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Istituto Neurologico Carlo Besta

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Primo corso di perfezionamento: **Neurologia Cognitiva**

 International School
of Neurological Sciences
Sezione di Neuro-oncologia, Epilessia e Nutrizione

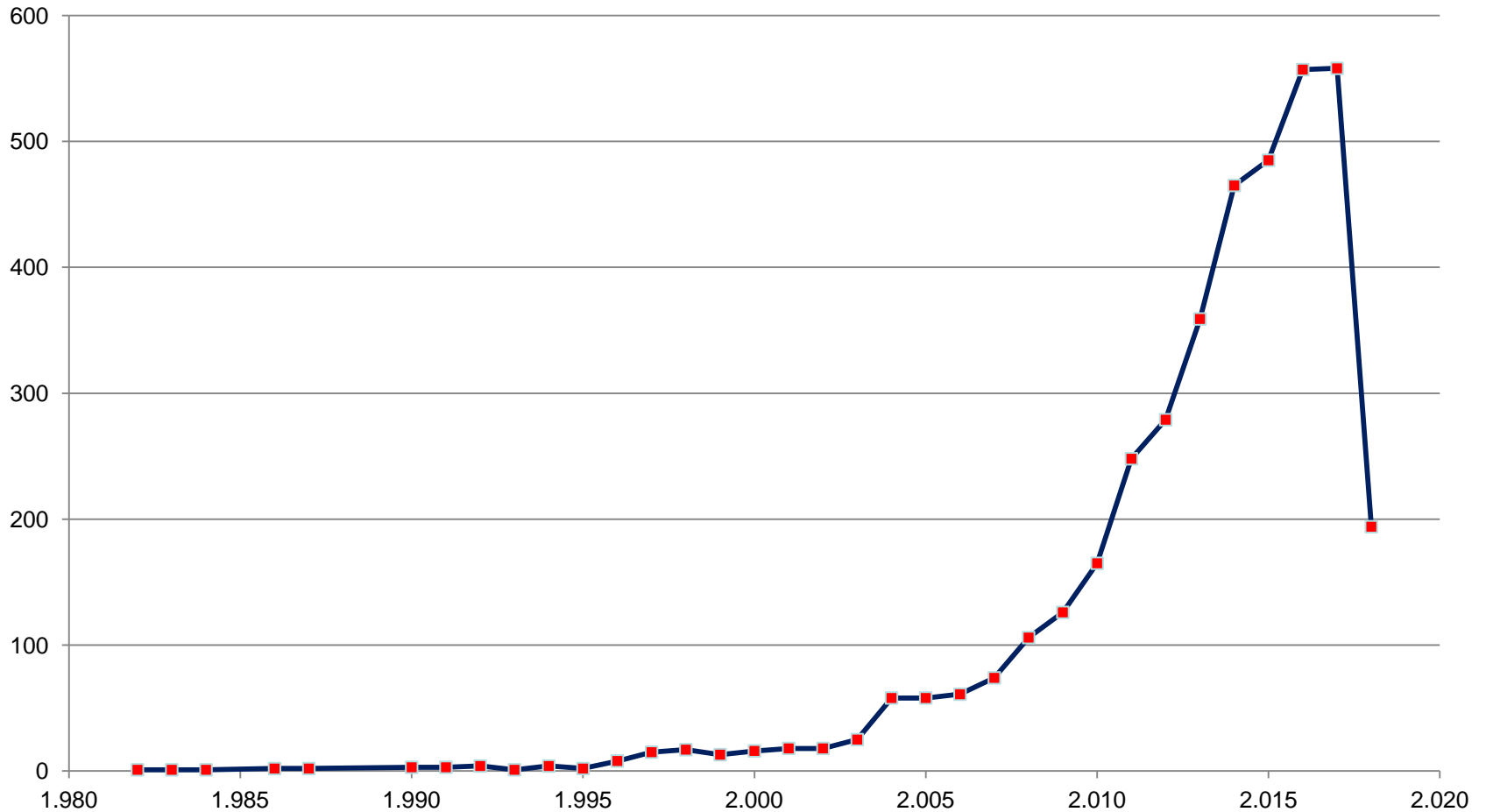
Connettività cerebrale ed attività gamma **Ferruccio Panzica**

ferruccio.panzica@istituto-besta.it

Fondazione IRCCS Istituto Neurologico C. Besta, Milano



Pubmed: (EEG OR MEG) AND (connectivity OR "brain networks" OR "graph theory" OR "functional networks")



Feature Review

Large-scale brain networks in cognition: emerging methods and principles

Steven L. Bressler¹ and Vinod Menon²

Much of our current knowledge of cognitive brain function has come from the modular paradigm, in which brain areas are postulated to act as independent processors for specific complex cognitive functions.

Accumulating evidence suggests that this paradigm has serious limitations and might in fact be misleading. Even the functions of primary sensory areas of the cerebral cortex, once thought to be pinnacles of modularity, are being redefined by recent evidence of cross-modal interactions.

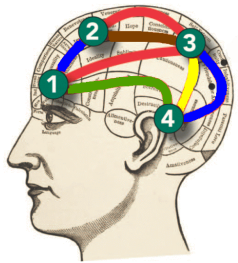
A new paradigm is emerging in cognitive neuroscience that moves beyond the simplistic mapping of cognitive constructs onto individual brain areas and emphasizes instead the conjoint function of brain areas working together as large-scale networks

CONNETTIVITA' CEREBRALE

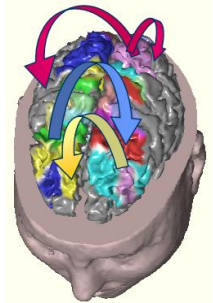
- Interazioni tra distinte e remote regioni cerebrali (reti funzionali) sono alla base di (e la chiave per comprendere) processi e funzioni.
- Alterazioni nelle interazioni tra componenti delle reti sono associate a malattie neurologiche o disfunzioni cognitive (epilessia, Alzheimer, Parkinson,.....)
- Il recupero funzionale può dipendere dalla topologia e adattabilità delle reti e dalle modalità di interazione (riorganizzazione, plasticità).

CONNETTIVITA' CEREBRALE

Connettività anatomica: insieme delle connessioni strutturali



Connettività Funzionale: misura statistica del grado di interazione tra attività in aree differenti



Connettività effettiva: influenza che un sistema esercita su un altro. Misura le interazioni e la loro direzione (chi guida chi) fra regioni cerebrali.

