Reti complesse ed epilessie

Ferruccio Panzica
Ferruccio.panzica@istituto-besta.it

Struttura di Ingegneria Biomedica,
UO Neurofisiopatologia ed Epilettologia diagnostica
Fondazione IRCCS Istituto Neurologico C. Besta, Milano

FONDAZIONE I.R.C.C.S. ISTITUTO NEUROLOGICO CARLO BESTA

Sistema Sanitario Regione Lombardia

Revised terminology and concepts for organization of seizures and epilepsies: Report of the ILAE Commission on Classification and Terminology, 2005–2009

*†Anne T. Berg, ‡Samuel F. Berkovic, §Martin J. Brodie, ¶Jeffrey Buchhalter, #**J. Helen Cross, ††Walter van Emde Boas, ‡‡Jerome Engel, §§Jacqueline French, ¶¶Tracy A. Glauser, ##Gary W. Mathern, ***Solomon L. Moshé, †Douglas Nordli, †††Perrine Plouin, and ‡Ingrid E. Scheffer

Epilepsia, 51(4):676–685, 2010

Generalized epileptic seizures are conceptualized as originating at some point within, and rapidly engaging, bilaterally distributed networks.

Focal epileptic seizures are conceptualized as originating within networks limited to one hemisphere. They may be discretely localized or more widely distributed

BRAIN CONNECTIVITY

- **Interactions between distinct and remote brain regions** organized in functional networks underlie brain processes and functions.

- Abnormalities in the interactions of network components play a critical role in neurological and psychiatric disorders.

- Damage to specific functional connectivity networks can lead to distinct neurological syndromes.

- Functional recovery (brain reorganization) may depend on the topology and adaptability of these networks and their interactions.

Anatomical connectivity: set of physical or structural connections

Functional Connectivity: statistical measure of interaction between activities in different areas.

Causality between two or more regions.

who drives whom?

Effective Connectivity: defined as the influence that one neural system exerts on another.

It describes the dynamic directional interactions (causal effects) among brain regions.

It is model dependent and time dependent

Connectivity is commonly characterized by ***synchrony*** between activities in distinct regions

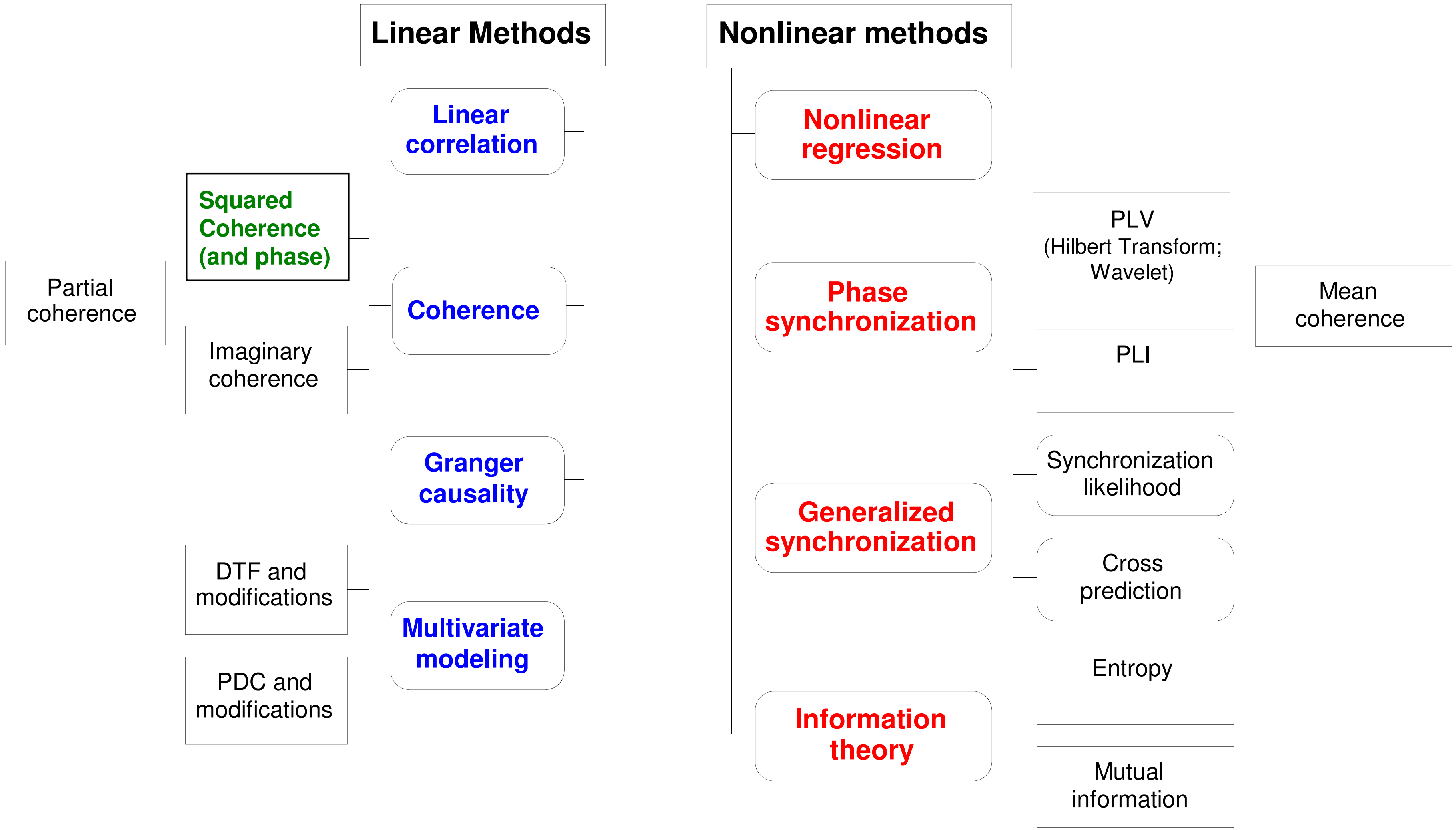
Synchrony measures the relation between the temporal structures of signals regardless of their amplitude.

Noise data: *2 signals are synchronized if the difference between their phases is nearly constant over a selected time window*

Couplings are:
- ✓ ***transient***
- ✓ ***dynamic*** (time-varying)
- ✓ ***frequency-specific***

Synchronization/connectivity: how to measure it?

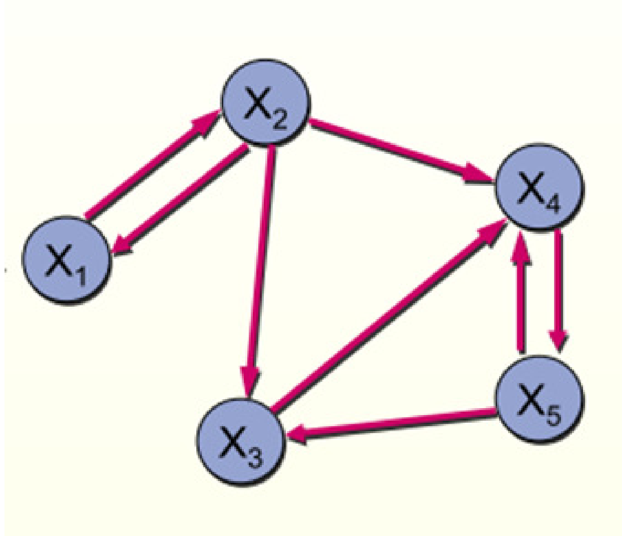
Several methods have been implemented, each having advantage and disadvantages, on the basis of the specific problem under analysis and of the assumptions about the underlying model of relationship between signals



Determining synchronization between all possible pairs of MEG sensors, HDEEG, EEG channels will produce huge matrices of correlation data, difficult to interpret and to handle statistically.

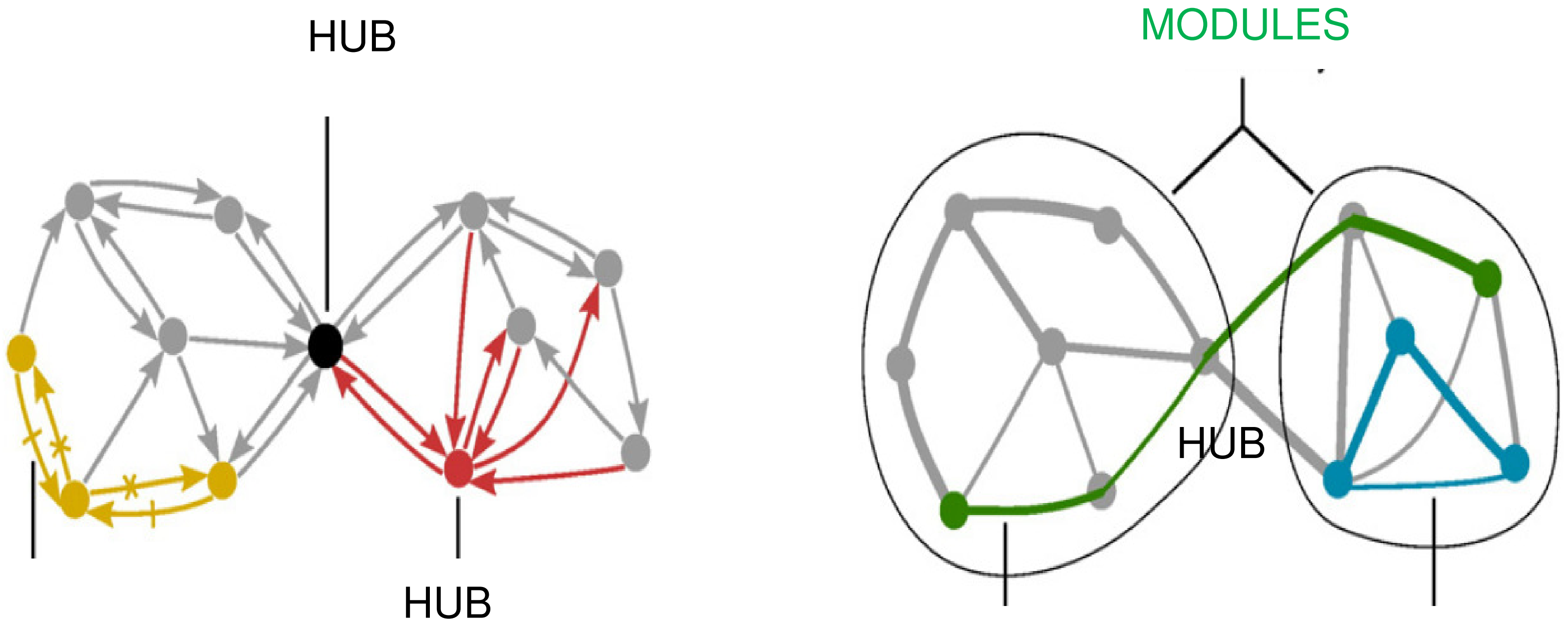
EEG: 19 channels → 342 measures
HDEEG: 128 channels → 16256 ”
MEG: 306 channes → 93330 ”

A network is a mathematical representation of a real-world complex system and is defined by a collection of nodes (vertices) and links (edges) between pairs of nodes.



