exist independently of the specific experimental context in which it is measured!

EEG Background is huge noise for ERP

- Each stimulus produces an evoked potential embedded in the EEG
- Since ERP are generally subtle in EEG, averaging of many epochs is needed to make them distinguishable
- Assumption: ERP amplitude adds constructively and EEG background noise diminishes destructively
- Each stimulus is followed by ERPs and every epoch is called trial or repetition
- SNR is increased \sqrt{N} times in amplitude (RMS) being *N* the number of trials









There are two main strategies on ERP analysis:



AEP Case study: Eriksen Flanker task stimuli



- Participants were required to respond to the center letter of a 5 letter array, designated as "target" with either a left-hand or right-hand response.
- Additional letters flanking the target letter either
 - favored the target response (compatible trials, HHHHH or SSSSS called congruent) or
 - primed the other response (incompatible trials, HHSHH or SSHSS called incongruent).
- Participant can realize to make an error and can correct it \rightarrow ERN has been associated with the conscious

detection of the commission of the error.

Stimulus	Type of Stimulus
ННННН	Congruent
SSHSS	Incongruent
SS <mark>S</mark> SS	Congruent
HHSHH	Incongruent

Grand mean average of 9 subjects (response locked)



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Grand mean average of 9 subjects (response locked)



How many trials are necessary?

















How many trials are necessary?



Influence of the number of repetitions/epochs on peak and latency calculated from the average epoch.



AEP: Visual ood-ball task





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time (ms)

MOVEMENT RELATED CORTICAL POTENTIAL

- They are a type of ERP related to the movement, independently if it is self-initiated or stimulus-related.
- They are **characterized** by **the maximum amplitude** and the **onset of the wave**. MRCPs appear for **1.5 or 2s** before the trigger onset and 0.5 to 1s afterwards and it is mainly located at channel Cz
- The amplitude ranges between 5 and 30 μ V and only occurs at frequencies around 0-5 Hz •





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Borràs et al. 2022

SENSORY MOTOR RHYTHMS (SMR)



- ٠ They reflect **changes** in the **activity** of local interactions between main neurons and interneurons during motor intention and execution in the **frequency domain**
- They are considered to **indicate activation and subsequent recovery** of the motor cortex during the process of • planning, execution and completion of the voluntary movement







Borràs et al. 2022

Even in MOTOR IMAGERY?







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Borràs et al. 2025

Is this affected by injury? (iSCI)





SINGLE-TRIAL ANALYSIS



Singe-trial analysis allows to

- Capture trial-by-trial variability → factors like fatigue, different attention or emotion along the experiment have influence on the subject performance
- Evaluate dynamic processes of brain activity
- Analyze rare events :
 - > AEPs suppresses of the unrelated component to the time-locked event markers
 - > AEPs can enhance artefacts time-locked with the external event (i.e. ocular/muscular artefacts)
- Enhance of statistical analysis power introducing new time-frequency features
- Analyze information at high frequencies not smoothed by averaging \rightarrow Connectivity studies
- Assess phase-based measures such as PLV, IC,. Cross-Frequency Coupling (CFC) ...

Single trial analysis is very suitable when individual variability, temporal dynamics, high frequency or rare events are of interest.



SINGLE-TRIAL ANALYSIS



Methodology:

the European Union



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- Time-frequency analysis: 2.
 - Short-Time Fourier Transform (STFT), Hilbert Transform (HT), Wavelet Transform (WT), Stockwell Transform (ST, or S-Transform)
- Time & frequency resolution limitations: 3.
 - Heisenberg uncertainty principle, or Cone of influence (COI)
- Feature extraction: 4
 - Based on magnitude and phase information
 - e.g. Relative power, spectral entropy, median frequency, inter-trial phase coherence (ITPC), phase-locking value (PLV), ...
- Feature averaging: 5.
 - Over time windows of interest: baseline, early/late response,...
- Statistical analysis on single-trial or averaged features. 6.

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Brain Connectivity

- ✓ What is brain connectivity?
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 - **EEG** connectivit
 - Studies on ELS connectivity
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What is brain connectivity?

- HYBRID NEURO
- Brain connectivity spans multiple scales, from microscopic connections between individual neurons to macroscopic networks that connect distinct brain regions
- The coexistence of two mechanisms (segregation and integration) provides very diverse and integrated information that shows a great complexity of patterns.
 - Segregation: specialized neurons grouped together to form segregated/separated zones
 - Integration: these zones are activated in coordination during different cognitive states

It has been hypothesised that the brain coordinates the flow of information dynamically by changing the strength, pattern, or the frequency with which different brain areas engage in oscillatory synchrony.