Le interazioni sono:

✓ ***transienti***

✓ ***Dinamiche (tempo-varianti)***

✓ ***Frequenze-specifiche***

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

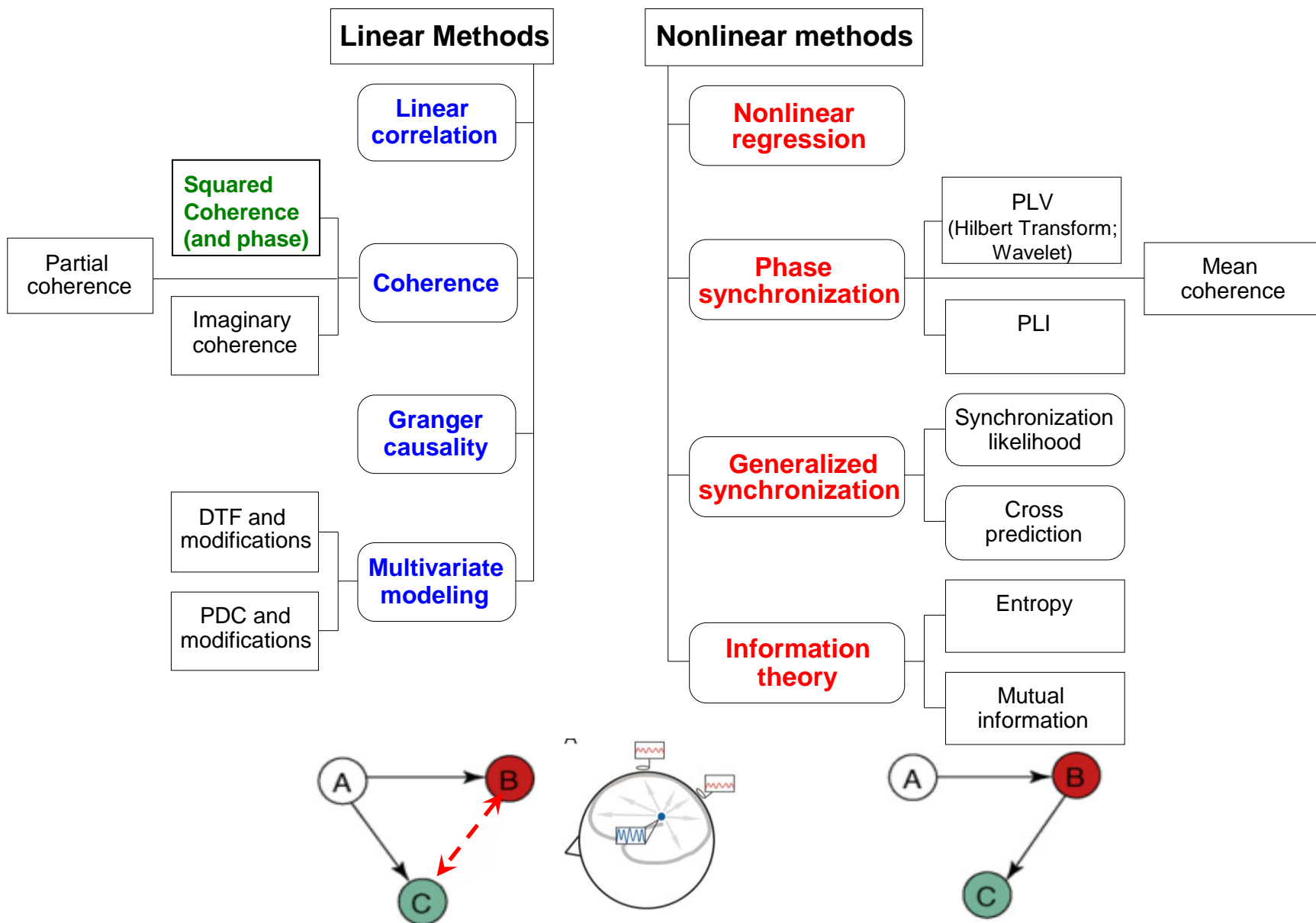
*†Anne T. Berg, ‡Samuel F. Berkovic, §Martin J. Brodie, ¶Jeffrey Buchhalter, #**J. Helen Cross,
††Walter van Emde Boas, ‡‡Jerome Engel, §§Jacqueline French, ¶¶Tracy A. Glauser, ##Gary
W. Mathern, ***Solomon L. Moshé, †††Perrine Plouin, and ‡Ingrid E. Scheffer

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

Connettività: analisi di due o più differenti segnali



Studio della Teoria della Mente (TOM) mediante EEG

Capacità di attribuire stati mentali (intenzioni, scopi, volontà, desideri conoscenze, senso di realtà,...) ad altri e a se stessi e, in base a tali stati, predire e comprendere i comportamenti e le interazioni sociali



(TNFP. E. Schiaffi)

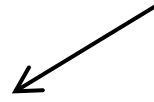
Protocollo EEG-TOM

- Soggetti sani volontari (16)
- Montaggio EEG 10-20 con poligrafia (flessore ed estensore del carpo bilaterale) → risposta al test
- 5 minuti di EEG basale
- Somministrazione delle vignette (10 fisiche-10 TOM-10 emp)

Analisi di coerenza (fisiche, TOM, emp., basale)

- ❑ Derivazioni selezionate: F3/4 - C3/4 → P3/4 - O1/2
- ❑ Finestra di analisi di 1.000 ms (0,5-1.5 s da opzione risposta)

RM- ANOVA separatamente destra e sinistra.

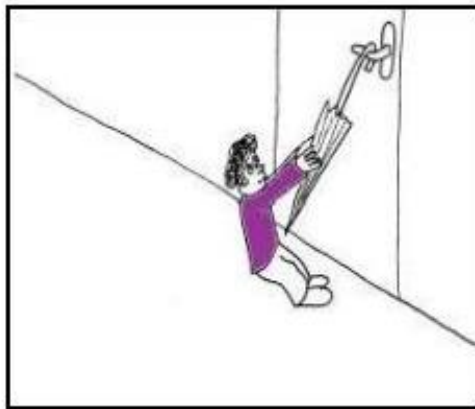
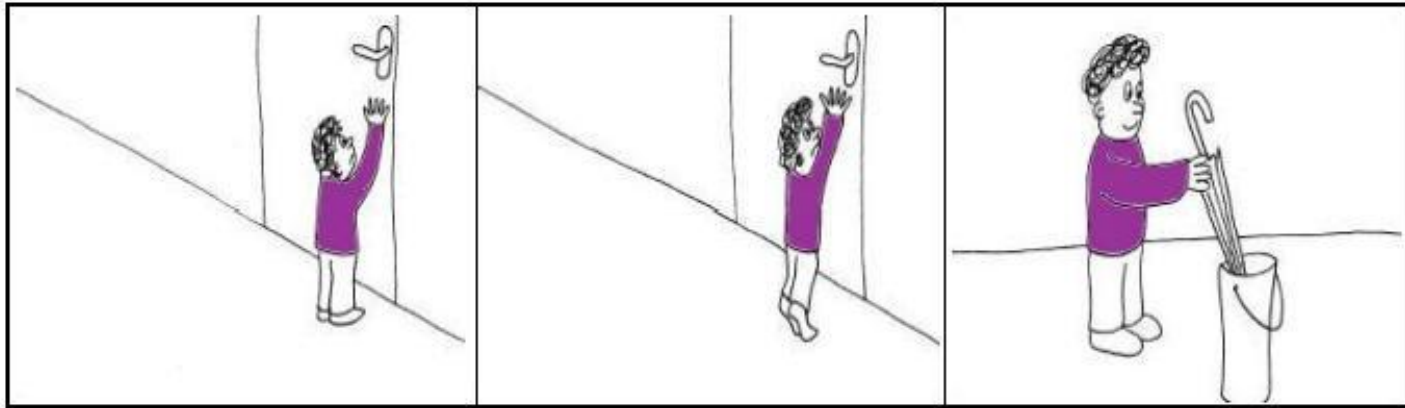


