SIPF
Società Italiana di Psicofisiologia e Neuroscienze Cognitive

UNIVERSITÀ DEGLI STUDI DI BARI ALDO MORO

Neuroelectric-metabolic EEG-NIRS features in physiological and pathological conditions.

New frontiers in network physiology: novel models of bioelectric interactions for personalized treatments

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Dipartimento di Fisica di Bari

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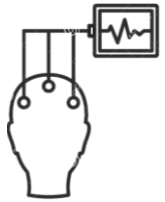

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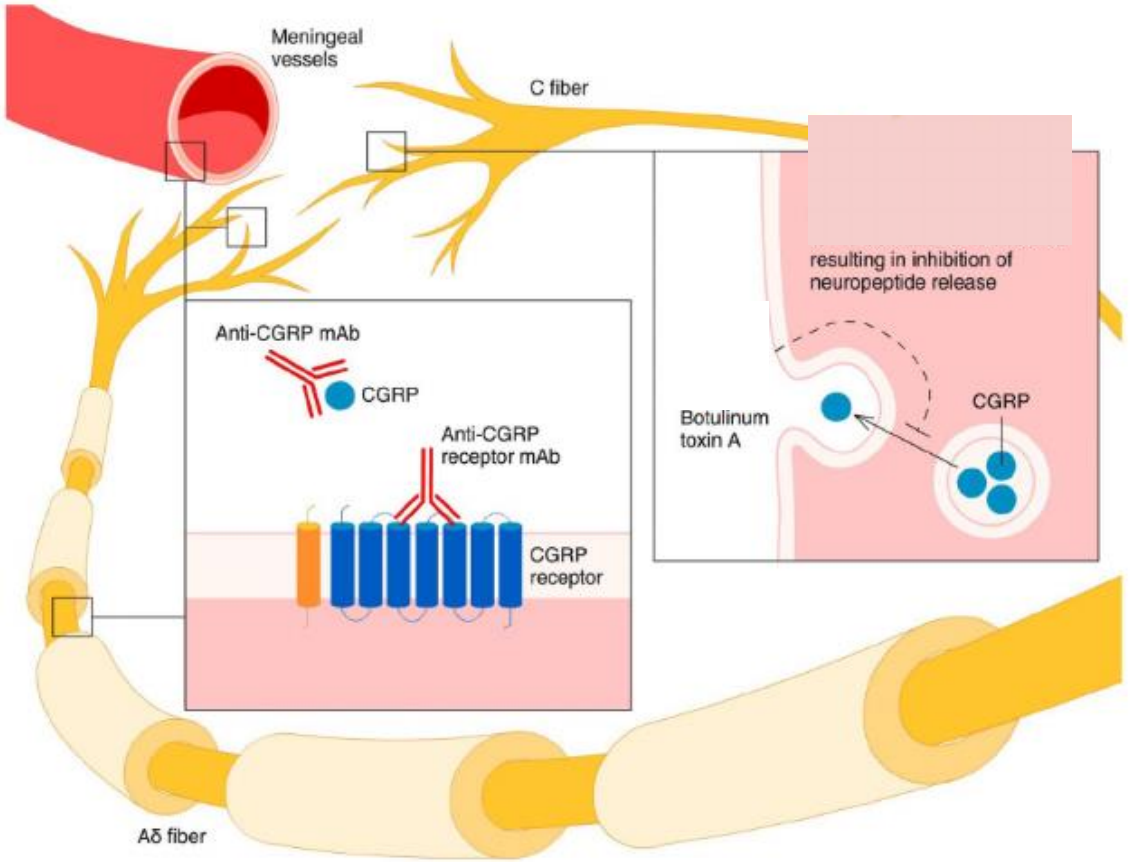
Introduction

The identification of Calcitonin Gene-Related Peptide (CGRP) as a possible target for migraine treatment has revolutionized the therapeutic scenario.

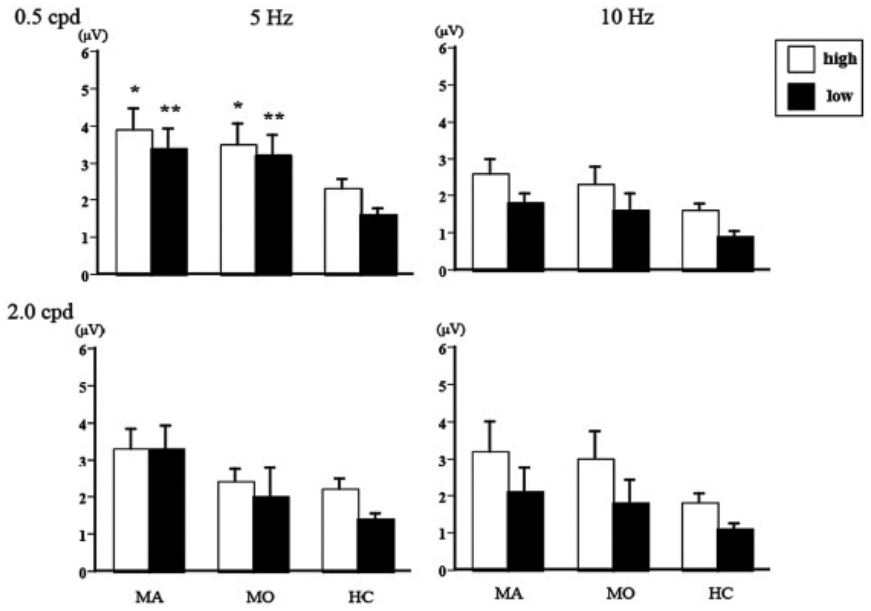


To date, all new therapies directed against CGRP or its receptor for the treatment of migraine have produced positive results.

Introduction

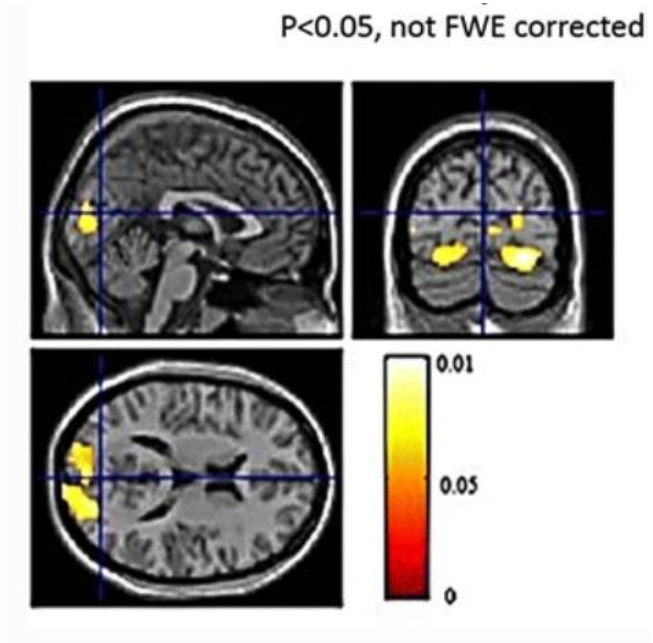
OCCIPITAL CORTEX IS A CRUCIAL SITE IN MIGRAINE: Increased amplitude of steady state visual evoked potentials, increased metabolic response and altered connectivity of occipital cortex were found

Abnormal visual processing in migraine with aura: A study of steady-state visual evoked potentials