Nodes in large-scale brain networks usually represent brain regions, while links represent anatomical, functional, or effective connections depending on the dataset

M. Rubinov, O. Sporns / NeuroImage 52 (2010) 1059–1069



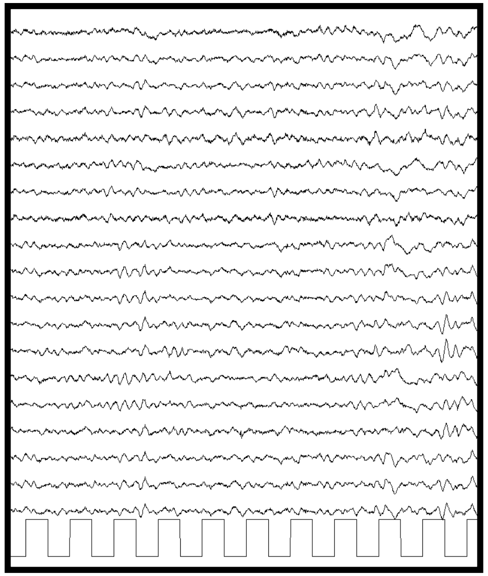
Two networks characteristics are increasingly studied in relation to epilepsy: “hubs” and “modules”.

Hubs are nodes with many connections and with a central position within a network. They are central for efficient communication.

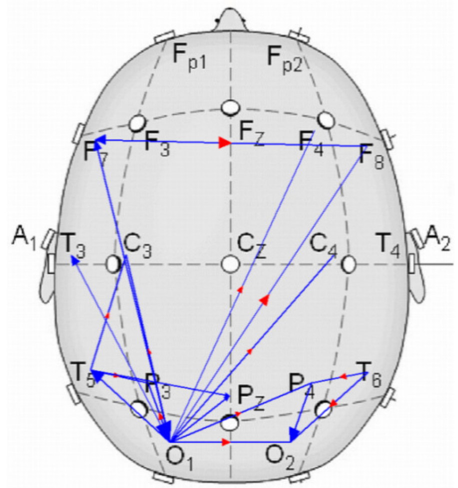
Modules are subnetworks that can be defined as a group of nodes that are more connected to each other than to other parts of the network

Experimental protocol

Multi-ch data acquisition and pre-processing.



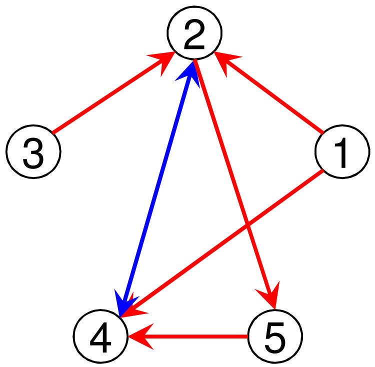
Measure of interaction, association,…. (synchronization) between couples of signals



Evaluation of strength and **<u>direction</u>** of connections.

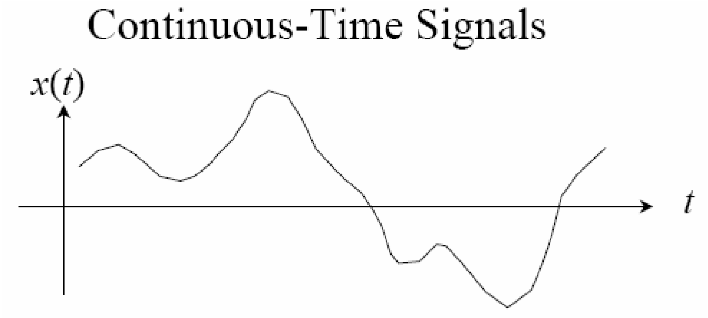
Graph-theory based indexes

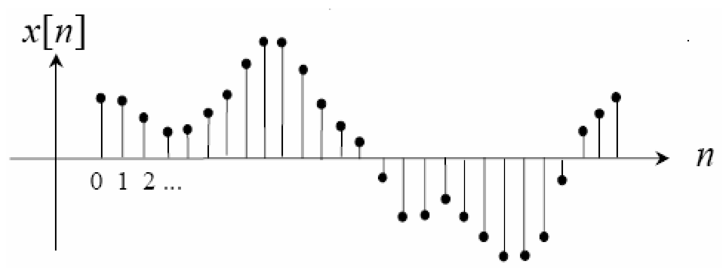
$$\begin{vmatrix} 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 1 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 1 & 1 & 0 & 0 & 1 \\ 0 & 1 & 0 & 0 & 0 \end{vmatrix}$$



Post-processing: statistics, classification,…. (event/resting; populations, follow-up)

Frequenza di campionamento =
= No. di conversioni effettuate in 1 s

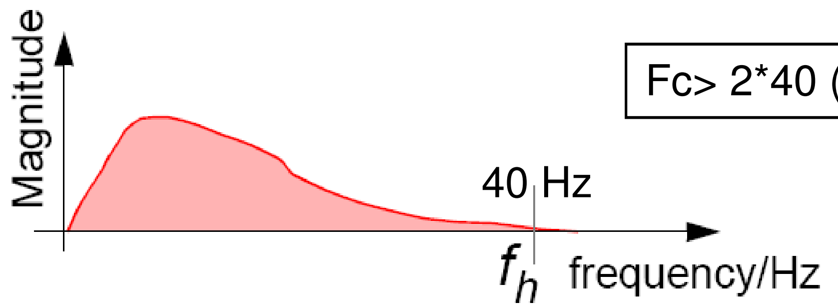




A quale frequenza dobbiamo campionare un segnale analogico per preservare le informazioni ?

Teorema di Nyquist (Shannon)

La frequenza di campionamento deve essere maggiore del doppio della più alta frequenza contenuta nel segnale analogico



Fc> 2*40 (=Fm) = 80 Hz

Prima della conversione ADC
frequenze > fc/2 devono essere eliminate

Segnale digitale: sottocampionamento

1. Definire il fattore di sottocampionamento
2. Filtrare il segnale per soddisfare il teorema del campionamento
3. Ridurre il numero di campioni

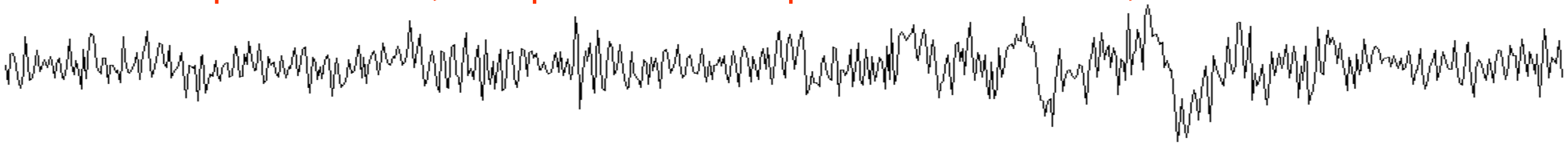
Aliasing

Originale, artefatto da alimentazione elettrica 50 Hz

P4-O2

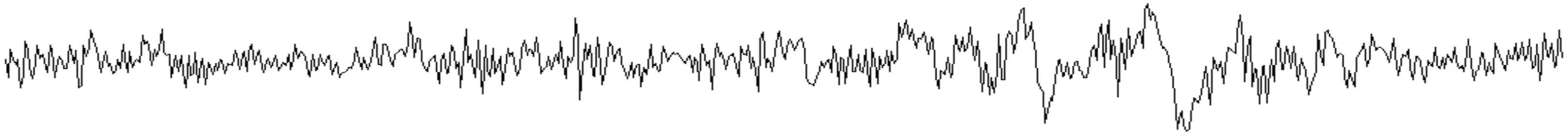
Sottocampionamento, Frequenza di campionamento 64 Hz; nessun filtro antialiasing