Esempio vignetta TOM

Neuronal correlates of theory of mind and empathy: A functional magnetic resonance imaging study in a nonverbal task

Birgit A. Völlm,^{a,*} Alexander N.W. Taylor,^a Paul Richardson,^a Rhiannon Corcoran,^b
John Stirling,^c Shane McKie,^a John F.W. Deakin,^a and Rebecca Elliott^a

NeuroImage 29 (2006) 90 – 98

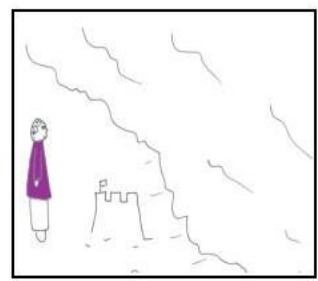
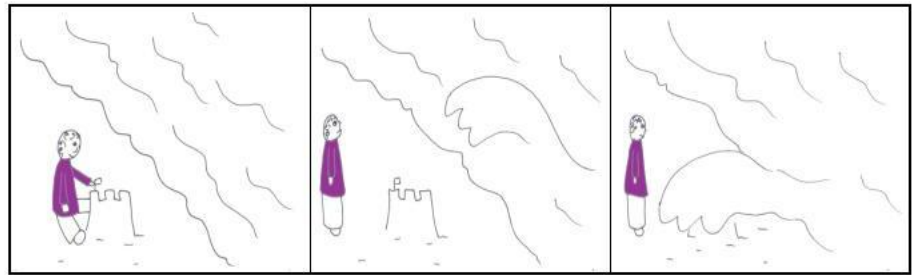


1

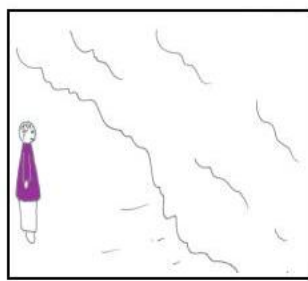


2

Esempio vignetta fisica

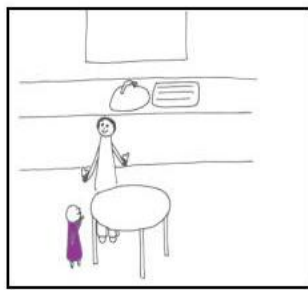
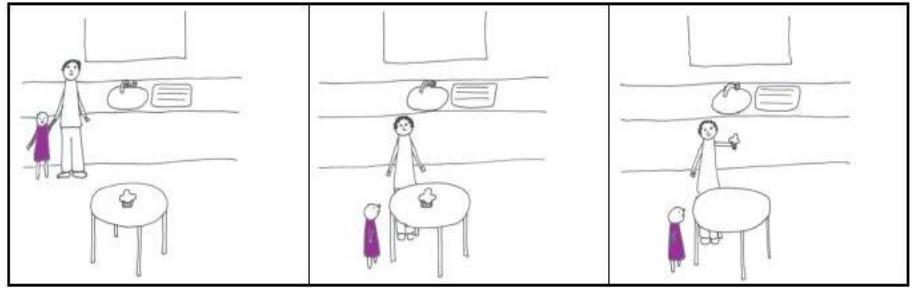


1

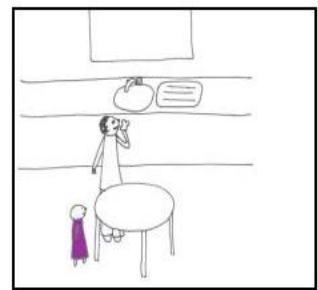


2

Esempio vignetta



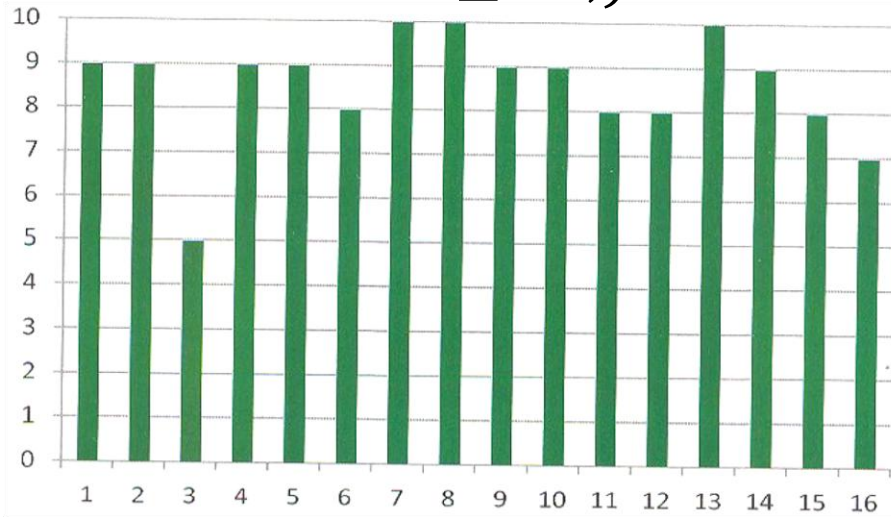
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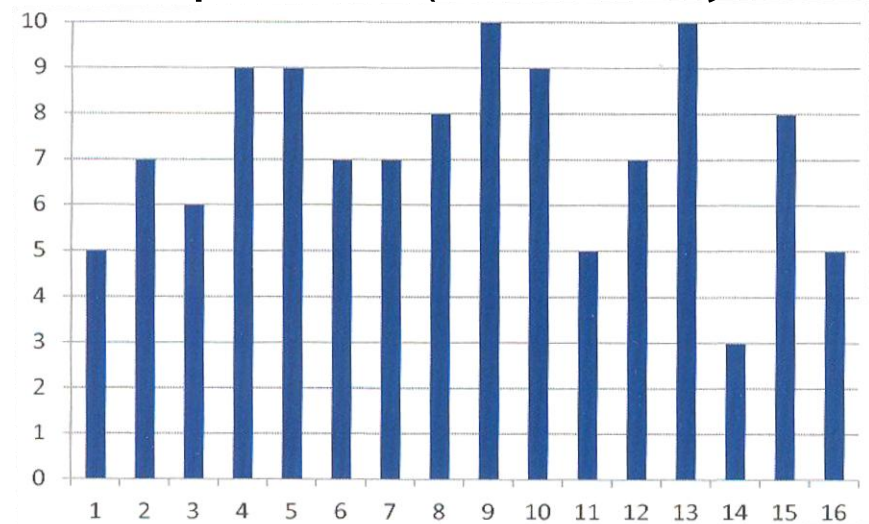
2