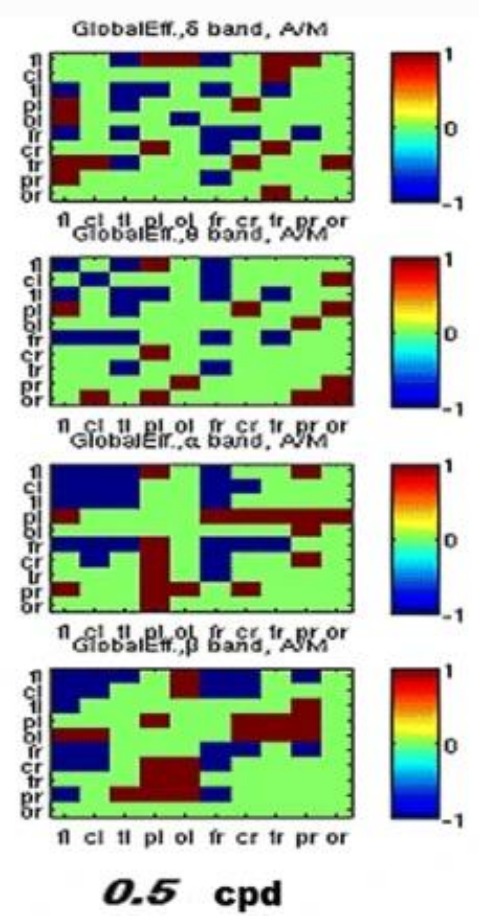


The mean amplitude at 5 and 10 Hz for 0.5 and 2.0 cpd and two different contrasts in migraine with aura (MA), without aura (MO) and healthy controls (HC)

(K. Shibita et al., Journal of the Neurological Sciences, 2008)



Statistical probability maps reporting the comparison of bold signal changes in migraine with aura vs migraine without aura



Comparison of global efficiency in migraine with aura vs migraine without aura

Brain networking analysis in migraine with and without aura

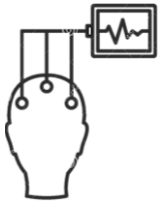
(M. De Tommaso et al., The Journal of Headache and Pain, 2017)

Introduction

CGRP antagonists act at peripheral level. How could they modify occipital cortex excitability in migraine?

In this study, our goal has been to test the effect of 3 Galcanezumab (GCA) therapy on migraine patients by evaluating cerebral electrical (Steady State Visual Evoked Potentials -SSVEPs) and hemodynamic activities (functional near infrared spectroscopy, fNIRS) during a visual stimulation

Data acquisition

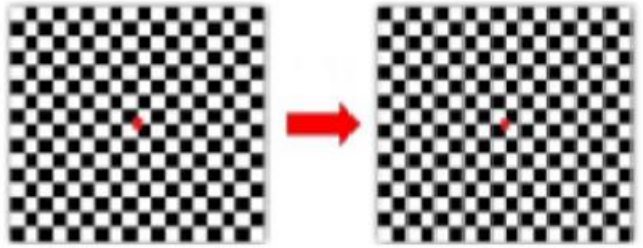


10 healthy volunteers and 15 drug patients were selected at the Headache Center of Applied Neurophysiology and Pain Unit of Bari Policlinico General Hospital from December 2020 to September 2022 during the routine clinical practice

Migraine patients underwent clinical and neurophysiological examination in basal condition (T0) , 1 hour after GCA injection (T1) and after 3 months of GCA treatment (T2). Controls were examined once.

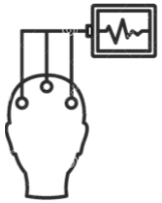
Patients received 240 mg of GCA the first time and then 120 mg monthly.

Checkboard pattern reversal stimulations of 60s preceded by 60 s of resting state were performed for each patient and for each condition.



At the time of the study inclusion, patients were having 8 days or more with migraine / month in the last 3 months, were assuming symptomatic drugs for more than 10 days/month and were experiencing resistance to at least three preventive drugs.

Data acquisition



	GENDER	AGE	DURATION	DIAGNOSIS	DRUGS	T0	DAYS/30	SIM/30	MIDAS	NRS	T2	DAYS/30	SIM/30	MIDAS	NRS
AI	F	29	20	MA	AED, AD, BB		13	13	79	10		17	16	113	10
BA	F	48	30	MA	AED, AD, BB,TB		12	12	26	7		8	8	12	4
DD	F	38	22	MA	AED,AD,CA		9	9	68	10		4	4	34	10
DE	F	47	25	CM	AED,AD,CA,TB		17	17	150	9		17	10	70	6
DI	F	48	25	MA	AED,AD,CA,BB		13	13	26	7		10	10	13	6
DL	F	47	24	MA	AED,AD		8	12	32	10		3	3	10	6
FA	F	57	40	CM	AED,AD,CA,TB		20	20	75	7		4	4	12	8
LE	F	42	30	CM	AED,AD,CA,BB,TB		27	27	30	8		6	6	10	6
MA	F	67	50	CM	AED,AD,CA,BB,TB		15	4	50	8		15	3	25	5
MO	F	47	30	CM	AED,AD,TB		25	25	56	8		12	10	25	7
MN	F	63	45	MA	AED,AD,CA,BB		10	12	5	6		5	0	0	4
PN	F	58	10	MA	AED,BB,AD		13	13	77	7		8	8	33	7
SM	M	56	30	CM	AED,BB,AD		15	15	108	10		5	5	50	8
Mean(SD)							15.5(8.7)	14.7(6.2)	60.1(39.2)	8.2(1.4)		8.7(5)	6.6(4.2)	31.3(31)	6.6(2)
T test							3.3	4.3	3.59	3.68					
p							0.006	0.001	0.004	0.003					

AED: antiepileptics-topiramate and/or valproate
AD: antidepressants-amitriptyline
BB: beta blockers-propranolol or atenolol
CA: calcium channel blockers-flunarizine;
TB: Botulin Toxin

MA: episodic migraine without aura
CM: Chronic Migraine

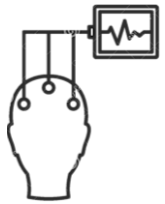
DAYS/30: average over 3 months of the number of headache days per month.

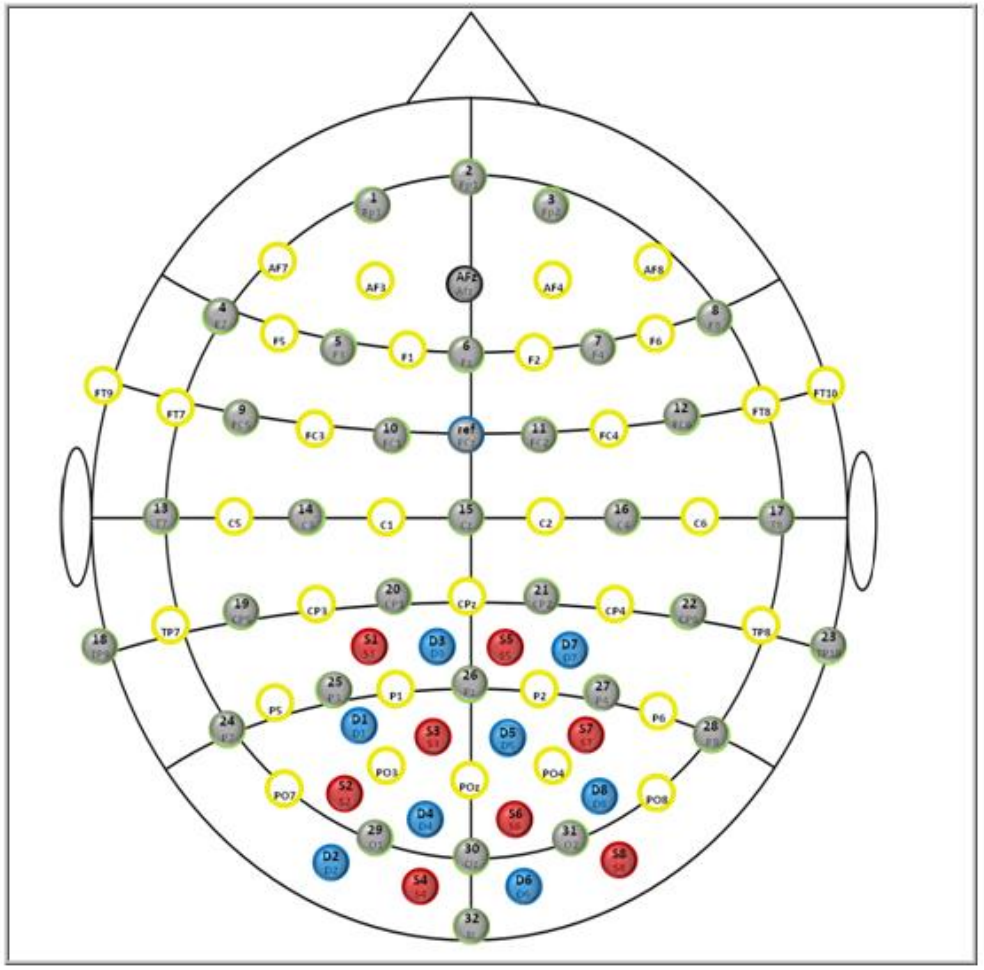
SIM/30: average over 3 month of the number of days per month with acute therapy

MIDAS: Migraine Disability Assessment, questionnaire measuring headache impact on patient's life.