P4-O2

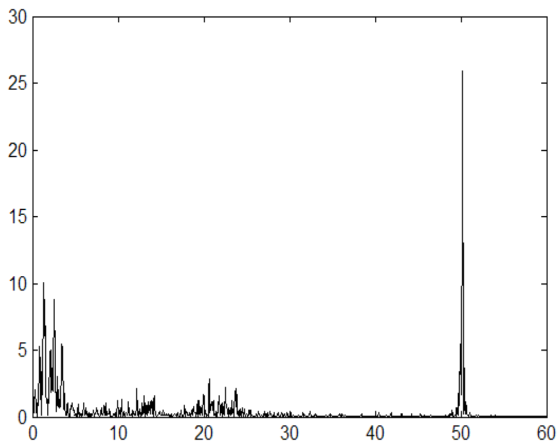


Sottocampionamento, Frequenza di campionamento 64 Hz; filtro antialiasing

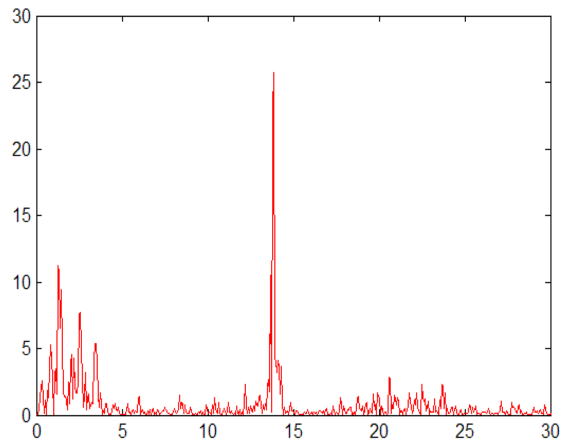
P4-O2



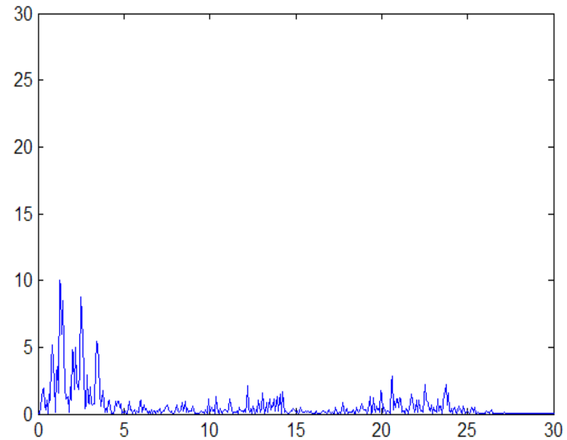
P4-O2, originale



P4-O2, Sottocamp.,NO filtro



P4-O2, Sottocamp.,SI filtro



$$f = \frac{f_c}{2} + x \Rightarrow f_{Ny} - x$$

$$50 = 32 + 18 \Rightarrow 32 - 18 = 14\,Hz$$

Clinical Neurophysiology 125 (2014) 1803–1808

Contents lists available at ScienceDirect

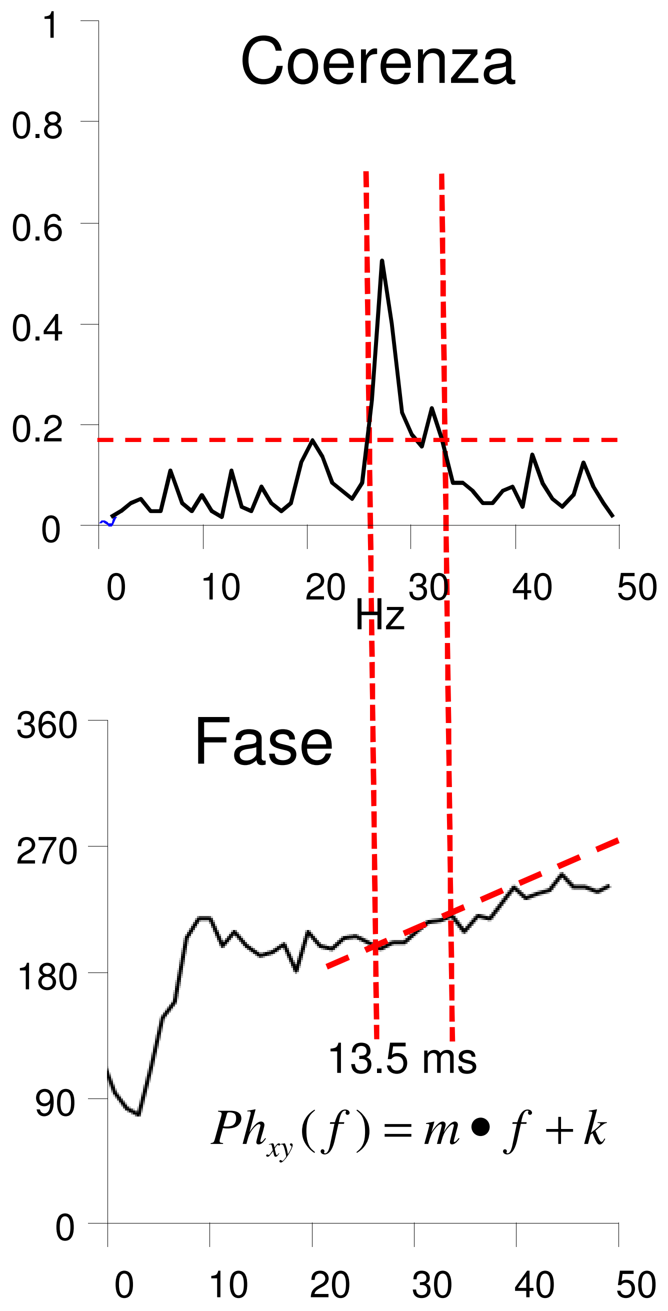
Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

EEG–EMG information flow in movement-activated myoclonus in patients with Unverricht–Lundborg disease

Ferruccio Panzica *, Laura Canafoglia, Silvana Franceschetti

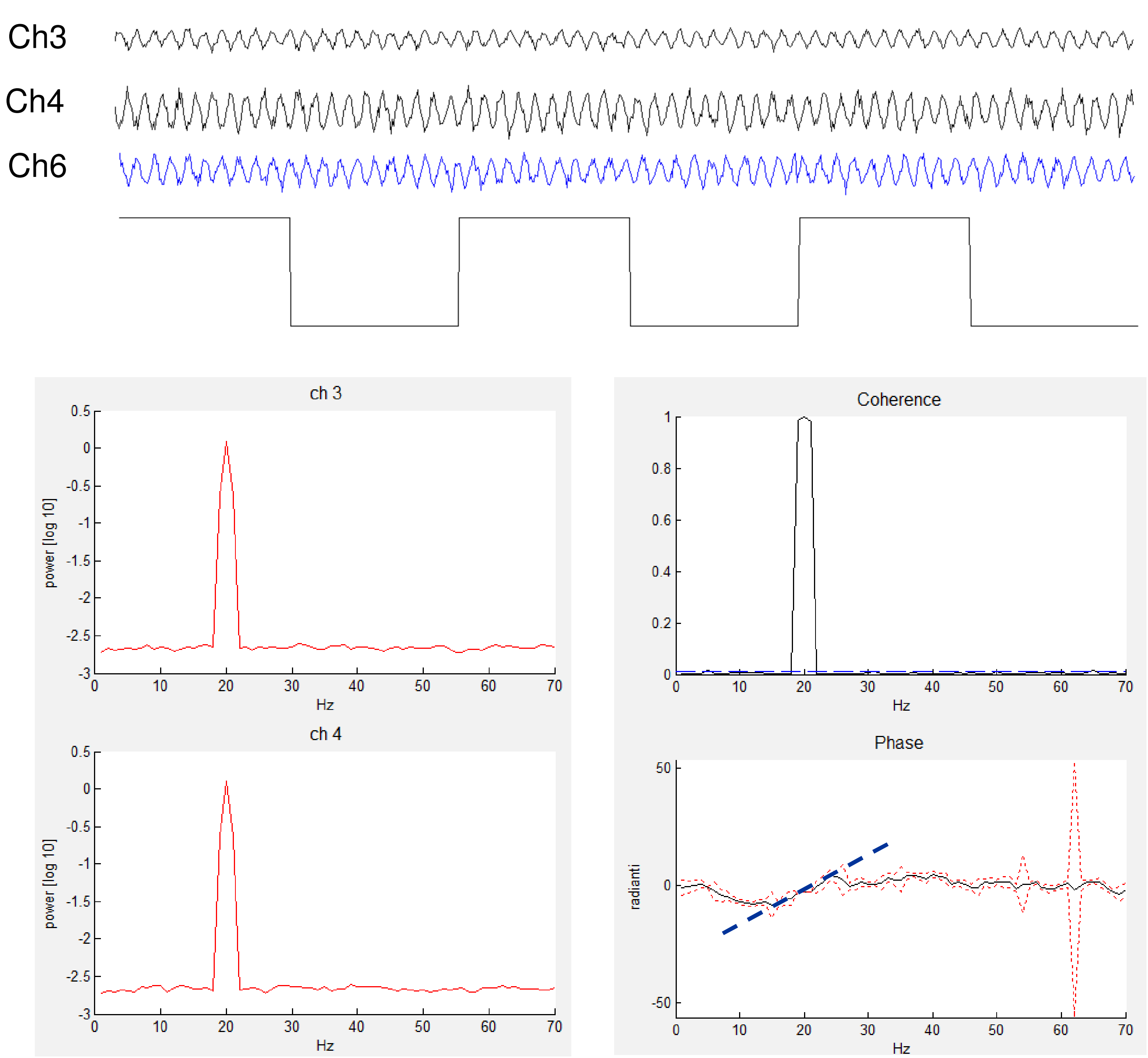
Department of Neurophysiology, C. Besta Neurological Institute IRCCS Foundation, Milan, Italy

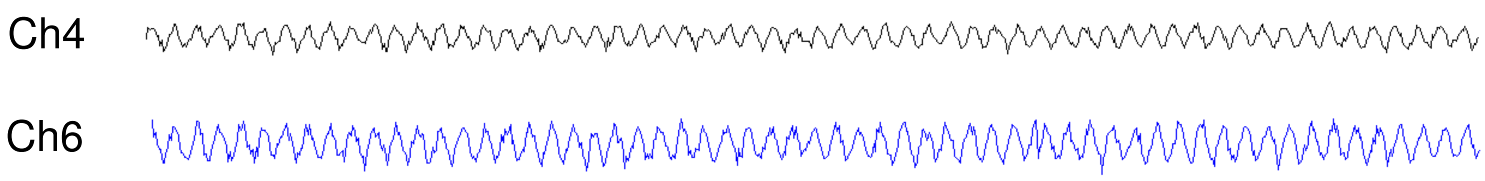


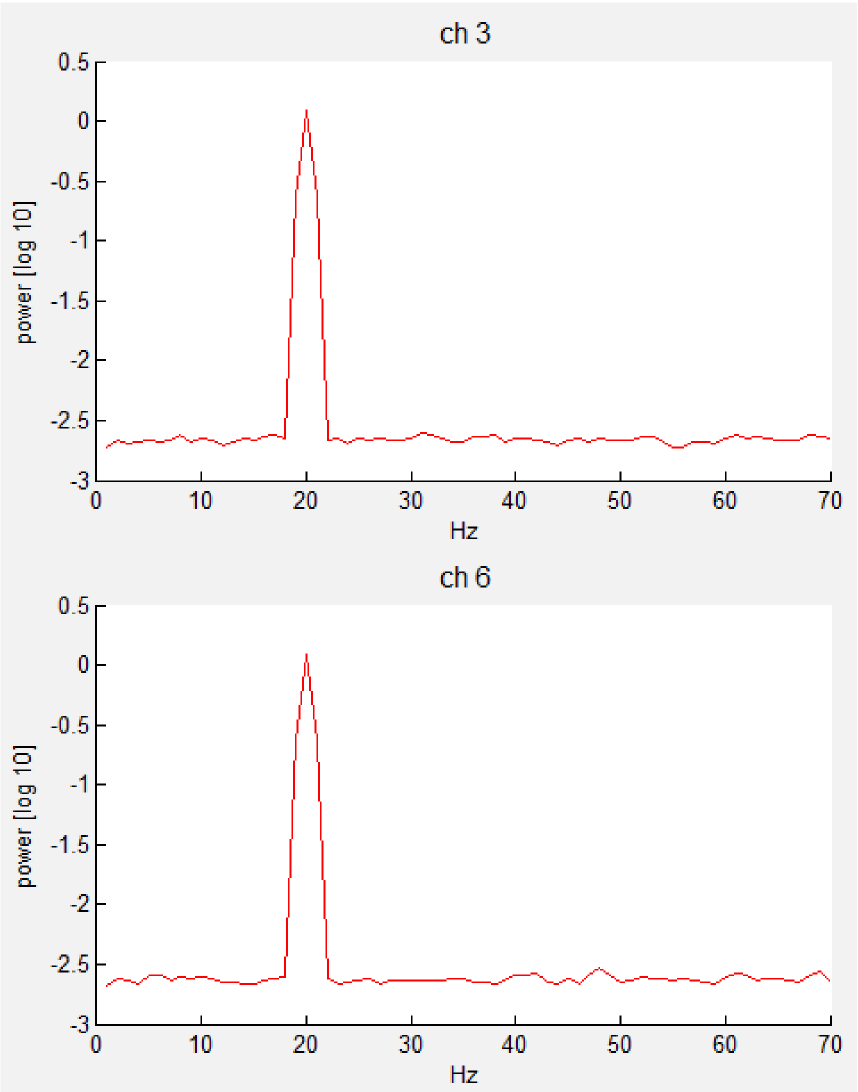
Misura il grado di relazione **lineare** tra due segnali in funzione della frequenza.

