

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?
	- \checkmark EG connectivity
	- \checkmark Case studies on EEG connectivity
	- ✓ Graph Theory
	- ✓ Examples

Outline

EEG recordings

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	- ✓ Examples

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:
	- \Box 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)
	- \Box EEG bandwidth: 0.5 80 Hz
	- \Box 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
	- \Box 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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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)**

Stim

- 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

*Obtained from Sarma et al 2020

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)

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.

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?

ERN

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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

 -15

0

100

200

300

400

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500 time (ms)

600

700

800

900

1000

MOVEMENT RELATED CORTICAL POTENTIAL @ NEURO

- 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 µV** and only occurs at frequencies around 0-5 Hz

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Borràs et al. 2022

SENSORY MOTOR RHYTHMS (SMR)

- 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

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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 :**
	- \triangleright AEPs suppresses of the unrelated component to the time-locked event markers
	- \triangleright 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.

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SINGLE-TRIAL ANALYSIS

Methodology:

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

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EBrain Connectivity

- ✓ What is brain connectivity?
- \checkmark EG connectivity
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- \checkmark Graph Theory
- ✓ Examples
- **What is brain connectivity?**
	- **EEG connectivi**

• **Studies on EEG connectivity**

- **Graph Theory**
- **Examples**

What is brain connectivity?

-
- 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.

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What is brain connectivity?

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Brain connectivity is not static! Its patterns change over time

What is brain connectivity?

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

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

 $0 - 3$ explosive growth 4 – 11 pruning/refining 12 – 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 relationshipsdependencies across different brain regions
- **Effective connectivity** cause-effect interactions between brain regions

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- **Examples**

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A Tutorial Review of Functional Connectivity Analysis Methods and Their Interpretational Pitfalls [Bastos & Schoffelen](https://doi.org/10.3389/fnsys.2015.00175) 2015 **A Tutorial Review of Connectivity Analysis in EEG Data: State of the Art and Emerging Trends** Chiarion [et al 2015](https://www.mdpi.com/2306-5354/10/3/372)

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Cross-correlation EEG connectivity

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](https://doi.org/10.1038/jcbfm.1993.4)

Coherence/Coherency EEG connectivity

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

$$
coh_{xy}(\omega) = \frac{\left| \frac{1}{n} \sum_{k=1}^{n} A_x(\omega, k) A_y(\omega, k) e^{i(\varphi_x(\omega, k) - \varphi_y(\omega, k))} \right|}{\sqrt{\left(\frac{1}{n} \sum_{k=1}^{n} A_x^2(\omega, k) \right) \left(\frac{1}{n} \sum_{k=1}^{n} A_y^2(\omega, k) \right)}}
$$

Coherence/Coherency EEG connectivity

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., 2008](https://doi.org/10.1103/PhysRevLett.100.234101) [Nolte et al., 2004](https://doi.org/10.1016/j.clinph.2004.04.029)

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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

Quantifies the relationship **Phase Synchronization**

between rhythms

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

not affected by instantaneous amplitude

[Rosenblum et al., 1996](https://doi.org/10.1103/PhysRevLett.76.1804)

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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**

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](https://youtube.com/watch?v=MTPE4k8X2tk)

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)

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

Ruiz-Gómez 2022

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Phase Locking Value EEG connectivity

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

$$
plv_{xy}(\omega) = \frac{\left| \frac{1}{n} \sum_{k=1}^{n} 1_x(\omega, k) 1_y(\omega, k) e^{i(\varphi_x(\omega, k) - \varphi_y(\omega, k))} \right|}{\sqrt{\left(\frac{1}{n} \sum_{k=1}^{n} 1_x^2(\omega, k) \right) \left(\frac{1}{n} \sum_{k=1}^{n} 1_y^2(\omega, k) \right)}}
$$

$$
= \left| \frac{1}{n} \sum_{k=1}^{n} e^{i(\varphi_x(\omega, k) - \varphi_y(\omega, k))} \right| \qquad \text{Lachaux et al.}
$$