NRS: Numerical Rating Scale (from 0 no pain to 10 maximal pain) describing headache intensity.

Data acquisition





Signal Acquisition

EEG data were acquired simultaneously with fNIRS data, using a co-recording cap and a black over-cap to mitigate possible interferences generated by ambient light on the fNIRS acquisition.

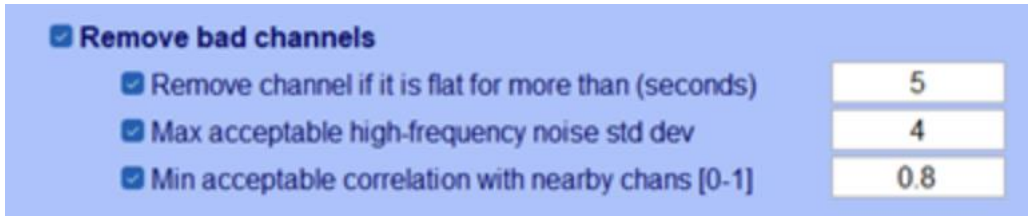
EEG data were recorded by 61 scalp electrodes, according to the enlarged 10–20 system (nasion as reference and Fpz as ground). Electrooculogram (EOG) was recorded, and EEG sampling rate was 256 Hz

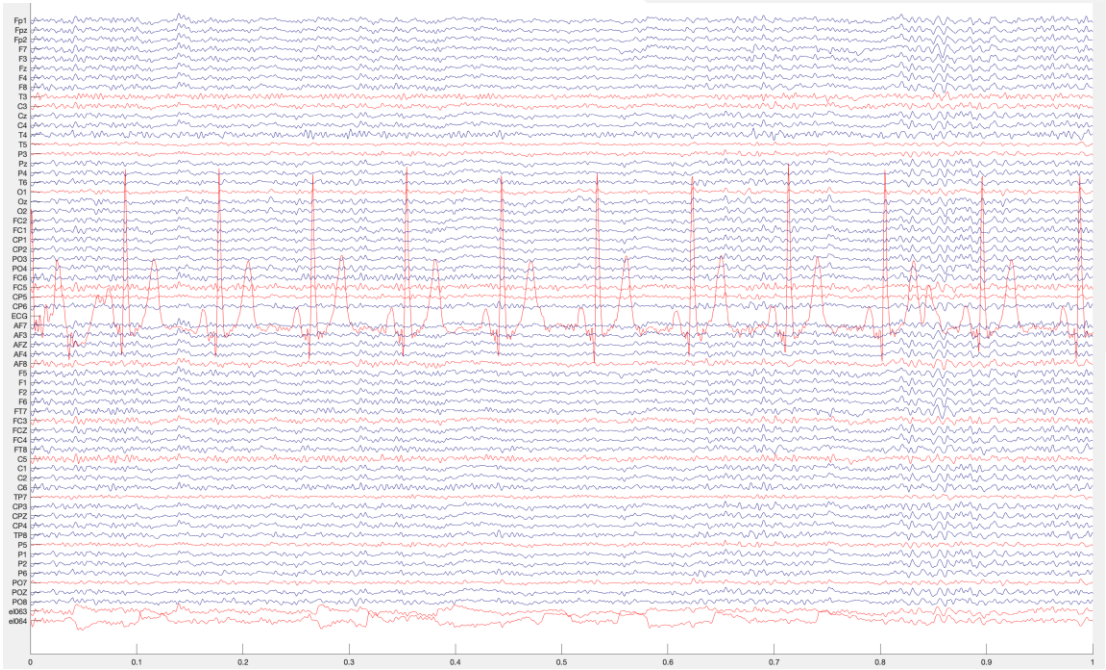
fNIRS data were recorded by 24 channels given by the arrangement of 8 sensors and 8 detectors. An inter-optode distance of 30 mm and a sampling rate of 7.8 Hz were used.

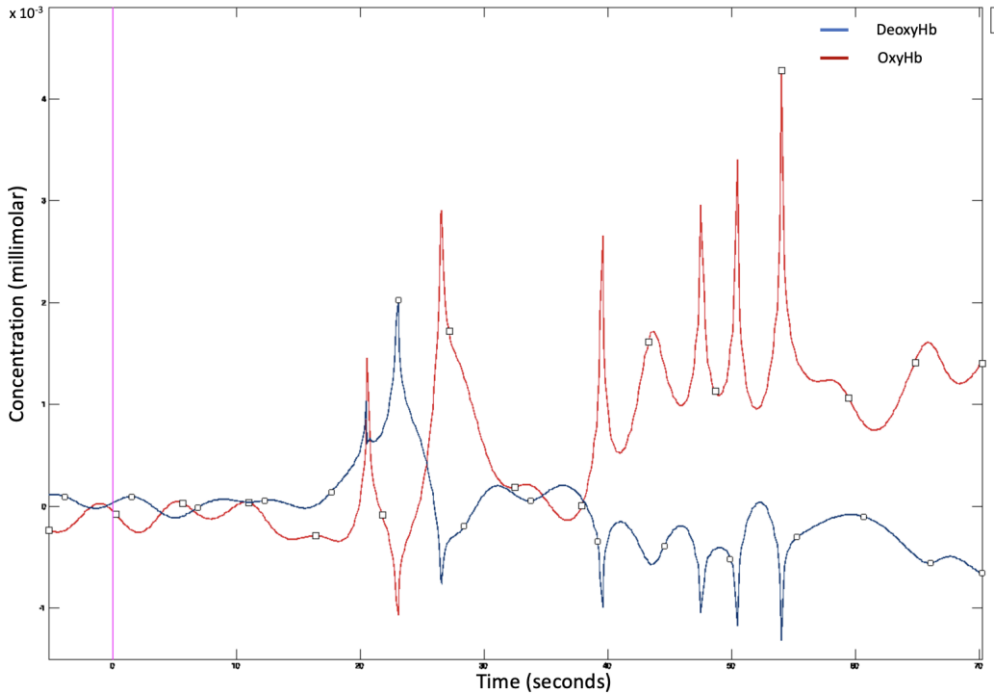
Data processing

EEG and fNIRS processing

EEG data were filtered between 1 and 30 Hz and artifact subspace reconstruction method were used to correct continuous data and reject bad channels and data segments. bad channels were interpolated and re-referenced to the average.







fNIRS data quality was evaluated checking the gain factor (ampliefied photo-current<8) and the coefficient of variation (100 times the standard deviation over the signal mean<7.5)