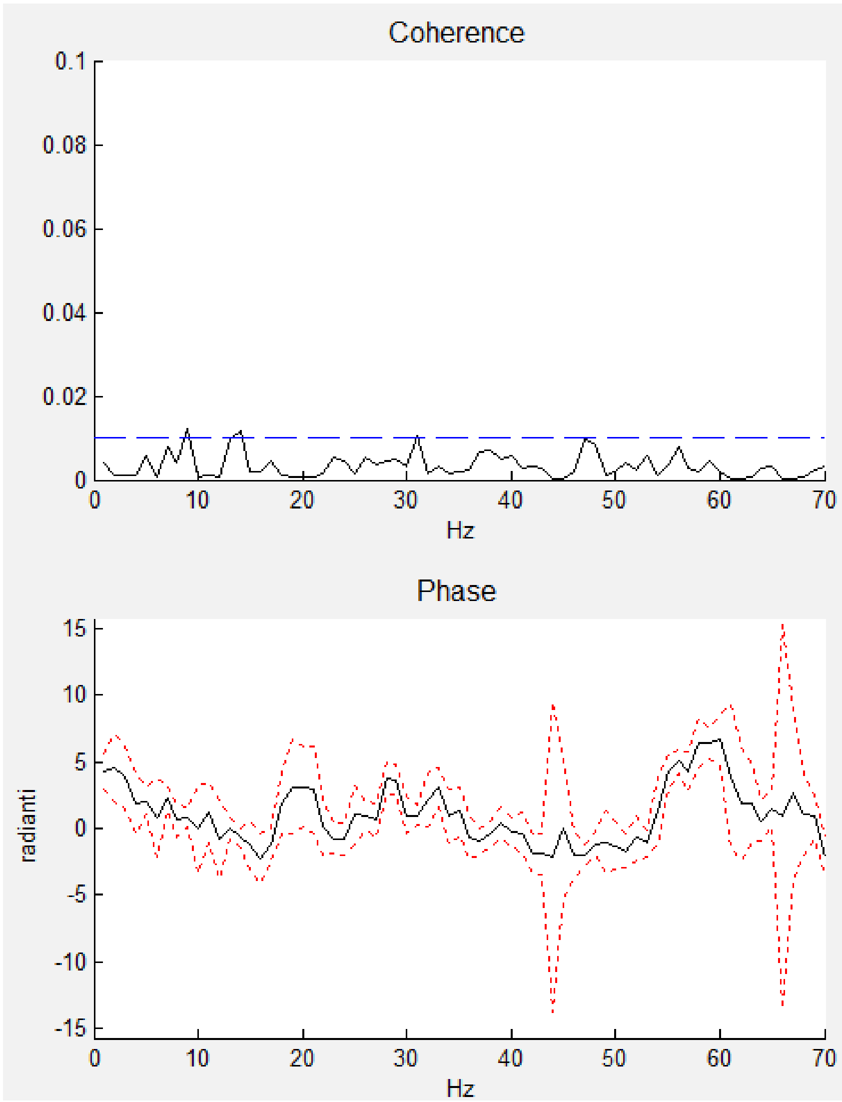
Valori sono compresi tra 0 e 1. Un elevato valore indica:
Connettività funzionale: interazione tra attività rilevate in differenti aree

Ritardo (tempo di propagazione) tra attività in aree diverse.


Ch3
Ch4
Ch6
ch 3
power [log 10]
Hz
ch 4
power [log 10]
Hz
Coherence
Hz
Phase
radianti
Hz


Ch4
Ch6


ch 3
power [log 10]
Hz
ch 6
power [log 10]
Hz


Coherence
Hz
Phase
radianti
Hz

METHODS

- ❖ 13 patients with EPM1A (9 females; mean age 35.4±15.5 years)
- ❖ 12 healthy (6 females; mean age 31.8 ± 10.5 years).

Polygraphic recordings at rest and during simple voluntary motor activities (L and R mild hand isometric extension, lasting 2 minutes each).

- ✓ Sampling frequency: 512 Hz;
- ✓ band pass filters: 1.6-120 Hz.

Connectivity analysis.

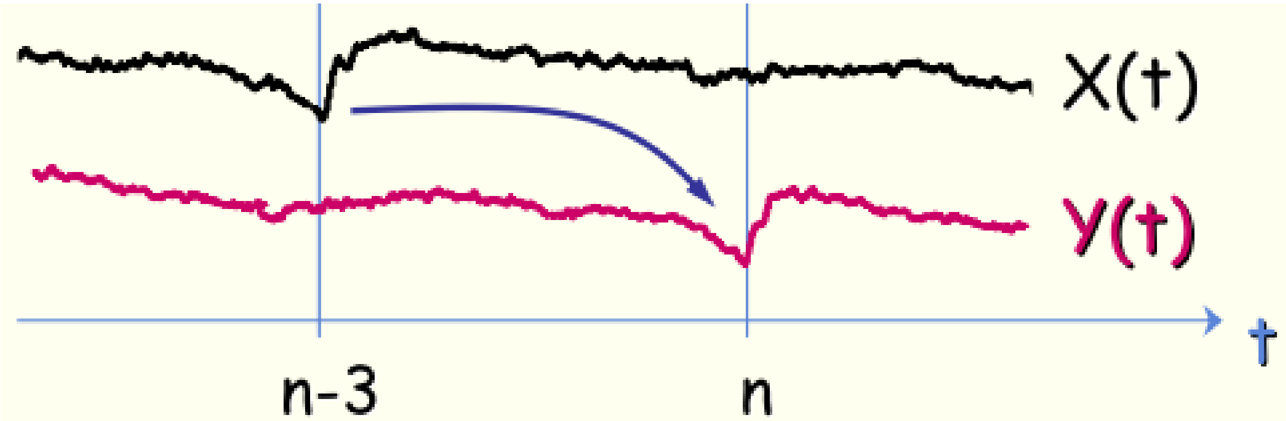
- ❑ As a pre-processing step, a spline surface Laplacian estimate was applied to the EEG channels in order to ensure reference-free and spatially sharpened data
- ❑ One minute of the EEG and EMG signals was selected, normalised by subtracting the mean and dividing by the standard deviation,
- ❑ then divided into non-overlapping 2-second epochs for analysis
- ❑ ***Generalized Partial Directed Coherence***

Granger causality

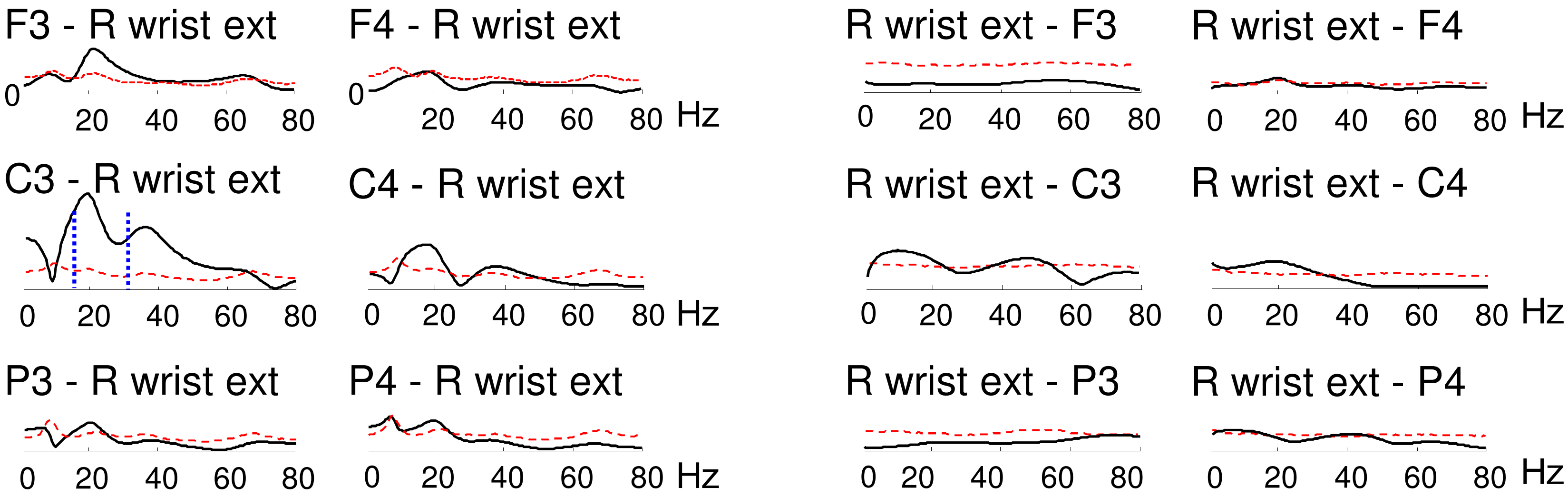
Probabilistic concept of causality derived from the common sense opinion that causes precede their effects in time and formulated in terms of prediction using linear stochastic models