Caudate nucleus Internal capsule Globus pallidus Putamen Claustrum Insula Corpus callosun Lateral ventricle Choroid plex Form Third contriel Medial medullary lamin Intermediate mas Third ventrice Optic track mamillari Amygdaloid nucleus

Thalamus

What is brain connectivity?

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Brain connectivity is not static! Its patterns change over time



What is brain connectivity?



Our brain Brain connectivity is not static! Its patterns change over time

- Changes as we age
- Is shaped by our experiences, environment, genetics, etc.



0-3 explosive growth4-11 pruning/refining12-18 consolidation



Refining and strengthening (integration and efficiency)



Loss of neural connections (especially white matter tracts)



Types of brain connectivity?

- Anatomical connectivity anatomic connextions physical pathways between neurons
- Functional connectivity
 statistical relationships dependencies across
 different brain regions
- Effective connectivity cause-effect interactions between brain regions

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EEG connectivity



linea	ir Ma		Different Approaches	
	n VS	onlinear	time domain information-theoretic domain	
static	MSS	dynamic	frequency domain pairwise	
			multivariate model based w	
Eurodod by	Grant agre	ement	mouer-paseu 2	

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EEG connectivity



A Tutorial Review of Functional Connectivity Analysis Methods and Their Interpretational Pitfalls <u>Bastos & Schoffelen 2015</u> A Tutorial Review of Connectivity Analysis in EEG Data: State of the Art and Emerging Trends <u>Chiarion et al 2015</u>





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EEG connectivity Cross-correlation



the concept of **FC** was used by **Karl Friston** on neuroimaging data

assessed via **correlation** or **covariance** (time)

statistical connections between the dynamic activity of neural units in different anatomical locations



Friston et al, 1993



EEG connectivity Coherence/Coherency

Coherence is the frequency domain equivalent to the time domain cross-correlation function

$$coh_{xy}(\omega) = \frac{\left|\frac{1}{n}\sum_{k=1}^{n}A_{x}(\omega,k)A_{y}(\omega,k)e^{i\left(\varphi_{x}(\omega,k)-\varphi_{y}(\omega,k)\right)}\right|}{\sqrt{\left(\frac{1}{n}\sum_{k=1}^{n}A_{x}^{2}(\omega,k)\right)\left(\frac{1}{n}\sum_{k=1}^{n}A_{y}^{2}(\omega,k)\right)}}$$



EEG connectivity Coherence/Coherency

COH estimates the similarities in the frequency content of two signals combining both amplitude and phase synchrony information



Close relatives

phase-slope index (PSI)

imaginary part of the coherency (IC)

Nolte et al., 2004



Nolte et al., 2008 Grant agreement no. 101079392 the European Union



EEG connectivity

Amplitude envelope correlation

Estimates the correlation based on the amplitude of the time series

Three-steps procedure:

- 1- Orthogonalization of each time series
- 2- Computation of power envelopes





3- Calculation of Pearson correlation between *log*-transformed power envelopes

EEG connectivity Phase Synchronization



Quantifies the relationship **between rhythms**

instantaneous phase extracted from signals $|n \emptyset_1 - m \emptyset_2| < const$

not affected by instantaneous amplitude

Rosenblum et al., 1996



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suitable tool for analysing the
interaction between brain units,
especially when the interaction is too
weak to be detected by other measures



EEG connectivity Phase Synchronization

Intuitive concept of phase synchronization



- Timing is important (not amplitude)
- *Consistency* in phase difference, not relative phase, is important (but relative phase is relevant)
- Synchronization is dynamic over time (by changes in frequency)



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Tutorial by Mike Cohen



EEG connectivity

Phase Synchronization/Synchronization likelihood

Phase-based connectivity metrics



SL estimates the likelihood of a system which is at the same state at two different times, and another system will also be in the same state at these times

PLI quantifies the asymmetry of the phase difference distributions of two time series (proposed to overcome SL limitations)

 $PLI_{X,Y} = |\langle sign \sin(\Delta \phi_{X,Y}) \rangle|$

Ruiz-Gómez 2022



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EEG connectivity Phase Locking Value

Same as coherence, but normalizing signals (unit amplitude in the Fourier domain)

$$plv_{xy}(\omega) = \frac{\left|\frac{1}{n}\sum_{k=1}^{n}1_{x}(\omega,k)1_{y}(\omega,k)e^{i\left(\varphi_{x}(\omega,k)-\varphi_{y}(\omega,k)\right)}\right|}{\sqrt{\left(\frac{1}{n}\sum_{k=1}^{n}1_{x}^{2}(\omega,k)\right)\left(\frac{1}{n}\sum_{k=1}^{n}1_{y}^{2}(\omega,k)\right)}}$$
$$= \left|\frac{1}{n}\sum_{k=1}^{n}e^{i\left(\varphi_{x}(\omega,k)-\varphi_{y}(\omega,k)\right)}\right|$$
Lachaux et al.