RISPOSTE ESATTE

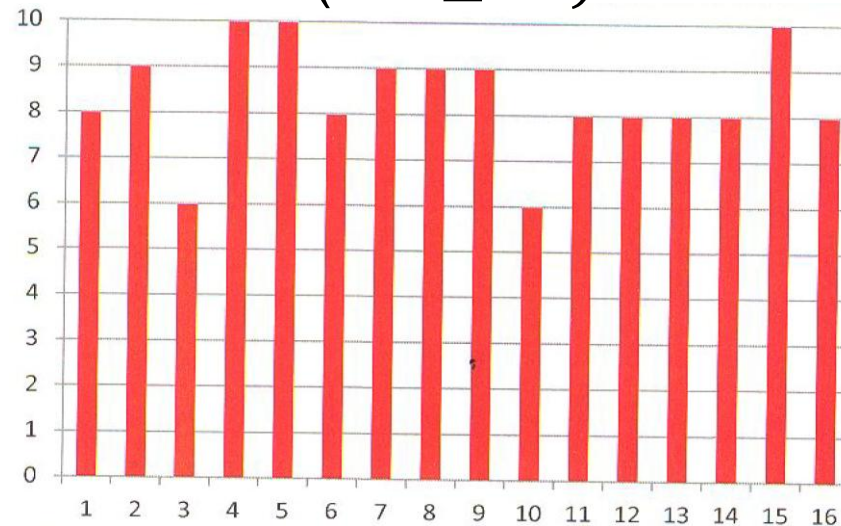
Fisiche 8.6 ± 1.3 ;



Empatiche (7.2 ± 2.0);



TOM (8.4 ± 1.2)

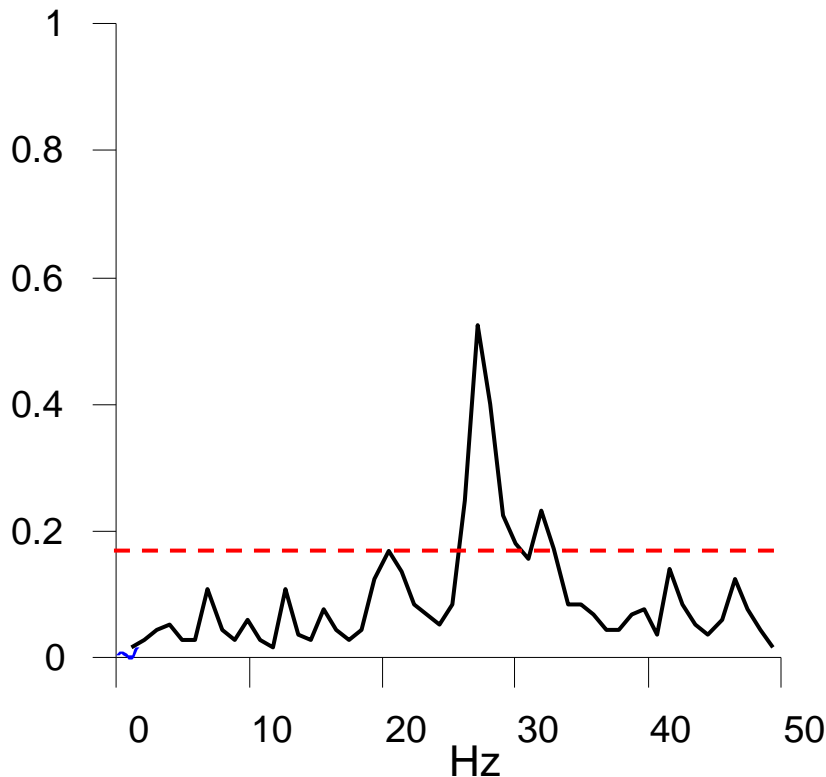


Coerenza (Connettività Funzionale)

Misura il grado di correlazione lineare tra due segnali nel dominio della frequenza.

valore compreso tra 0 e 1

è una misura statistica



Banda δ : 0.5 – 4 Hz
Banda θ : 4-8 Hz
Banda α : 8-13 Hz
Banda β : 13-30 Hz
Banda γ : > 30 Hz

Fisiche

F4-C4 vs P4-O2

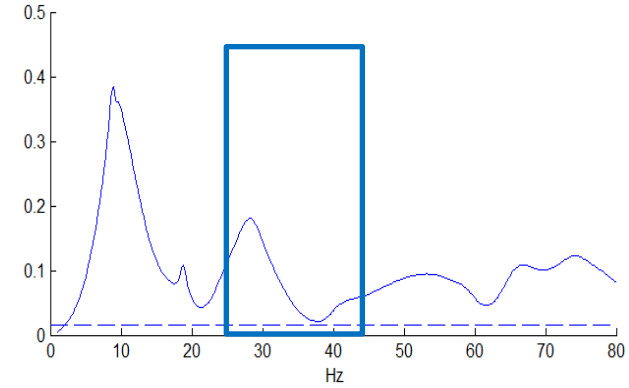
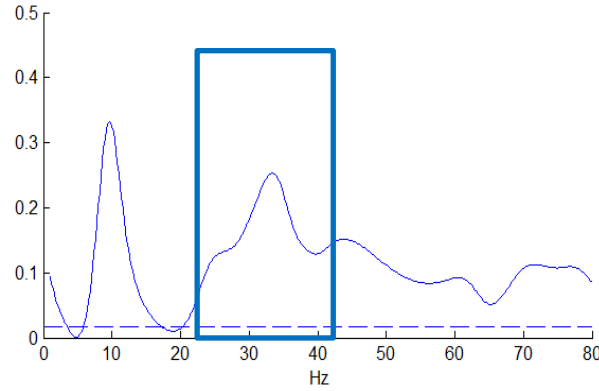
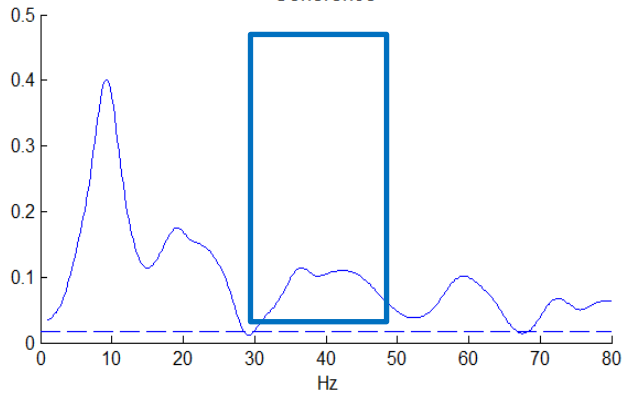
TOM