"A process X_t is said to Granger cause another process Y_t

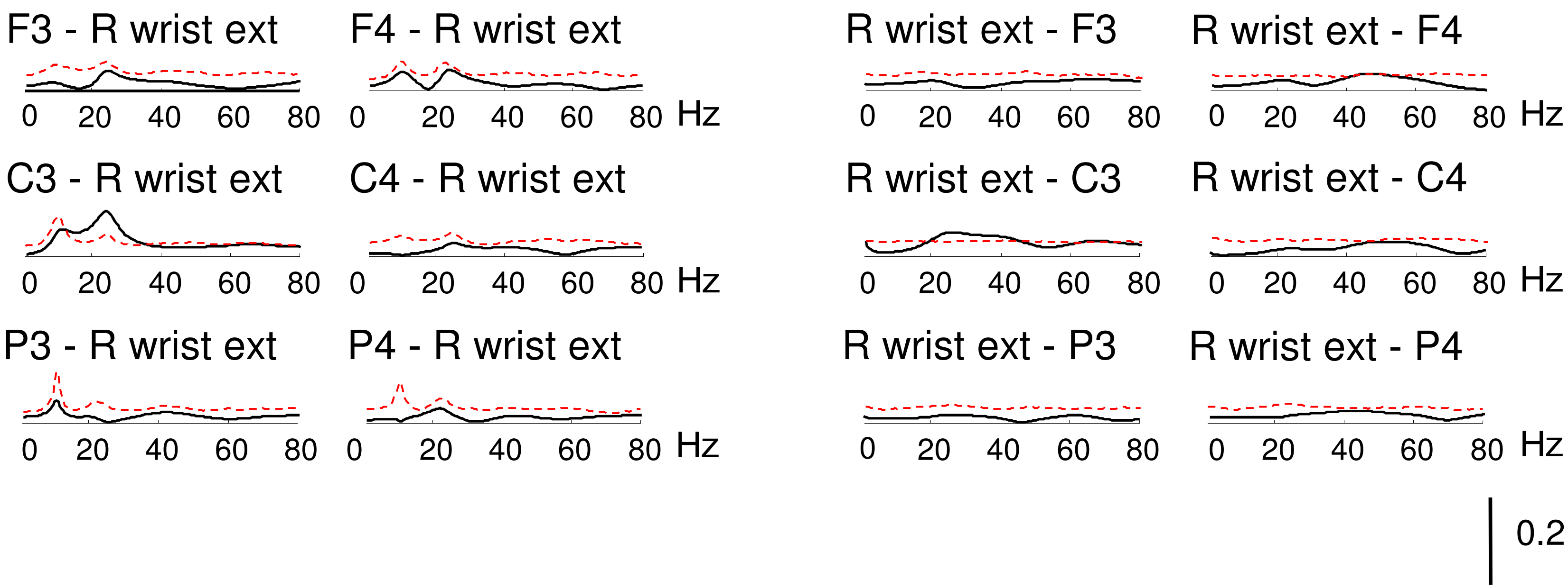
if future values of Y_t can be predicted better using past values of X_t and Y_t than using the past of Y_t alone."



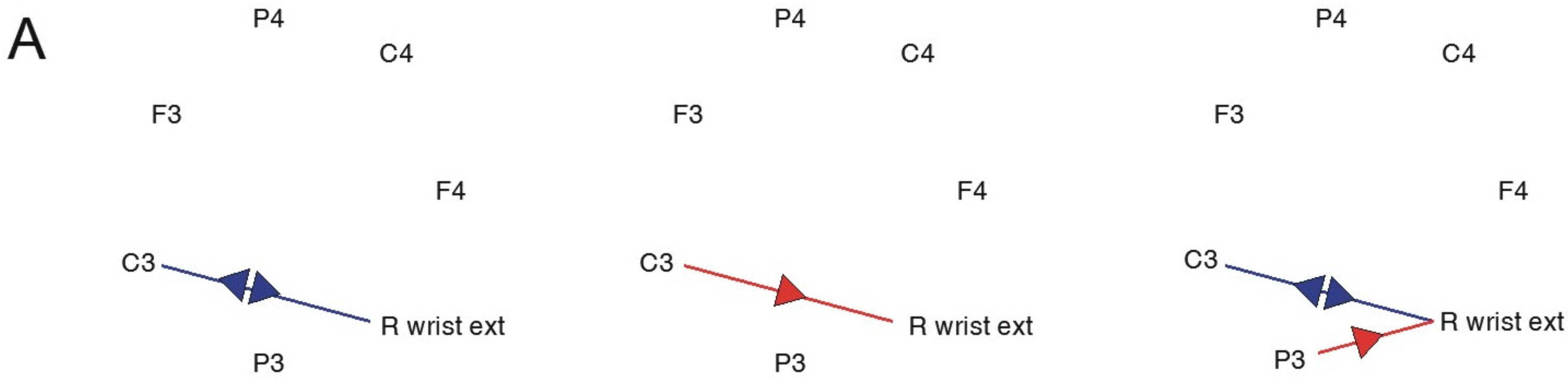
EPM1 patient



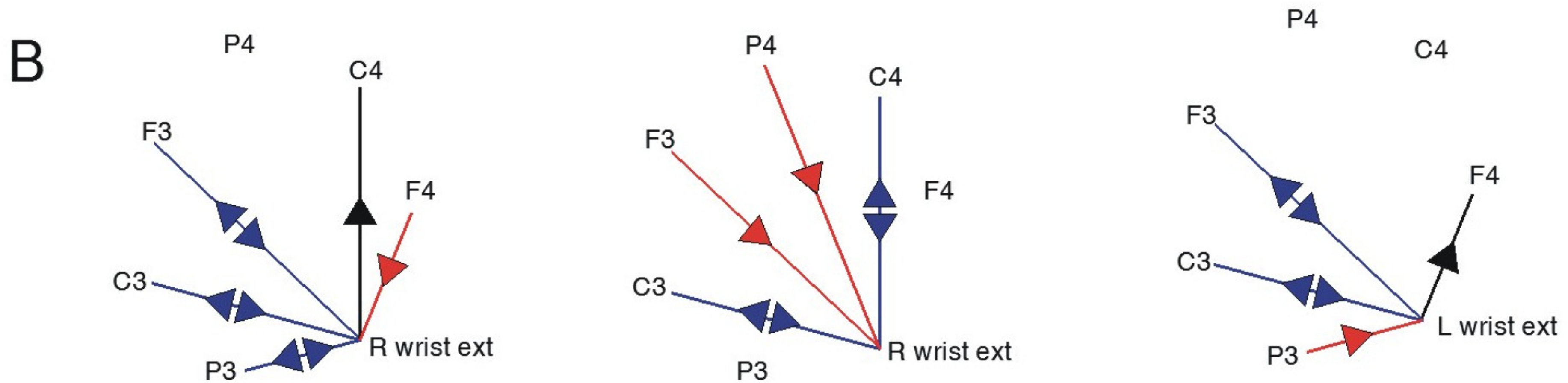
Healthy Subject



Controls

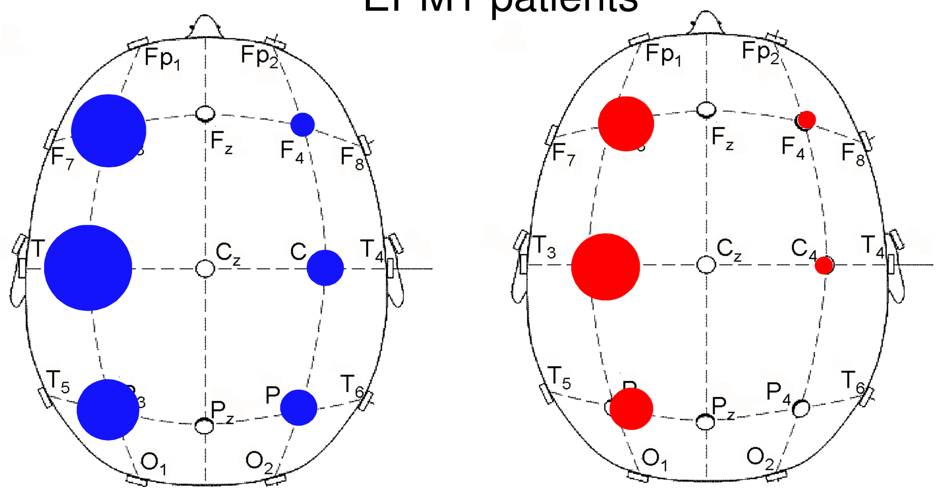


EPM1 patients

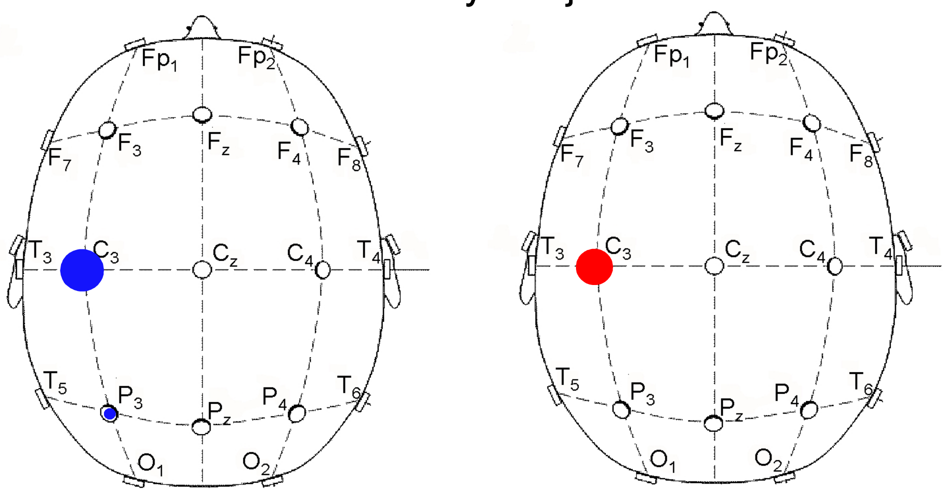


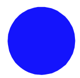
EEG→ EMG outflow   EMG→ EEG outflow

EPM1 patients



Healthy subjects



 = 10 subjects

EEG → EMG

	Patients	Controls	P
Electrodes	3.4 ± 1.0	0.58 ± 0.7	0.000001
Peak freq. (Hz)	20.9±3.9	19.7±3.4	NS
Peak amplitude	0.19 ± 0.06	0.10±0.04	0.003
Area	3.63±1.42	1.17±0.91	0.001
Total flow	5.71±2.74	1.36±1.10	0.0001

- All EPM1 patients showed a significant influence from the periphery towards the contralateral C-P regions
- In 10 cases also towards the contralateral frontal region
- In 5 towards the ipsilateral hemisphere.

Significant feedback from the periphery only in 4/12 controls, limited to the contralateral central area

↑ EEG → EMG

Enhanced recruitment of pre-motor and ipsilateral motor cortices because of the greater difficulty in performing the motor task

↑ EMG → EEG

Supplementary cortical input due EMG outflow acting on intrinsically hyperexcitable and larger neuronal pools and directly reaching the cortical motor areas.

The strong and extensive synchronisation constrains the ability of neurons to code information in time and space, as they preferentially fire locked to the beta rhythm → segregation

The hypersynchronous oscillatory discharge of motor units leads to jerks and jerky tremor, rather than the sustained posture and smooth movement normally achieved by the relatively asynchronous and fractionated activation of motor units.