PLV looks for latencies at which the phase difference between the signals varies little across trials

., 1999

Close relatives

Phase Lag Index (PLI)

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Weighted Phase Lag Index (wPLI)

Vink et al., 2011



EEG connectivity Phase Lag Index



Vink et al., 2011

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EEG connectivity Mutual Information

$$H(X) = -\sum_{x} p(x) \log(p(x))$$

$$H(X,Y) = -\sum_{x,y} p(x,y) \log(p(x,y))$$

$$MI_{xy} = I(X, Y) = H(X) + H(Y) - H(X, Y)$$
$$= \sum_{x} \sum_{y} p(x, y) \log\left(\frac{p(x, y)}{p(x)p(y)}\right)$$



Kraskov et al., 2004



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EEG connectivity Mutual Information



- SD conserves all the original data statistical properties but the property of interest.
- CMIF is calculated from original data and SD (many times) and, then, subtracted to get the final CMIF which measures the non-linear coupling/connectivity





Alonso et al, 2007

EEG connectivity Mutual Information



Amplitude adjusted Fourier transform method (AAFT):

- Preserving the magnitudes of the FT in order to conserve first and second order statistics (linear properties)
- changing randomly the phases of the FT to remove nonlinear properties; and
- transforming back to the time domain.



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Alonso et al, 2007



EEG connectivity Granger Causality/Transfer Entropy

What about **directionality/causality**?

X Granger-causes Y if predicting Y based on past Y and past X **performs better** than predicting solely on past Y

Granger 1969

Transfer entropy is a version of mutual information operating on conditional probabilities

Schreiber 2000

Granger causality and transfer entropy are equivalent for Gaussian variables
<u>Barnett et al., 2009</u>

$$TE_{x \to y} = \sum_{x_{n+1}} p(y_{n+1}, y_n, x_n) log \left(\frac{p(y_{n+1}, x_n, y_n) p(y_n)}{p(x_n, y_n) p(y_{n+1}, y_n)} \right)$$

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Alonso et al., 2015

- What is brain connectivity?
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Drug Effect: alprazolam Mutual Information

Linear and nonlinear components present opposite trends

Objective

Describe short-term changes caused by alprazolam

Results

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Alprazolam induced significant changes in EEG connectivity in comparison with placebo.

Linear changes were negatively correlated and nonlinear changes were positively correlated with drug plasma concentrations; the latter showed higher correlation coefficients.

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Drug Effect: Ayahuasca Transfer Entropy





Alonso et al., 2015

Drug Effect: Ayahuasca

Transfer Entropy



Alonso et al., 2015

0,881



TE

0,834

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Schizophrenia Coherence, PLV



To explore the coupling patterns of brain dynamics during an auditory oddball task in schizophrenia (comparing between after and before the stimulus)



Bachiller et al., 2015

Results

SCH patients fail to change their coupling dynamics between stimulus response and baseline when performing an auditory cognitive task

Different behaviour is observed in controls

This may reflect impaired communication among neural areas.







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Grant agreement no. 101079392 the European Union



Rett Syndrome Coherence, Mutual Information

Objective

investigate the effect of different types of repeated cognitive stimulation in RTT patients on EEG brain connectivity

Results

Active Task (AT) leads to increase of nonlinear couplings (suggesting a nonlinear functional structure consequence of active stimulation).

Gaming activities may elicit greater attention and increased functional connectivity among brain regions.





Tost et al., 2024

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lacksquare

What is a network



A mathematical representation of a real-world complex system, such as the brain

Defined by:

- Nodes (vertices): represent brain regions, electrodes...
- Links (edges) between pairs of nodes: represent anatomical, functional, or effective connectivity

All networks are represented by their **adjacency (connectivity) matrices**. Rows and columns denote nodes, matrix entries denote links.







Types of networks

Depending on the weight of the links:

- 1. Weighted networks: links have information about connection strengths
- 2. Binary networks: just denote the presence or absence of connections

Depending on the directionality of the links:

- Directed networks: no symmetric adjacency matrices; show anatomical or causal directionality (tract tracing studies)
- 2. Undirected networks: symmetric adjacency matrices (other neuroimaging techniques: EEG, MEG, fMRI...)

structural datasets: tract tracing effective datasets: inference of causality from functional data

weighted directed networks



weighted undirected networks structural datasets: diffusion MRI, structural MRI functional datasets: functional MRI, MEG, EEG



Brain networks



Different major networks control brain function both during task processing and while at rest



Graph Theory parameters



An individual graph theory parameter may characterize one or several aspects of global and/or local brain connectivity

Basic concepts and notation:

- **N** is the set of all nodes in the network. **n** is the number of nodes
- *L* is the set of all links in the network. *I* is the number of links
- (*i*, *j*) is a link between nodes *i* and *j*
- **a**_{*i*,*i*} is the connection between nodes *i* and *j* for binary networks, $\mathbf{a}_{i,i} = 1$ when link (i,j) exists, $\mathbf{a}_{i,i} = 0$ otherwise for weighted networks, $\mathbf{a}_{i,i} = \mathbf{w}_{i,i}$ and $0 < \mathbf{w}_{i,i} < 1$



Rubinov and Sporns, 2010. 'Complex network measures of brain connectivity: uses and interpretations' Brain Connectivity Toolbox for MATLAB (brain-connectivity-toolbox.net)

Graph Theory parameters

<u>Measures of centrality</u>: based on node degree, quantify the total "wiring cost" of the network

Global strength (average node degree):

$$\mathbf{s} = \frac{1}{N} \sum_{i \in N} s_i = \frac{1}{N} \sum_{i \in N} \sum_{j \in N} w_{ij}$$



2. <u>Measures of functional integration:</u> average shortest path length between

all pairs of nodes in the network. Quantify the ability to rapidly combine specialized information from distributed brain regions (global connectivity)

Characteristic path length:

$$L = \frac{1}{n} \sum_{i \in \mathbb{N}} L_i = \frac{1}{n} \sum_{i \in \mathbb{N}} \frac{\sum_{j \in \mathbb{N}, j \neq i} d_{ij}}{n-1}$$



Graph Theory parameters



3. <u>Measures of functional segregation:</u> based on

triangle counts, quantify

- The presence of information hubs based on the number of triangles
- the ability for specialized processing to occur within densely interconnected groups of brain regions (local connectivity)

Fraction of node's neighbours that are also neighbours of each other

Clustering coefficient:

$$C = \frac{1}{n} \sum_{i \in \mathbb{N}} C_i = \frac{1}{n} \sum_{i \in \mathbb{N}} \frac{2t_i}{k_i(k_i - 1)}$$





Higher transitivity/clustering coefficient: greater number of connections within the module (forming triangles)

Normalization Procedure



To obtain measures that are independent of network size, a **randomization procedure** should be carried on:

- Generate a set of surrogate random networks derived from the original networks by randomly reshuffling the edge weights preserving the basic characteristics of the original network (size, density, and degree distribution)
- 2. Compute the desired parameter in the surrogate networks (at least 50 or more)
- 3. Obtain the **parameter ratio** by dividing the original value and the mean value of the random graphs





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igodol



Chen J. et ál., 2019. 'Topological reorganization of EEG functional network is associated with the severity and cognitive impairment in Alzheimer's disease'



Alzheimer's disease and MCI (I)

Chen J. et ál., 2019. 'Topological reorganization of EEG functional network is associated with the severity and cognitive impairment in Alzheimer's disease'



0.3

1.

2.

Schizophrenia



Gomez-Pilar et ál., 2017. 'Functional EEG network analysis in schizophrenia: Evidence of larger segregation and deficit of modulation'

Auditory odd-ball 3-stimulus paradigm (P300) EEG

- 1. Connectivity: event-related Coherence (ERC) from CWT
- 2. Graph metrics: clustering coefficient (CIC), path length (PL)

Results:

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- More segregated cortical activity prior to stimulus onset for patients (higher CIC in baseline)
- Less segregated cortical activity in response for patients (lower CIC in response)
- Complex cognitive capacities for patients (larger integration activity between distant brain regions is needed)

Granh Parce and

no.10107939392

C: controls SP: schizophrenia Patients FEP: first episode patients CP: chronic patients



Alzheimer's disease and MCI (II)



Ruiz-Gómez SJ et ál., 2021. 'A new method to build multiplex networks using Canonical Correlation Analysis for the characterization of the Alzheimer's disease continuum'

Resting state EEG

1. Connectivity: PLI

2. Graph metrics: global strength (s), characteristic path length (L) and clustering coefficient (C)

- Lower integration in AD networks (higher L) compared to HC subjects
- Decreases in global segregation for the AD group (lower C)





Schizophrenia



Ruiz-Gomez and Mijancos, 2025

TMS: Repetitive Single Pulses

- 1. Connectivity: PLV from CWT coefficients
- 2. Graph metrics: Global strength (G) and path length (L)

Results:

- <u>Baseline:</u> SCZ networks are more connected: higher values of G and lower values of L
- <u>Response</u>: more similar networks between SCZ and HC. The cerebral response to the TMS stimulus is different for each group



Motor execution



Ruiz-Gomez and Borràs, 2025

Six different movements performed during few seconds repetitively.

- 1. Connectivity: PLV from CWT coefficients
- 2. Graph metrics: Global strength (G), Cluster correlation (C) and path length (L)





BIOsignal Analysis for Rehabilitation and Therapy (BIOART) Group

Thanks!











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