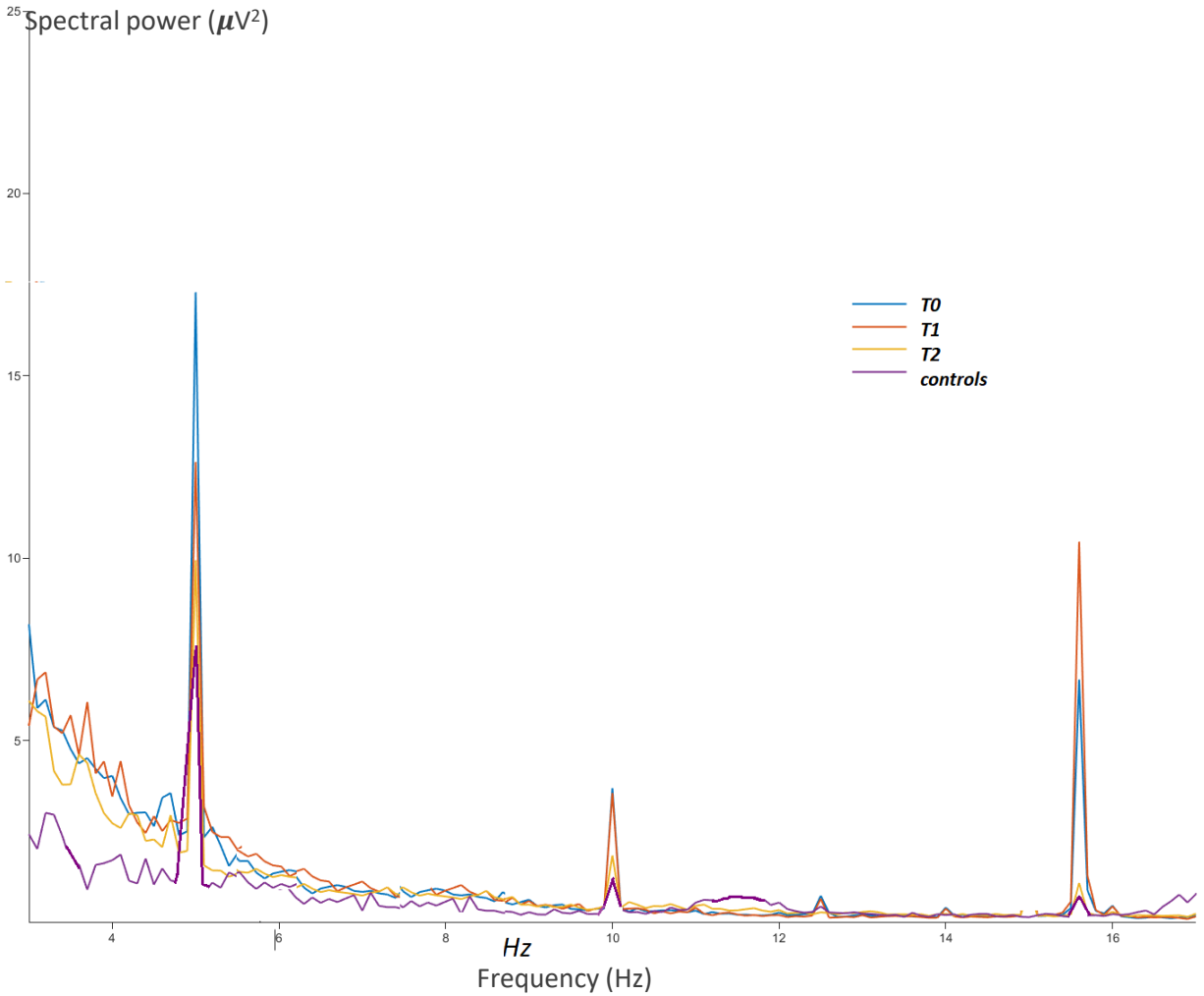
Discontinuities and artifacts were removed, and signals were filtered (0.08-0.2).

Signals were converted to optical intensities which in turn were converted to oxy and deoxyhemoglobin concentration changes. Baseline was corrected.

Statistical Analysis

EEG analysis

We estimated the spectral power using the Fast Fourier Transform (FFT), averaging 10 sec samples from the recording session. Then, we applied a baseline correction in the frequency domain.



The spectral power of fundamental frequency (F) at 5 Hz, double frequency (2F) at 10 Hz and triple frequency at 15 Hz was averaged over parieto-occipital electrodes (P3, P4, Pz, O1, Oz and O2)

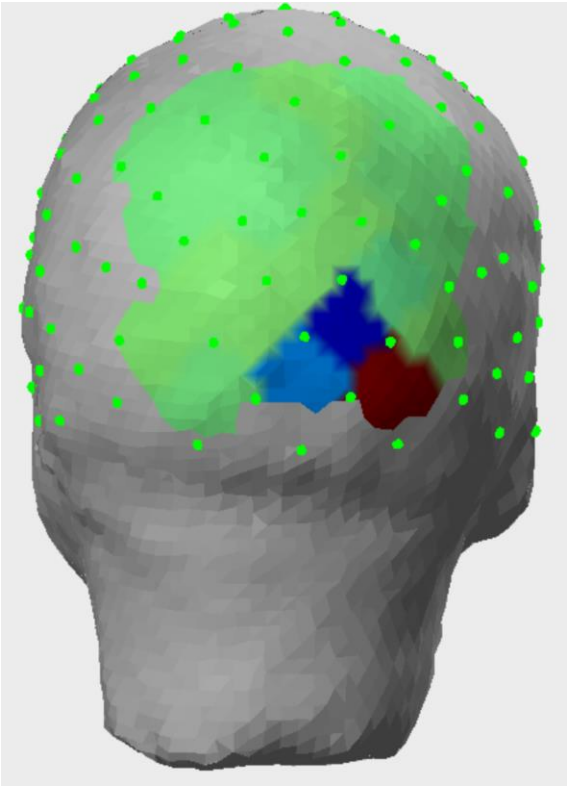
We performed an ANOVA test with Bonferroni correction to evaluate statistical differences in the spectral power computed among T0, T1, T2 and controls

Finally, We carried out a topographical analysis at F, 2F and 3F powers for the different conditions.

Statistical Analysis

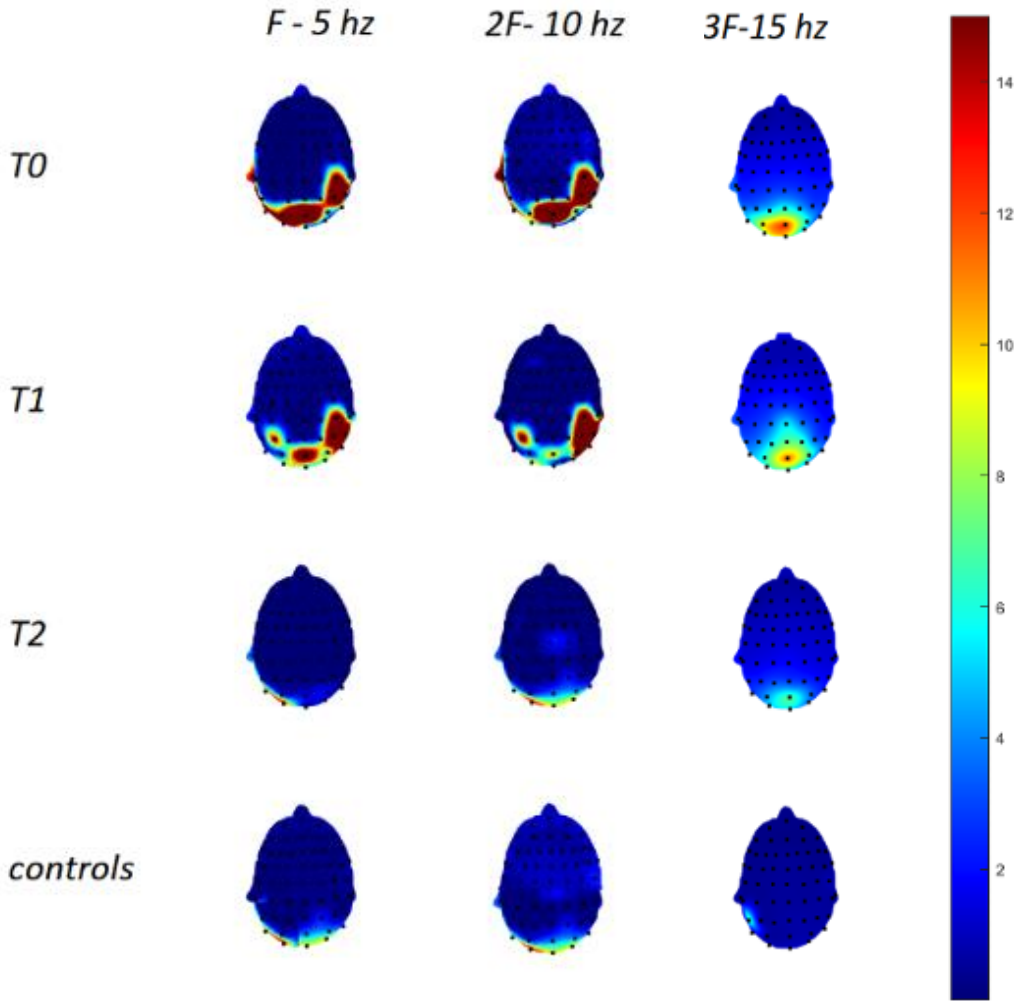
fNIRS analysis

To compute the degree of hemodynamic activation of each channel compared with the baseline, we used a Generalized linear model (GLM), choosing the Hemodynamic Response Function (HRF) to model the response during the visual stimulation.



the results obtained from the GLM were used to evaluate, using the Student's t test, if there were fNIRS channels wherein oxy and deoxyhemoglobin changed in a statistically significant way (p-value < 0.05 corrected for multiple comparison) for the comparisons: T0 vs T2, T1 vs T2, Controls vs T2, Controls vs T0.