Brown, Current Opinion in Neurobiology 2007, 17:656–664

Epilepsia, 53(2):359–367, 2012
doi: 10.1111/j.1528-1167.2011.03352.x

FULL-LENGTH ORIGINAL RESEARCH

Enhanced frontocentral EEG connectivity in photosensitive generalized epilepsies: A partial directed coherence study

*†Giulia Varotto, *Elisa Visani, *Laura Canafoglia, *Silvana Franceschetti, *Giuliano Avanzini, and *Ferruccio Panzica

*Department of Neurophysiology, Epilepsy Centre, C. Besta Neurological Institute IRCCS Foundation, Milan, Italy; and †Department of Bioengineering, Politecnico di Milano, Milan, Italy

SUMMARY

Purpose: Photosensitive epilepsy (PSE) is the most common form of reflex epilepsy presenting with electroencephalography (EEG) paroxysms elicited by intermittent photic stimulation (IPS). To investigate whether the neuronal network undergoes dynamic changes before and during the transition to an EEG epileptic discharge, we estimated EEG connectivity patterns in photosensitive (PS) patients with idiopathic generalized epilepsy.

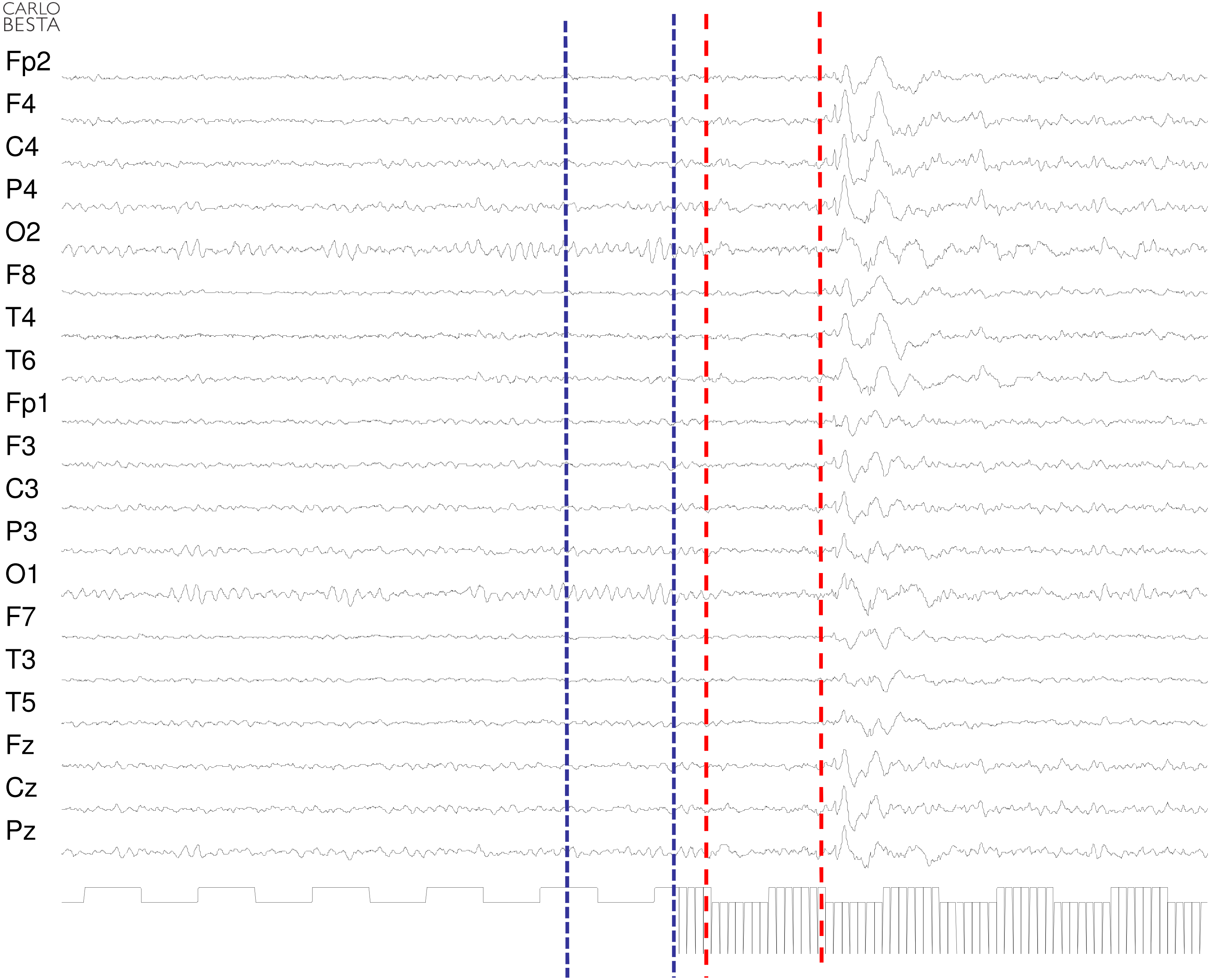
Methods: EEG signals were evaluated under resting conditions and during 14 Hz IPS, a frequency that consistently induces photoparoxysmal responses (PPRs) in PS patients. Partial directed coherence (PDC), a linear measure of effective connectivity based on multivariate autoregressive models, was used in 10 PS patients and 10 controls. Anterior versus posterior (F3, F4, C3, C4, and P3, P4, O1, O2) and interhemispheric connectivity patterns (F4, C4, P4, O2, and F3, C3, P3, O1) were estimated with focus on beta and gamma band activity.

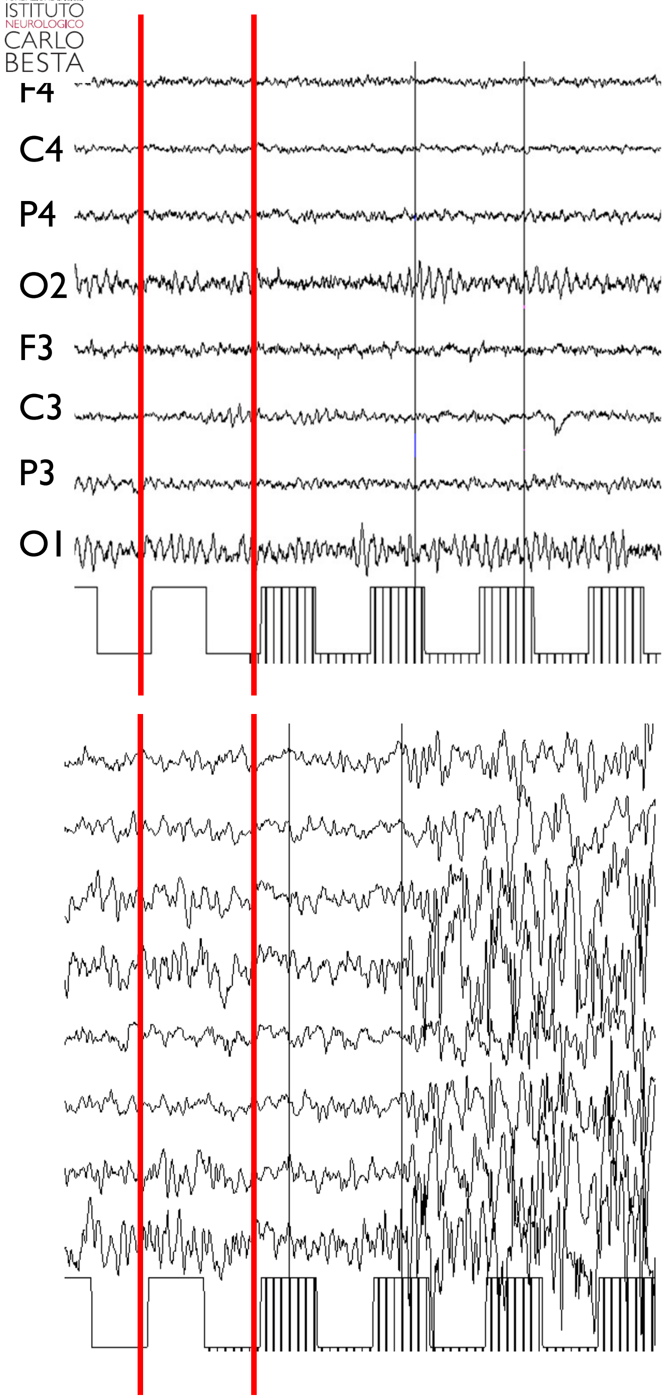
Key Findings: PDC analysis revealed an enhanced connectivity pattern in terms of both the number and strength of outflow connections in the PS patient group. Under resting condition, the greater connectivity in the PS patients occurred in the beta band, whereas it mainly involved the gamma band during IPS (i.e., the frequencies ranging from 40–60 Hz that include the higher harmonics of the stimulus frequency). Both at rest and during IPS, the differences between the PS patients and controls were due primarily to clearly increased connectivity involving the anterior cortical regions.

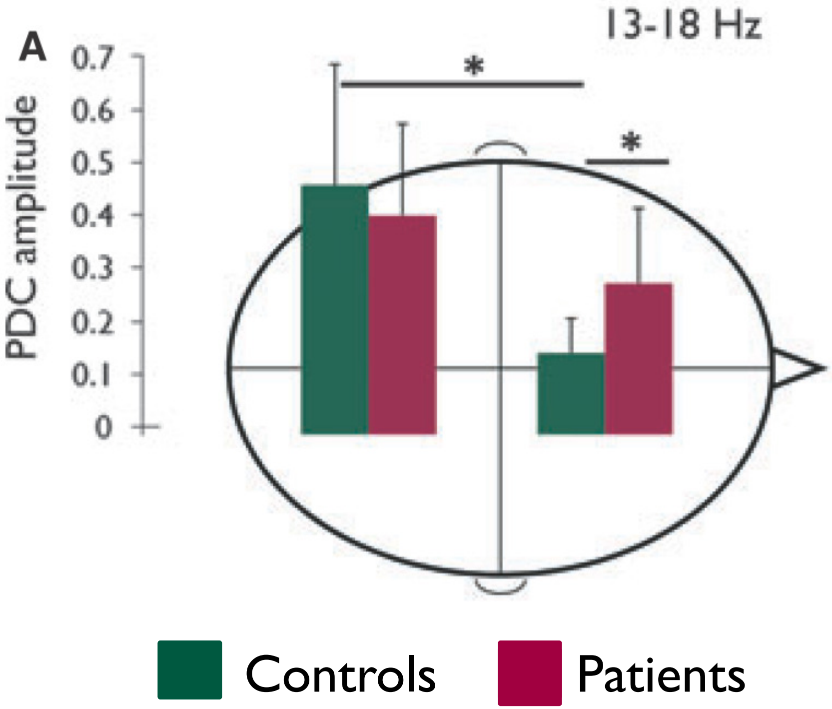
Significance: Our findings indicate that PS patients are characterised by abnormal EEG hyperconnectivity, primarily involving the anterior cortical regions under resting conditions and during IPS. This suggests that, even if the occipital cortical regions are the recipient zone of the stimulus and probably hyperexcitable, the anterior cortical areas are prominently involved in generating the hypersynchronization underlying the spike-and wave discharges elicited by IPS.