empatiche

Coherence

Coherence

Coherence

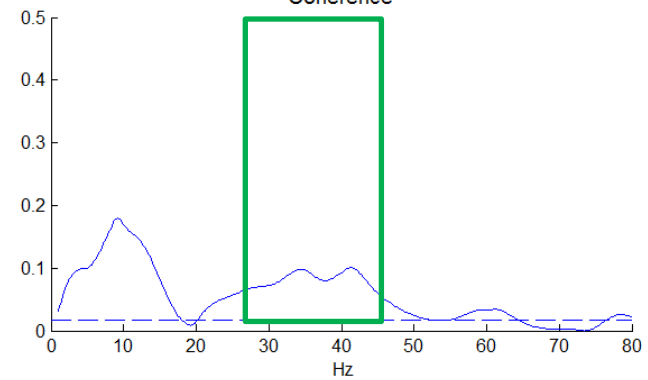
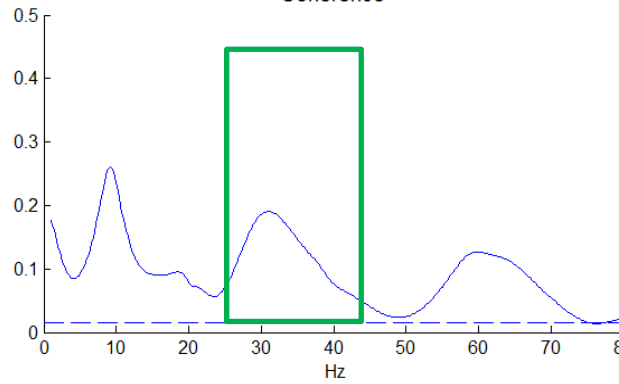
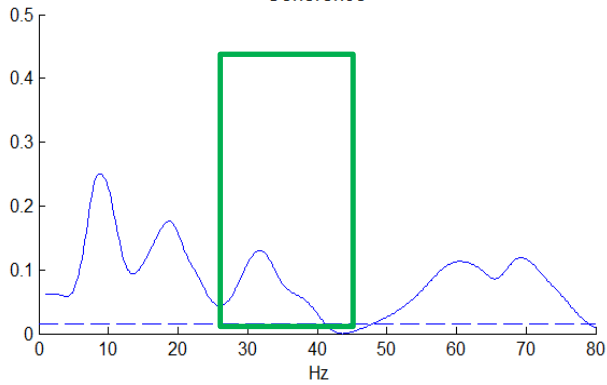


F3-C3 vs P3-O1

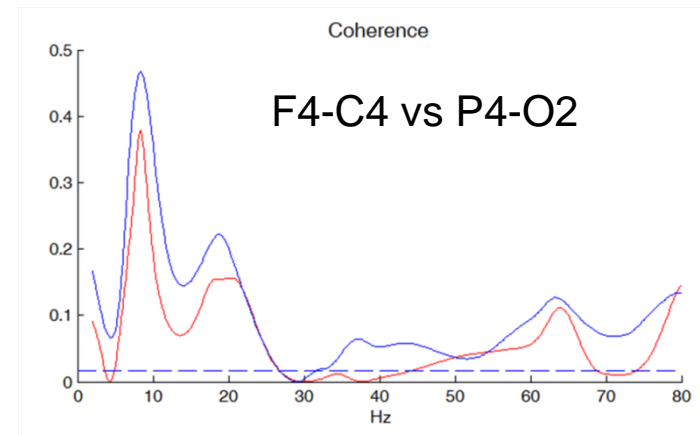
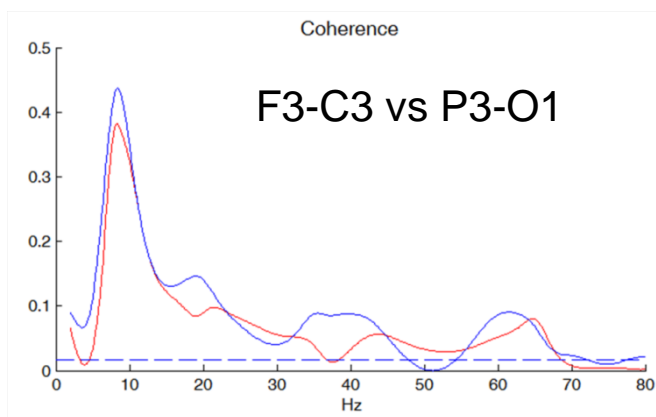
Coherence