Results

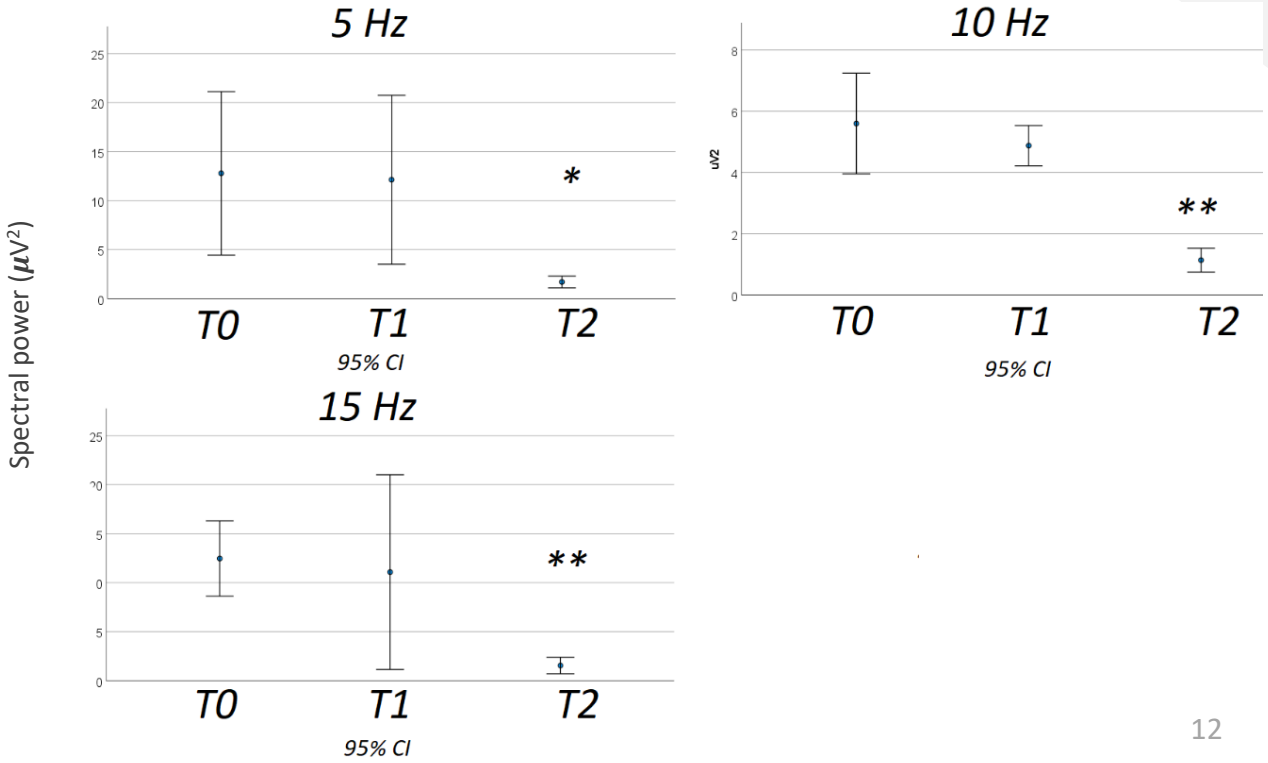


(M. De Tommaso, M. La Rocca et al., The Journal of Headache and Pain, 2022)

EEG results

We can observe a significant reduction of the spectral power at T2, as compared to T0 and T1 conditions for all the 3 frequencies (* p<0.05; ** p<0.01).

The spectral power was significantly lower also in controls compared with migraine patients at T0 and T1

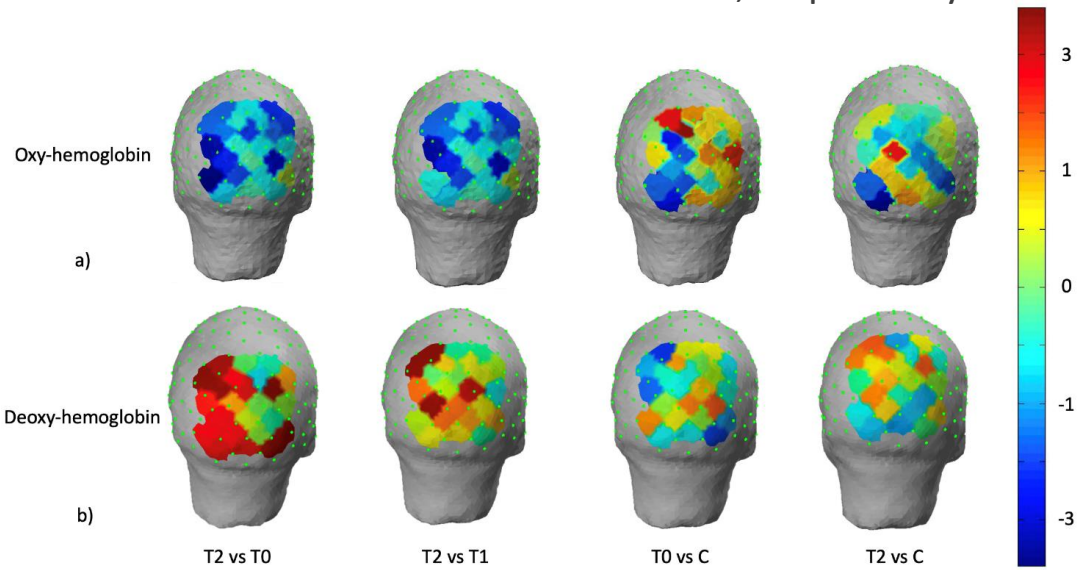


Migraine case study

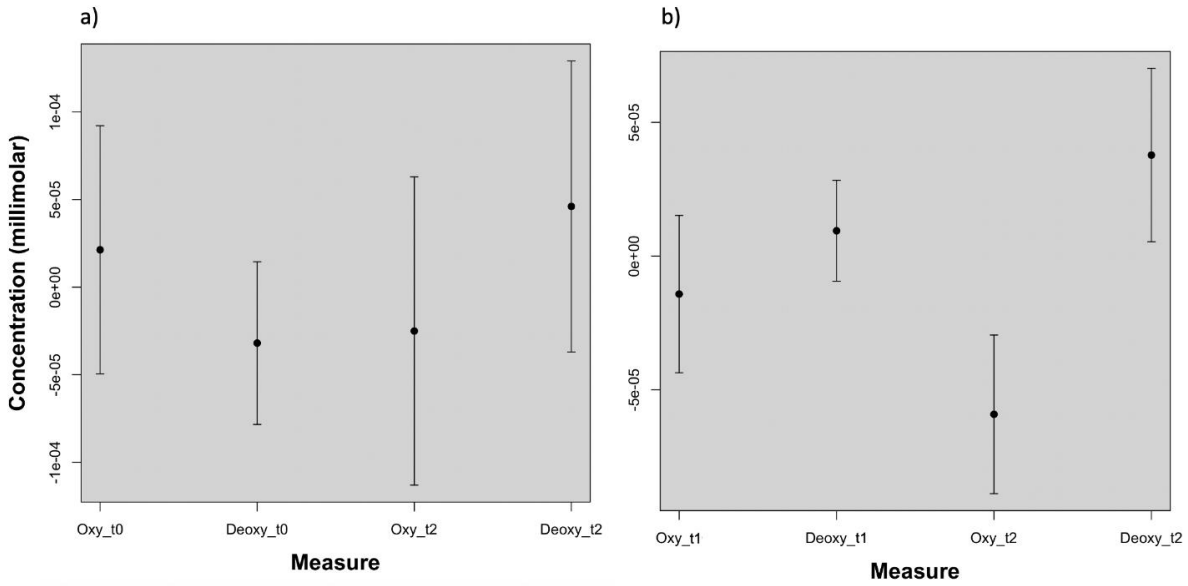
Statistical analysis for fNIRS data

(M. De Tommaso, M. La Rocca et al., The Journal of Headache and Pain, 2022)

T-statistic map of the brain regions wherein the significant increases and decreases in deoxy and oxyhemoglobin concentrations are indicated in intense red and in intense blue, respectively.