KEY WORDS: EEG, Photosensitive epilepsy, PPR, PDC, Connectivity.

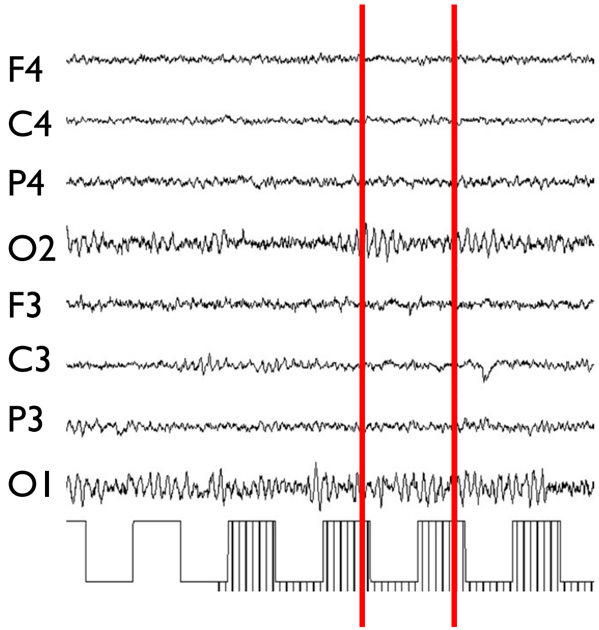
FONDAZIONE IRCCS ISTITUTO NEUROLOGICO CARLO BESTA

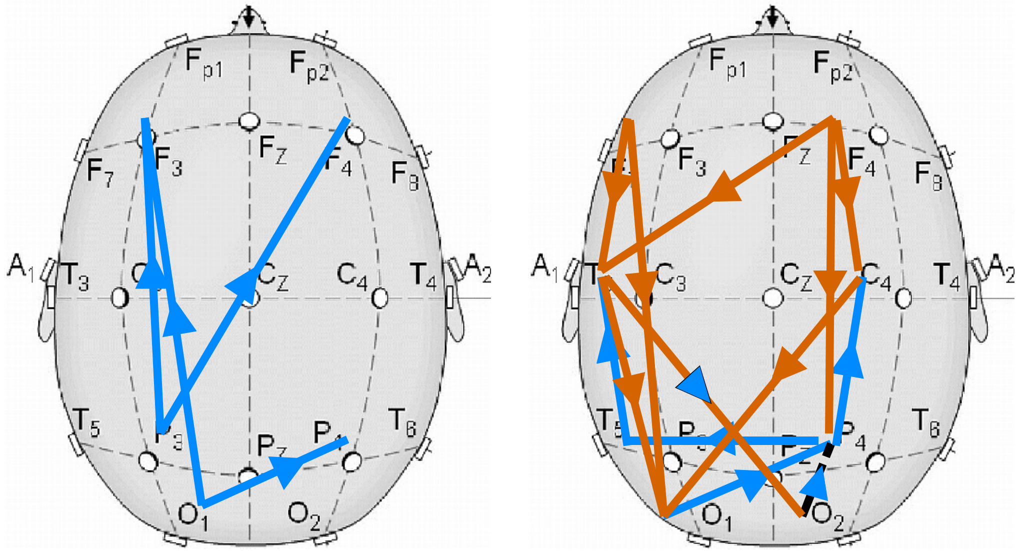


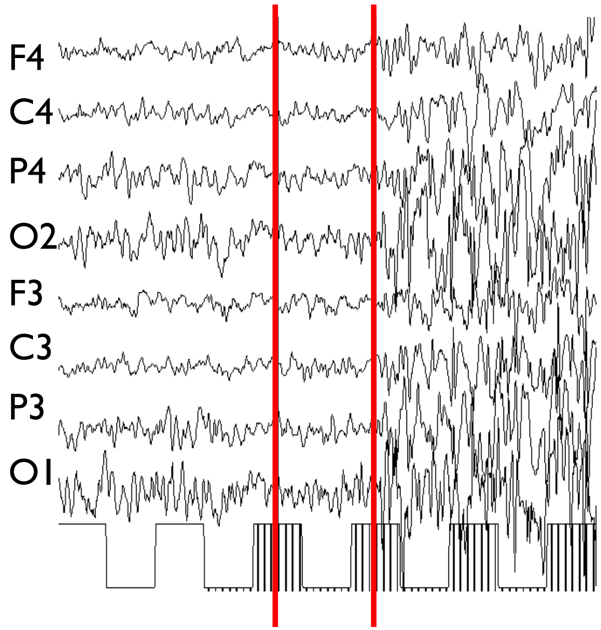

F4
C4
P4
O2
F3
C3
P3
O1

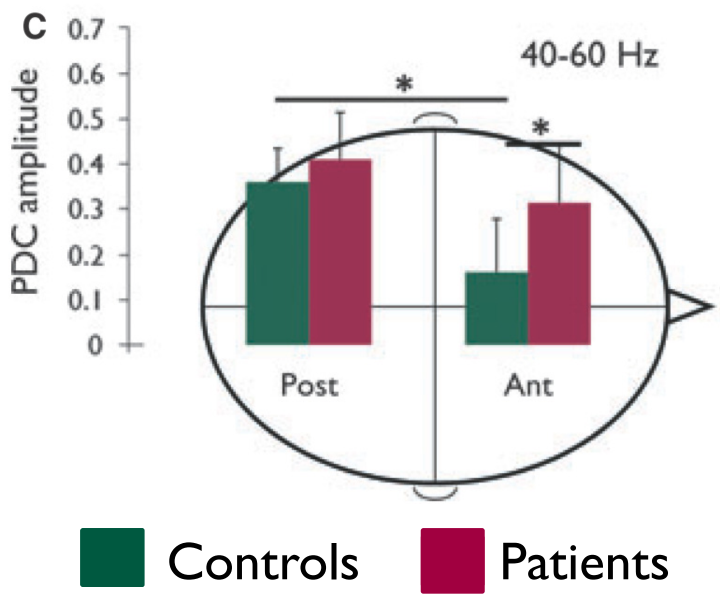

A
13-18 Hz
PDC amplitude
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
*
*
Controls
Patients

FONDAZIONE I.R.C.C.S.
ISTITUTO
NEUROLOGICO
CARLO
BESTA









PS patients are characterised by abnormal EEG hyper-connectivity mainly involving the anterior cortical regions at rest (beta band) and during IPS (gamma band).

• PPR requires a hyperexcitable occipital recipient zone, but the anterior cortical areas are involved in generating the hyper-synchronization underlying the SW discharges elicited by IPS.

• The abnormally synchronized activity at rest in the anterior cortical regions may reflect defectively controlled high-frequency oscillatory processes coupling neuronal assemblies in an extended network and predispose toward generalized epileptic discharges.

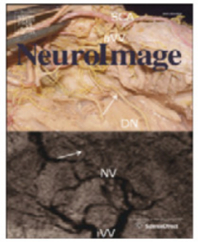
• IPS may act as an appropriate stimulus to engage the network in generating the gamma frequencies, leading to PPR

NeuroImage 61 (2012) 591–598

Contents lists available at SciVerse ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

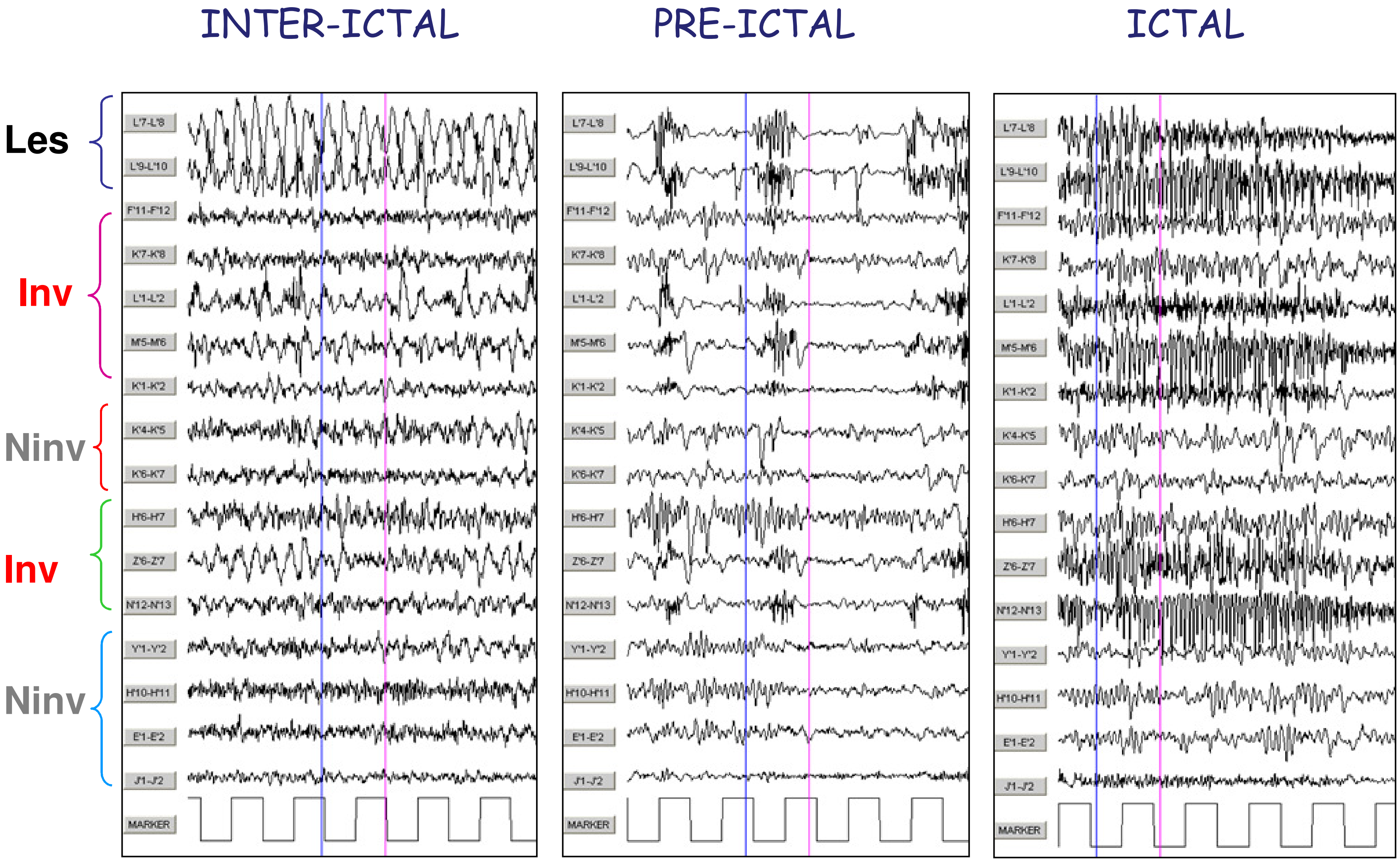


Epileptogenic networks of type II focal cortical dysplasia: A stereo-EEG study

Giulia Varotto [a,c], Laura Tassi [d], Silvana Franceschetti [a], Roberto Spreafico [b], Ferruccio Panzica [a,*]