Coherence

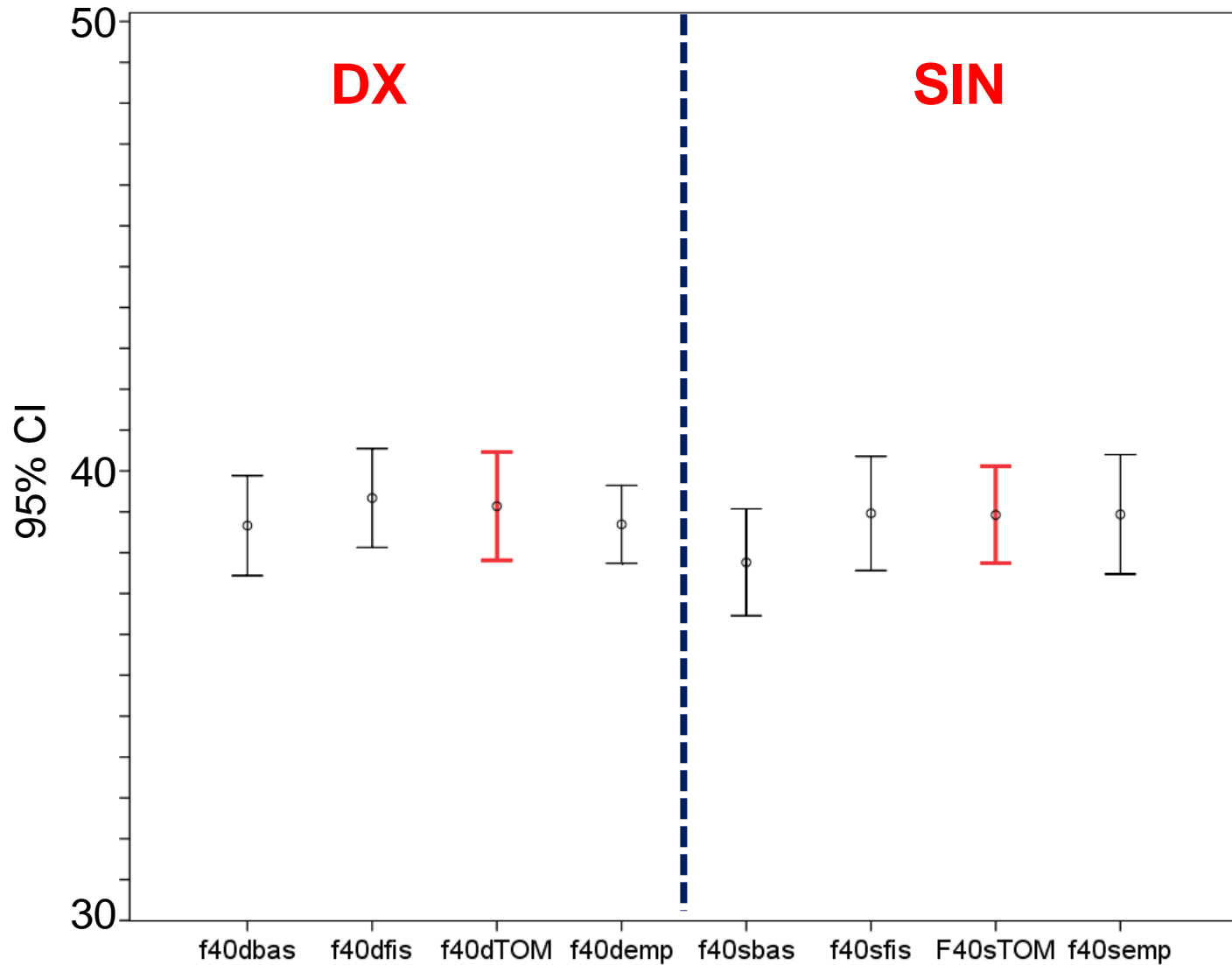
Coherence



PRE-TOM



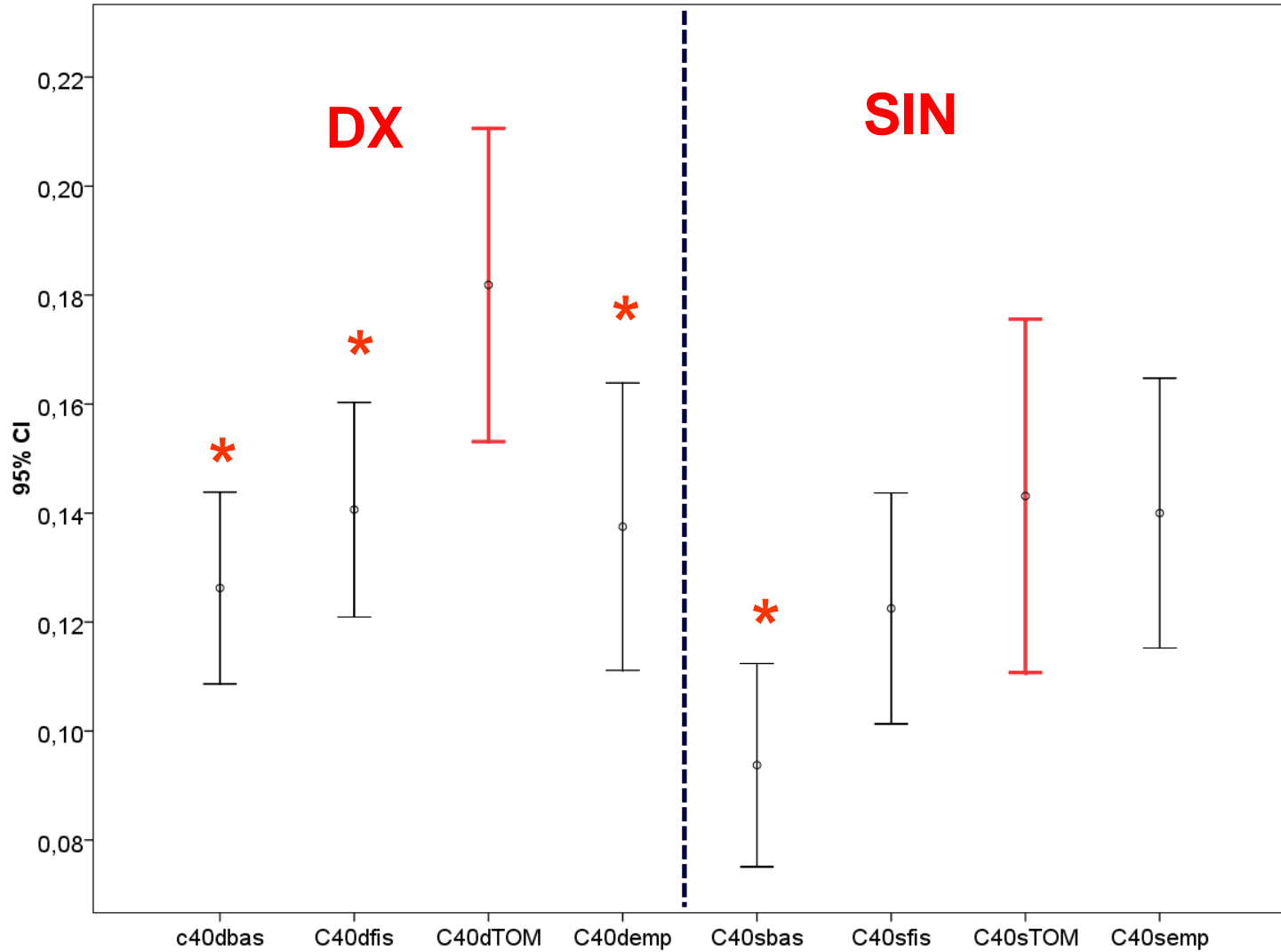
Frequenza coerenza FC – PO risposte esatte



dbas	38,56 ± 2,29
dfis	39,23 ± 2,27
dTOM	39,03 ± 2,48
demp	38,59 ± 1,79

sbas	37,66 ± 2,45
sfis	38,86 ± 2,62
sTOM	38,82 ± 2,22
semp	38,83 ± 2,74

Coerenza FC – PO risposte esatte



dbas	0.12 ± 0.03
dfis	0.14 ±,037
dTOM	0.18 ± ,053
demp	0.14 ±,049

sbas	0.09±,035
sfis	0.12 ±,039
sTOM	0.14 ± 0.06
semp	0.14 ± 0.05

Statistica risposte esatte

Misura:MEASURE 1

(I) Coherence dx	(J) Coherence dx	Differenza media (I-J)	Deviazione standard Errore	Sig. ^a	Intervallo di confidenza per la differenza al 95% ^a	
					Limite inferiore	Limite superiore
1	2	,054 [*]	,012	,003	,017	,092
	3	,046 [*]	,012	,009	,010	,082
	4	,049 [*]	,014	,018	,007	,092
2	1	-,054 [*]	,012	,003	-,092	-,017
	3	-,008	,016	1,000	-,056	,039
	4	-,005	,018	1,000	-,058	,048
3	1	-,046 [*]	,012	,009	-,082	-,010
	2	,008	,016	1,000	-,039	,056
	4	,003	,019	1,000	-,054	,060
4	1	-,049 [*]	,014	,018	-,092	-,007
	2	,005	,018	1,000	-,048	,058
	3	-,003	,019	1,000	-,054	,054

Fattori entro soggetti

Misura:MEASURE 1

Coherence dx	Variabile dipendente
1	C40dTOM
2	c40dbas
3	C40dfis
4	C40demp

Misura:MEASURE 1

(I) coherence SX	(J) coherence SX	Differenza media (I-J)	Deviazione standard Errore	Sig. ^a	Intervallo di confidenza per la differenza al 95% ^a	
					Limite inferiore	Limite superiore
1	2	,040 [*]	,012	,028	,003	,077
	3	,022	,013	,734	-,019	,062
	4	,011	,018	1,000	-,043	,065
2	1	-,040 [*]	,012	,028	-,077	-,003
	3	-,018	,010	,541	-,049	,012
	4	-,029	,015	,432	-,074	,016
3	1	-,022	,013	,734	-,062	,019
	2	,018	,010	,541	-,012	,049
	4	-,011	,016	1,000	-,058	,037
4	1	-,011	,018	1,000	-,065	,043
	2	,029	,015	,432	-,016	,074
	3	,011	,016	1,000	-,037	,058