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

., 1999

Close relatives

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Phase Lag Index (PLI) Weighted Phase Lag Index (wPLI) [Stam et al., 2007](https://doi.org/10.1002/hbm.20346) **[Vink et al., 2011](10.1016/j.neuroimage.2011.01.055)**

Phase Lag Index EEG connectivity

[Vink et al., 2011](10.1016/j.neuroimage.2011.01.055)

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Mutual Information EEG connectivity

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

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

$$
MI_{xy} = I(X, Y) = H(X) + H(Y) - H(X, Y)
$$

= $\sum_{x} \sum_{y} p(x, y) \log \left(\frac{p(x, y)}{p(x)p(y)} \right)$

[Kraskov et al., 2004](https://doi.org/10.1103/PhysRevE.69.066138)

Mutual Information EEG connectivity

Alonso et al, 2007

• SD conserves all the original data statistical properties but the property of interest.

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• 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

Mutual Information EEG connectivity

Amplitude adjusted Fourier transform method (AAFT):

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

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Alonso et al, 2007

Granger Causality/Transfer Entropy EEG connectivity

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](https://doi.org/10.2307%2F1912791)

Transfer entropy is a version of mutual information operating on conditional probabilities [Schreiber 2000](https://doi.org/10.1103/PhysRevLett.85.461)

Granger causality and transfer entropy are equivalent for Gaussian variables [Barnett et al., 2009](http://dx.doi.org/10.1103/PhysRevLett.103.238701)

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

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[Alonso et al., 2015](https://doi.org/10.1093/ijnp/pyv039)

- **What is brain connectivity?**
	- **EEG connectivi**
- **Studies on EEG connectivity**
- **Graph Theory**
- **Examples**

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](https://doi.org/10.1093/ijnp/pyv039)

Drug Effect: Ayahuasca Transfer Entropy

[Alonso et al., 2015](https://doi.org/10.1093/ijnp/pyv039)

TE 0,834 0,881

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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](https://doi.org/10.1088/1741-2560/12/1/016007)

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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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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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:

- **1. 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…)

weighted undirected networks structural datasets: diffusion MRI, structural MRI

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. *l* is the number of links
- *(i, j)* is a link between nodes *i* and *j*

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ai,j is the connection between nodes i and j for binary networks, ai,j = 1 when link (i,j) exists, ai,j = 0 otherwise for weighted networks, $a_{i,j} = w_{i,j}$ *and* $0 < w_{i,j} < 1$

57 *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

1. Measures of centrality: based on node degree, quantify the total "*wiring cost*" of the network

Global strength (average node degree):

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

2. Measures of functional integration: 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:

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

Graph Theory parameters

- **3. Measures of functional segregation:** 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:

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

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:

- 1. 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

- **What is brain connectivity?**
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- **Examples**

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'

 0.8 **ACI** Resting state EEG (eyes closed) AD₁ AD₂ 0.6 aver_CC MCI: mild cognitive impairment AD1: mild AD 1. Connectivity: Phase AD2: moderate to severe AD Coherence (PC) 0.2 2. Graph metrics: average delta theta alpha beta gamma clustering coefficient (aver_CC) **CC in alpha band**HC **MCI** AD₂ 0.6 cc 0.5

 0.4

 0.3

Schizophrenia

 0.5

p-value

C: controls

SP: schizophrenia Patients

FEP: first episode patients

CP: chronic patients

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 (ClC), path length (PL)

Response

Results:

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

Cluster coefficient spatial distribution Independent-samples t-test $C vs. CP$ FEP $C vs. SP$ C vs. FEP CP vs. FEP SP 0.5 **CLC CLC**

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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) 4 Results:

- 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:

- Baseline: SCZ networks are more connected: higher values of G and lower values of L
- Response: 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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