Plots reporting the values of oxy and deoxyhemoglobin levels averaged over the channels proved to be significant for the comparisons T0 vs T2 and T1 vs T2

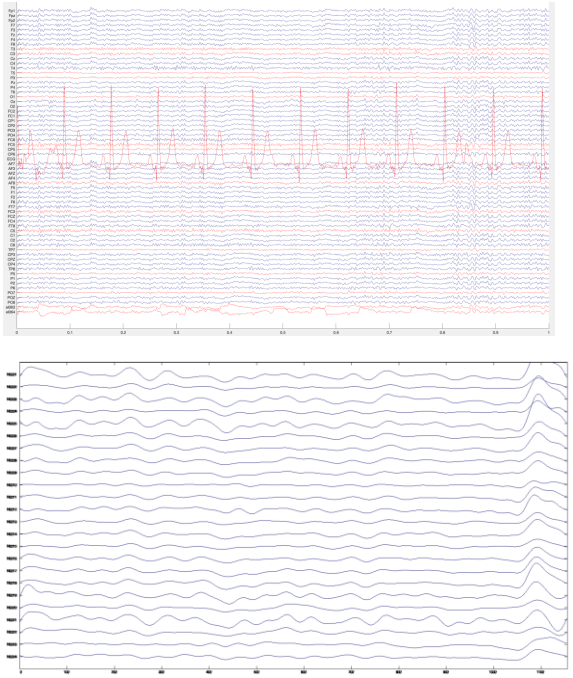


The paired Student's t test showed a significant reduction of the oxyhemoglobin concentration at T2 compared with T0 and T1 and a significant increase in deoxyhemoglobin at T2 on different occipital channels ($p<0.05$).

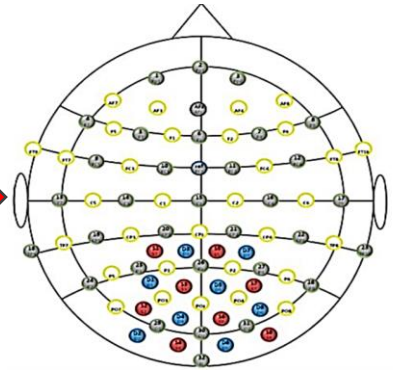
Connectivity study

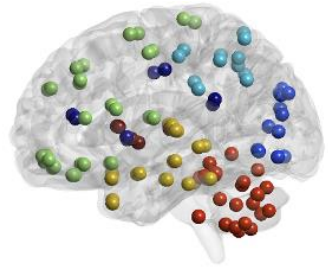
EEG connectivity

Processed EEG and fNIRS signal

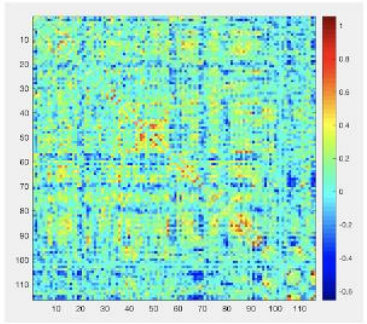


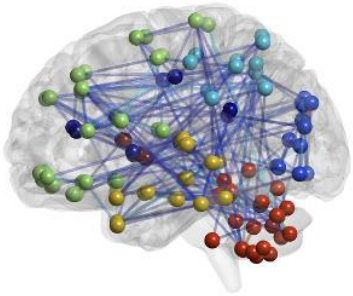
EEG electrodes to define network nodes





magnitude squared coherence was used to define network links





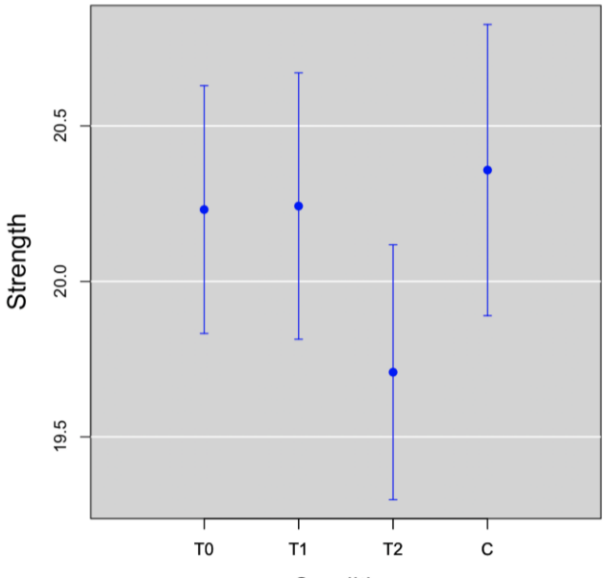
Network metrics:
Strength
Global Efficency
Clustering Coefficient

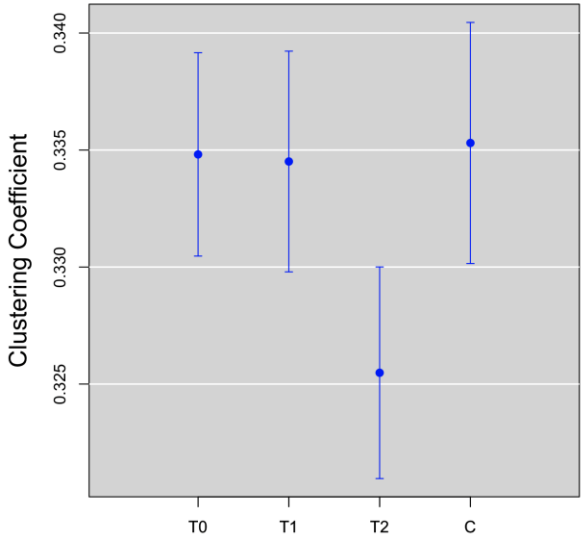
For each EEG frequency band (delta, theta, alpha, beta), we built a weighted network

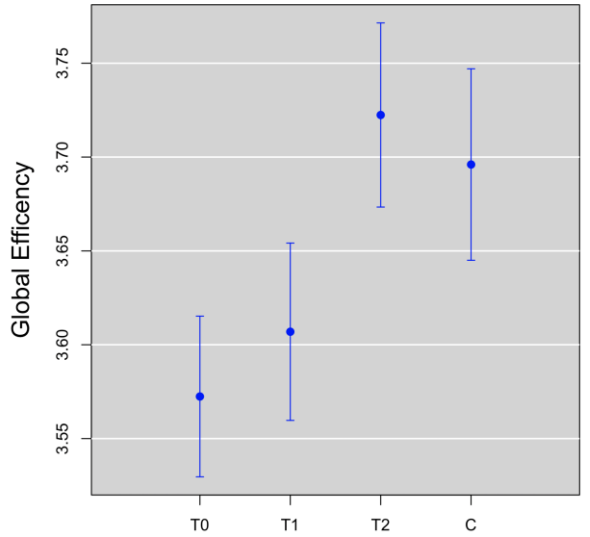
Connectivity study

EEG connectivity

Theta band (4-7 Hz)