Fattori entro soggetti

Misura:MEASURE 1

coherence SX	Variabile dipendente
1	C40sTOM
2	C40sbas
3	C40sfis
4	C40semp

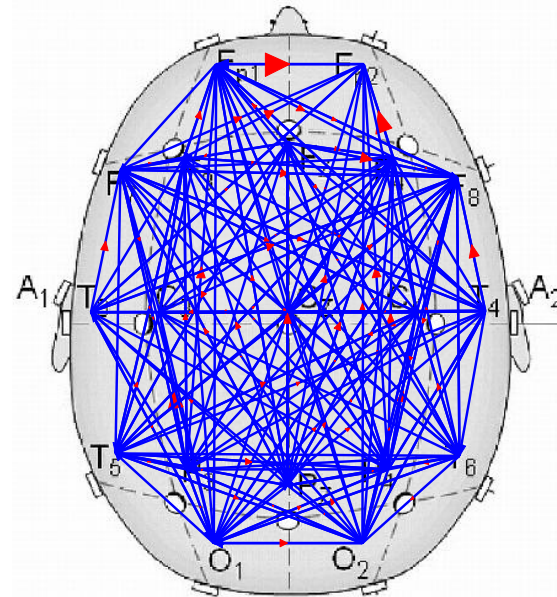
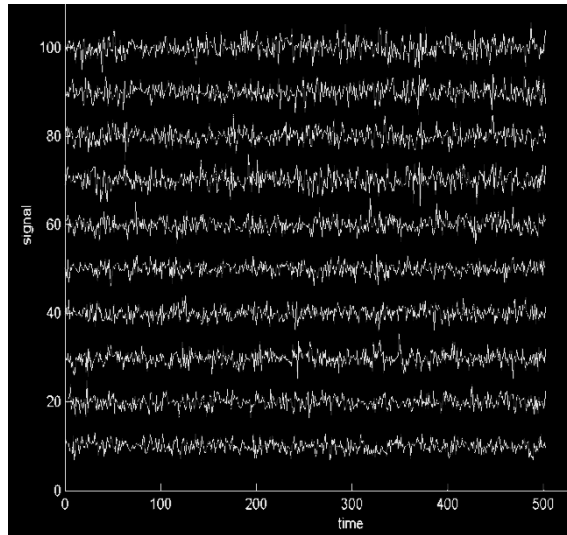
Basato sulle medie marginali stimate

*. La differenza media è significativa al livello .05.

a. Correzione per confronti multipli: Bonferroni.

- Gamma activation is a fundamental process (operator) in the cognitive communication and functioning in the whole brain.
 - Recent observations of
 - increased long-distance connectivity in the gamma band during cognitive processing
 - disruption (under/over-coupling) of long-distance connectivity in the gamma band in neurological diseases with cognitive impairment
- open new research opportunity for understanding of processes of perception, attention, memory, and learning.

Dalla connettività alle reti



EEG: 19 canali → 342 misure

HDEEG: 128 canali → 16256 ”

MEG: 306 canali → 93330 ”

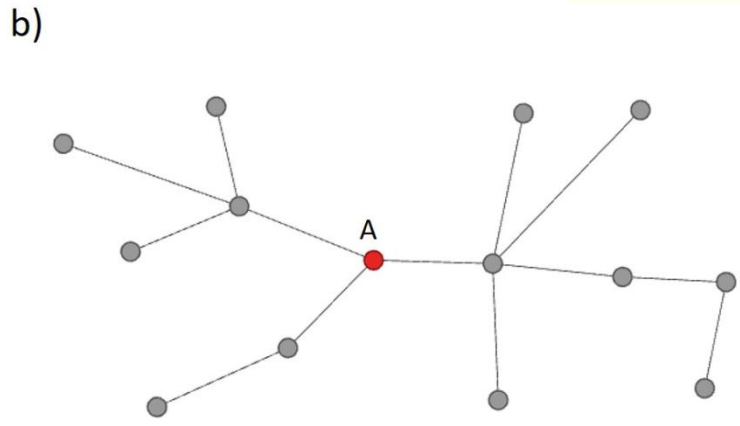
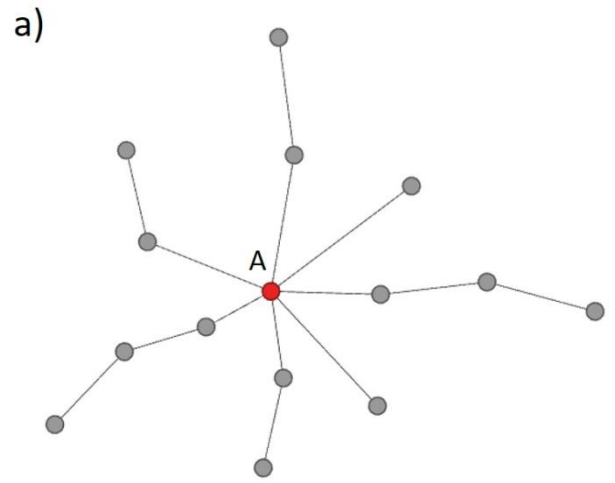
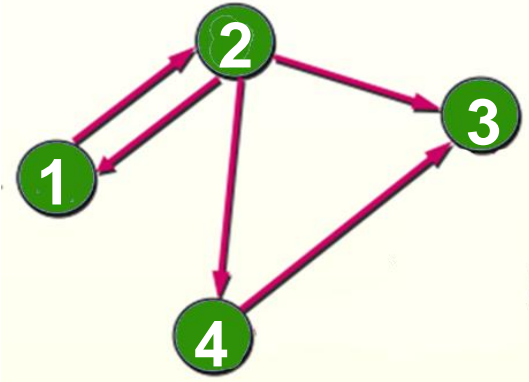
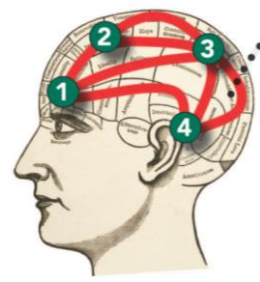
Difficoltà di estrazione delle informazioni