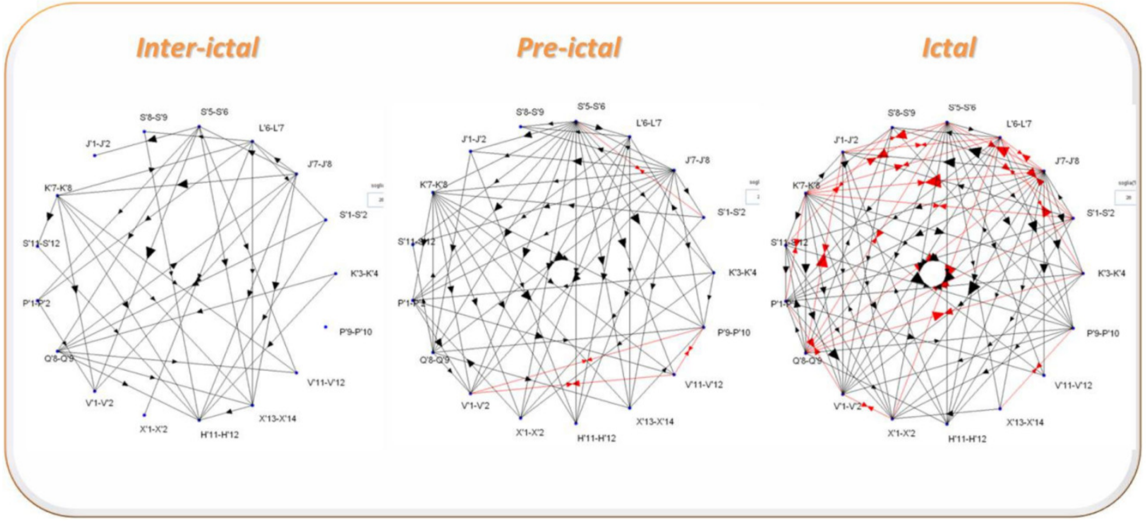
[a] *Neurophysiology and Diagnostic Epileptology Unit, Epilepsy Centre, C. Besta Neurological Institute IRCCS Foundation, Milan, Italy*
[b] *Clinical Epileptology and Experimental Neurophysiology Unit, C. Besta Neurological Institute IRCCS Foundation, Milan, Italy*
[c] *Department of Bioengineering, Politecnico di Milano, Milan, Italy*
[d] *"C. Munari" Center of Epilepsy Surgery, Niguarda Hospital, Milan, Italy*

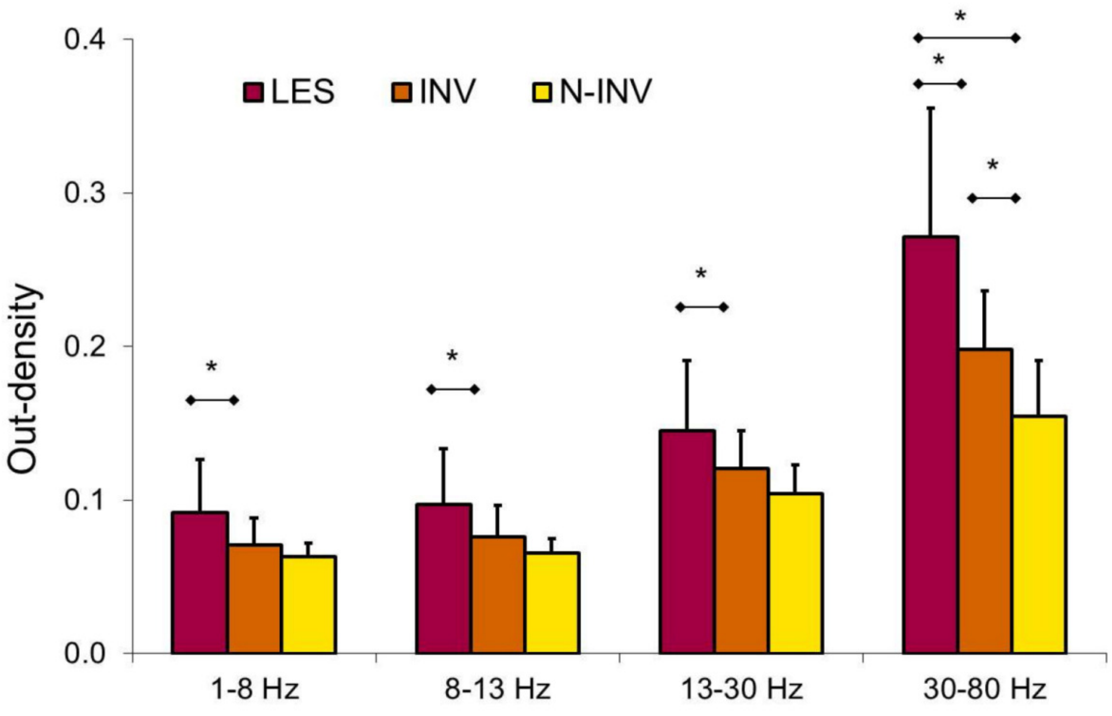
FONDAZIONE I.R.C.C.S. ISTITUTO NEUROLOGICO CARLO BESTA



Epileptic phenomenon are associated with abnormal changes in brain synchrony mechanisms and seizures in humans are associated with **abnormal synchronization of distant structures**.

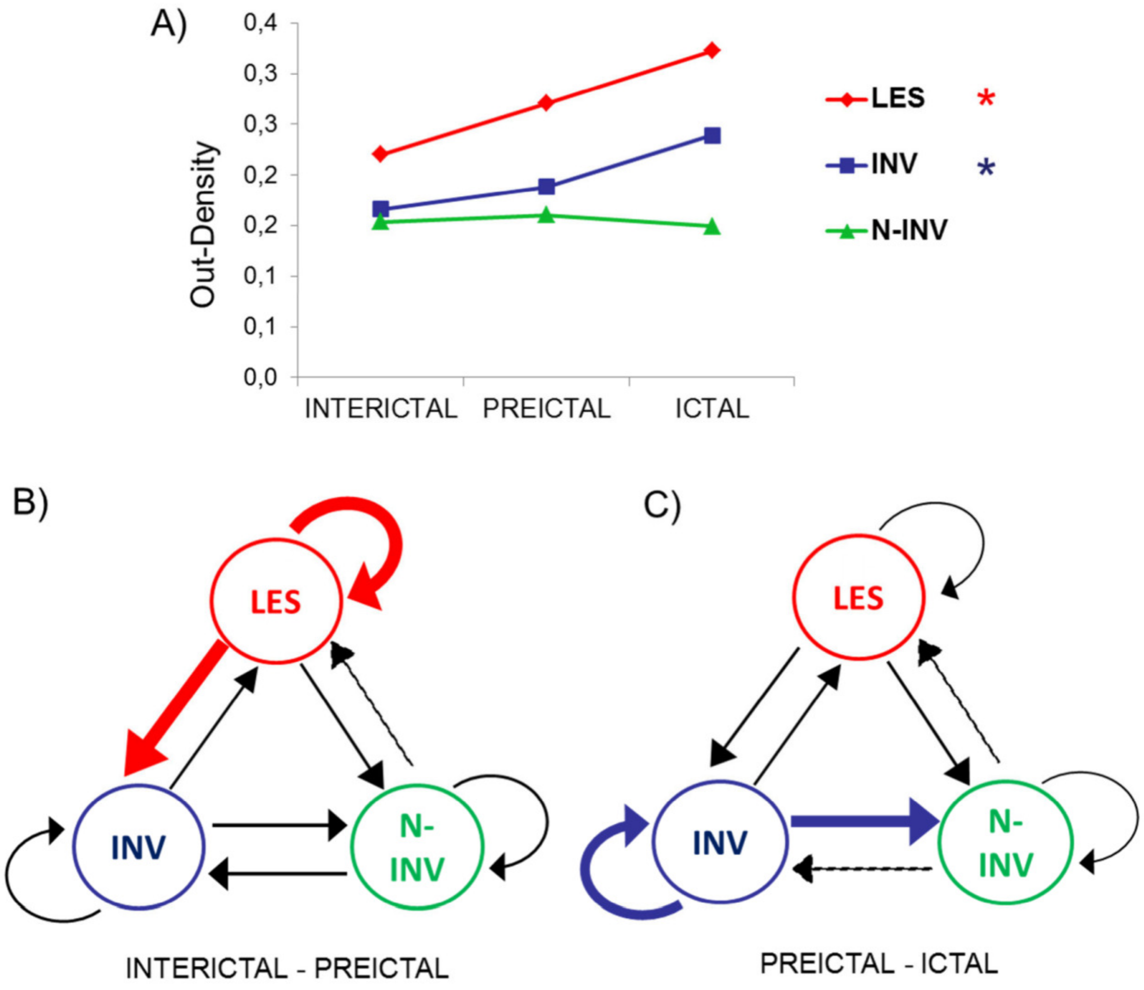
- Can abnormal couplings be identified?
- How do coupling and directions evolve during the interictal to ictal transition and the seizure?
- **Do some area play a leading role in the seizure generation process**?





- Epileptogenic area showed abnormal out-going connectivity
- The main significant changes occurred in the gamma band.

Temporal Dynamic changes



the dysplasia play a leading role in generating and propagating ictal EEG activity by acting as an hub.

The other cortical regions involved in the ictal activity essentially act as “secondary” generators.

A) Asterisks indicate a significant increase. B) and C): graphic representation of the significant (colored arrows) and non-significant (black arrows) increases between two temporal conditions (Varotto et al., Neuroimage 2012)