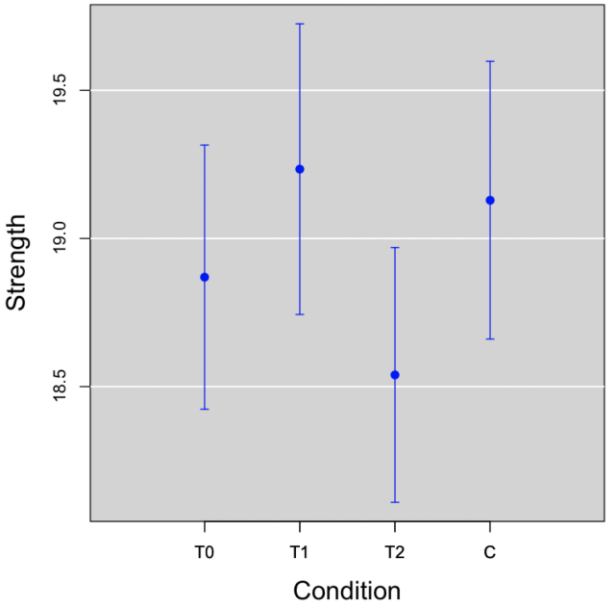


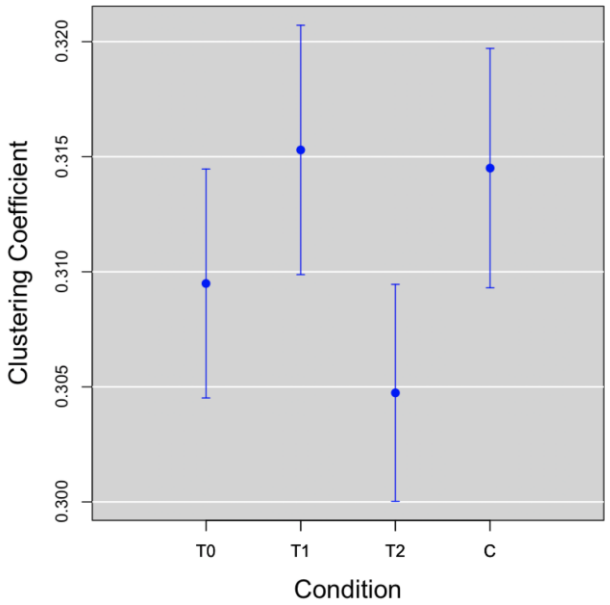


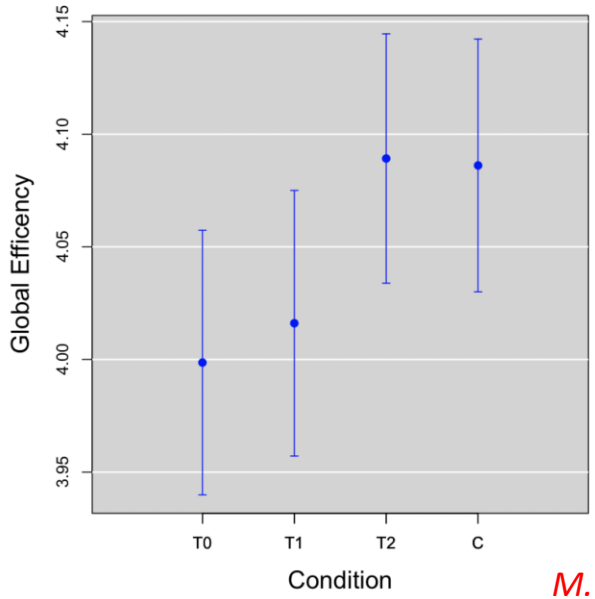


For both bands, GCA has the effect to increase network integration and decrease node coeherence and network segregation.

Alpha band (8-12 Hz)







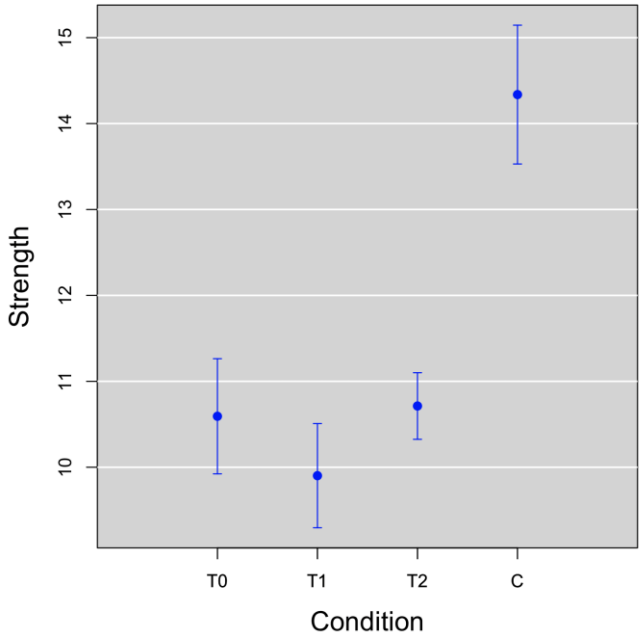
The beneficial effect seems to be due to the increase of the communication efficency of the network

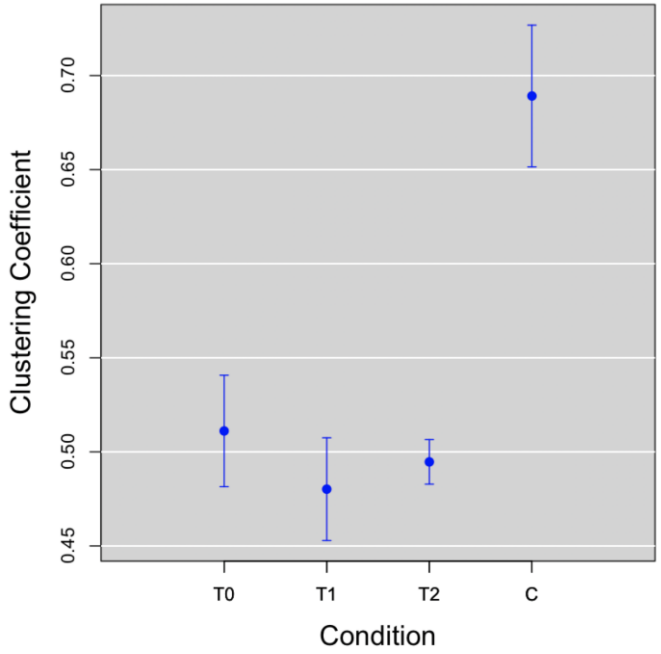
M. La Rocca et al., Cephalalgia, 2023)

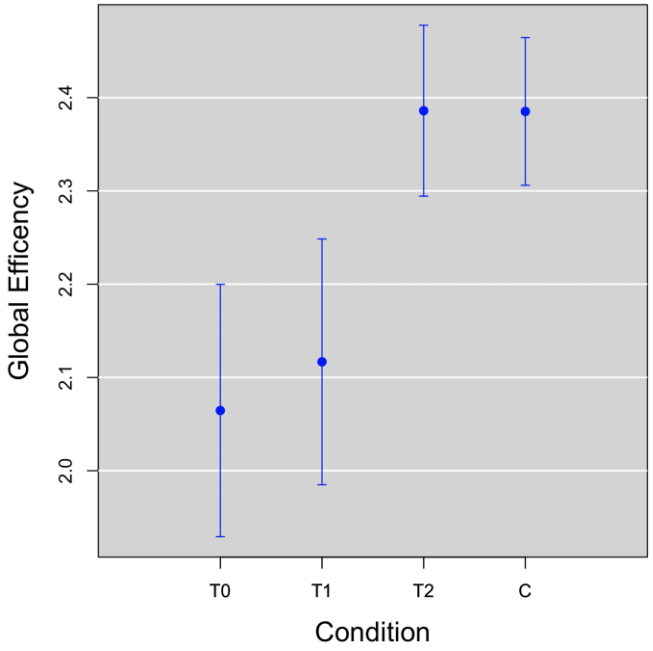
Connectivity study

NIRS connectivity

GCA seems to have the effect to increase integration on fNIRS networks making global efficiency comparable with that of the controls' fNIRS networks







This fNIRS network tendency is like that found for EEG networks

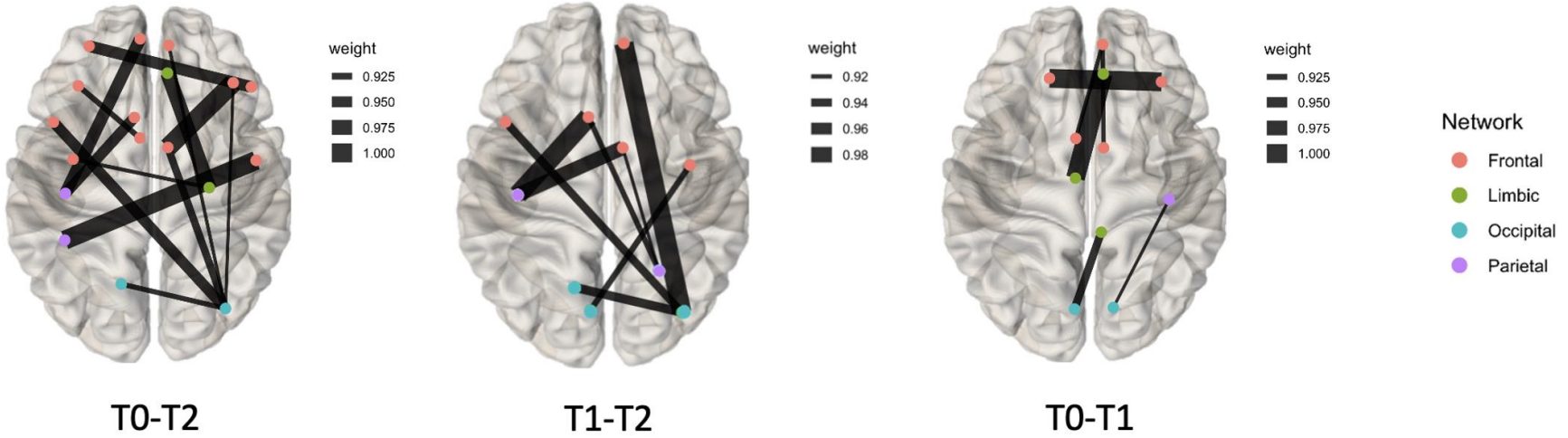
No statistical differences were found in network strength and clustering coefficient between T0, T1 and T2. On the contrary, controls' network strength and clustering coefficient is significantly greater.

Communication efficency seems a crucial factor in migraine *(M. La Rocca et al., Cephalalgia, 2023)*

Connectivity study

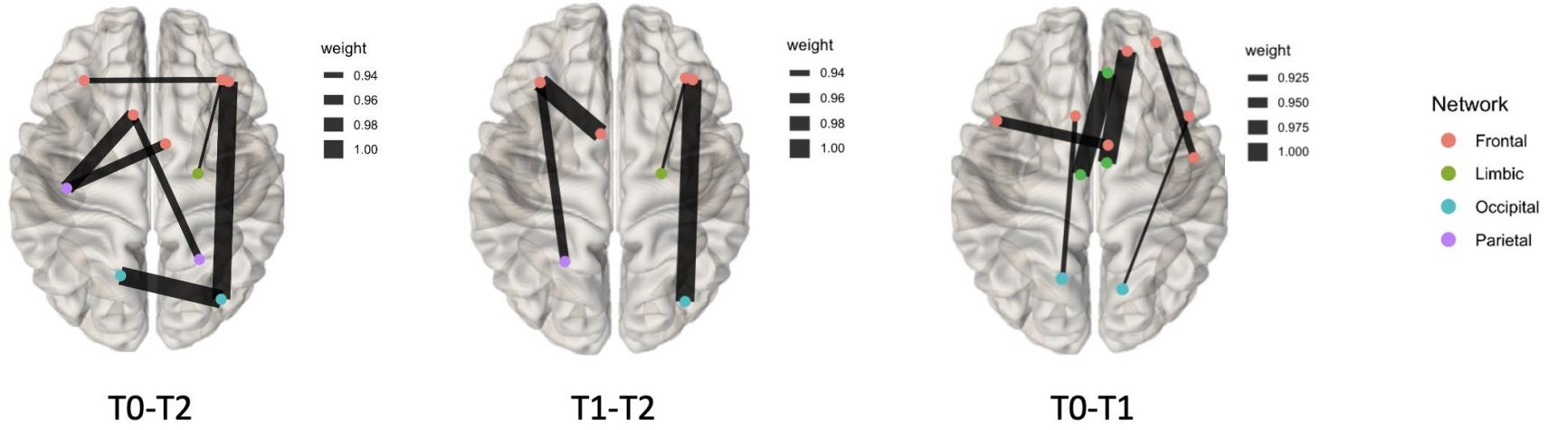
EEG connectivity

Differences in coherence between conditions greater than the 90th percentile of the distribution of the differences



Theta band (4-7 Hz)

T0-T2 T1-T2 T0-T1



Alpha band (8-12 Hz)

T0-T2 T1-T2 T0-T1

M. La Rocca et al., Cephalalgia, 2023)

The differences between T0 and T2 and T1 and T2 tend to be more intense, more numerous and for these differences the more intese links tend to connect the frontal and the occipital cortex confirming the role of the occipital cortex in migraine.

Connectivity study

Correlation with clinical data

- Our patients showed on average a reduction in headache days, acute drug consumption and disability. However, the association between clinical and neurophysiological effects of GCA was not significant.

- Correlation between the strength of connections and headache intensity at T2 might indicate that a minor anti-nociceptive effect could influence network connections

- The anti-correlation between global efficiency and monthly drug use might indicate that patients with less frequent use of symptomatics show a better global efficiency.

These correlations, although not exhaustive could support the hypothesis that an efficient and specific antinociception in the periphery, could potentially act on the brain network dysfunctions.

Conclusions and future steps

- This is the first study attempting to evaluate the effects of GCA in migraine patients by studying the electrical and metabolic activity of the occipital cortex (crucial site for migraine pathogenesis) using EEG and fNIRS data.

- After 3 months of treatment, we observed, in different areas of the occipital cortex, a significant decrease in electrical and hemodynamic activity that, from the comparison with a control group, seems to revert into normal ranges suggesting a medium-term effect of GCA.

- Connectivity anlysis gives an add value to the study underlying that migraine patients' brain networks have a reduced communication efficiency which is restored after 3 moth of GCA treatment.

- Connectivity analysis highlights also the correlation between network strength and anti-nociceptive effect, and the anti-correlation between global efficiency and monthly drug use.

- The poor correspondence with clinical efficacy after 3 months may be explained by the fact that the possible central effect of GCA could be slower than the peripheral mechanisms.

Conclusions and future steps

- To shed light on this aspect and best investigate GCA short and long effects, we are going to acquire more data and we plan to consider a longer and a shorter follow-up.
- We plan to use connectivity analysis to study the mutual interaction between the electrical and hemodynamic signals as well as the mutual interaction among the different EEG frequency bands.
- Since the methodology to study brain connectivity is very versatile, we are also considering to apply it to other scopes:

Transcranial direct current stimulation (tDCS) effects on cerebral vasomotor reactivity

Stroke
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Stroke Association
A Division of American Heart Association

Cortical Neuromodulation Modifies Cerebral Vasomotor Reactivity
Fabrizio Vernieri, Giovanni Assenza, Paola Maggio, Francesco Tibuzzi, Filippo Zappasodi, Claudia Altamura, Marzia Corbetto, Laura Trotta, Paola Palazzo, Matilde Ercolani, Franca Tecchio and Paolo Maria Rossini

tDCS effects on on cortical hemodynamic activity in fibromyalgia

brain sciences

Effect of Single Session of Anodal M1 Transcranial Direct Current Stimulation—TDCS—On Cortical Hemodynamic Activity: A Pilot Study in Fibromyalgia

by Marianna La Rocca [1,2], Livio Clemente [3], Eleonora Gentile [3], Katia Ricci [3], Marianna Delussi [3] and Marina de Tommaso [3,*]

UNIBA team

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Physics Department
“M. Merlin”

Thank you for your attention