Teoria dei grafi

RETI

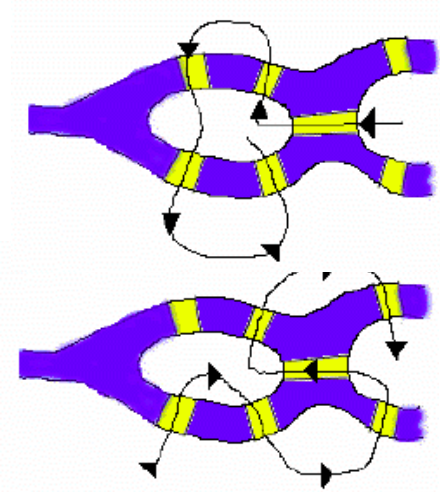
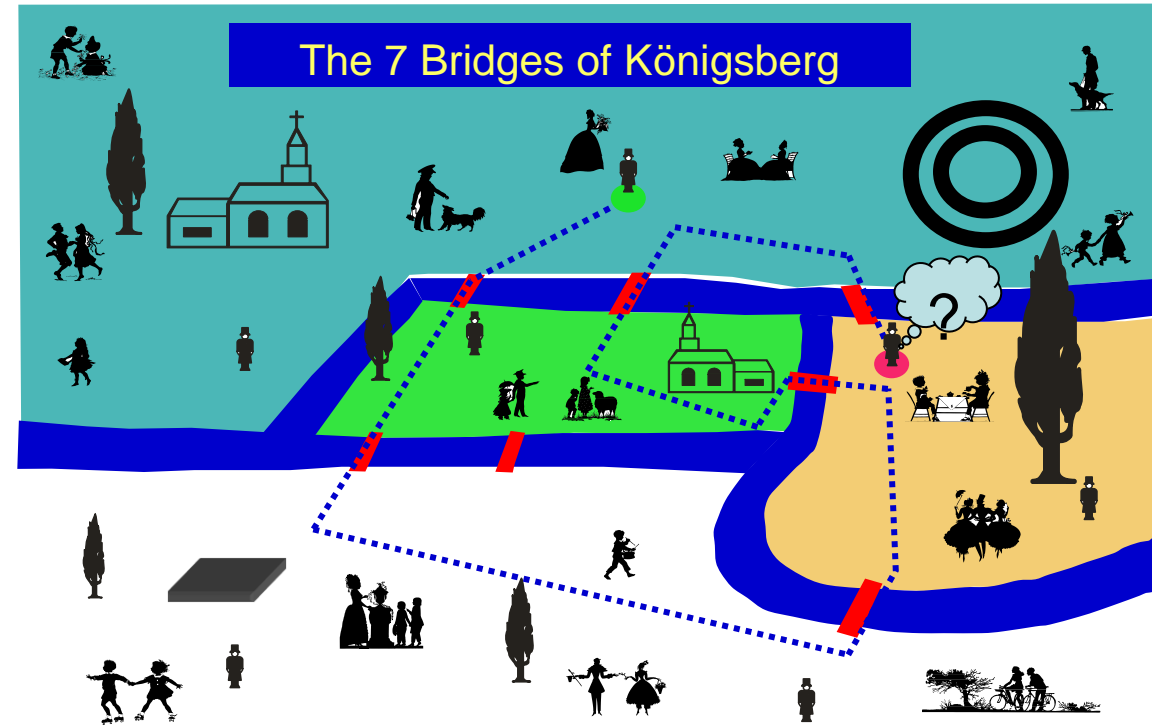
Rappresentazione di un sistema definito mediante collezione di **nodi (vertici)** e collegamenti tra i diversi nodi



HUBS: nodi con molte connessioni e/o posizione centrale all'interno di una rete.

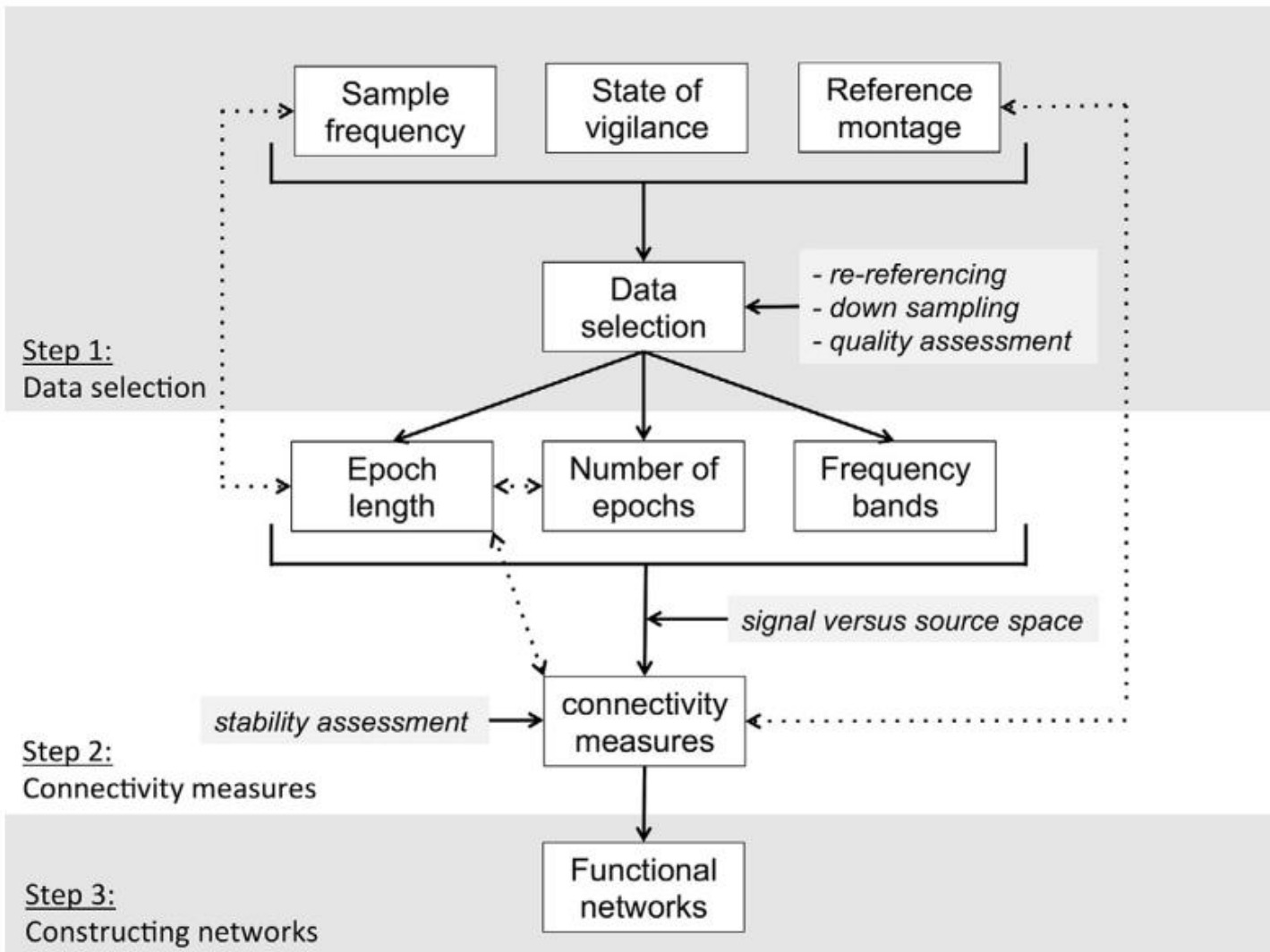
Essenziali per una comunicazione efficiente

7 ponti di Königsberg



river Pregel ran through the city such that in its centre was an island, and after passing it, the river broke into 2 parts. 7 bridges were built so that people could get from one part to another.

People wondered whether or not one could walk around the city in a way that would involve crossing each bridge exactly once



E. van Diessen et al. / *Clinical Neurophysiology* xxx (2014) xxx–xxx

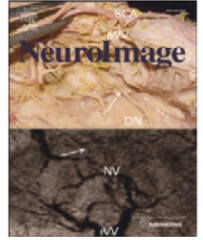
statistics, classification,....



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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

Ten patients who underwent SEEG at the Claudio Munari
Epilepsy Surgery Centre of Niguarda Hospital



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



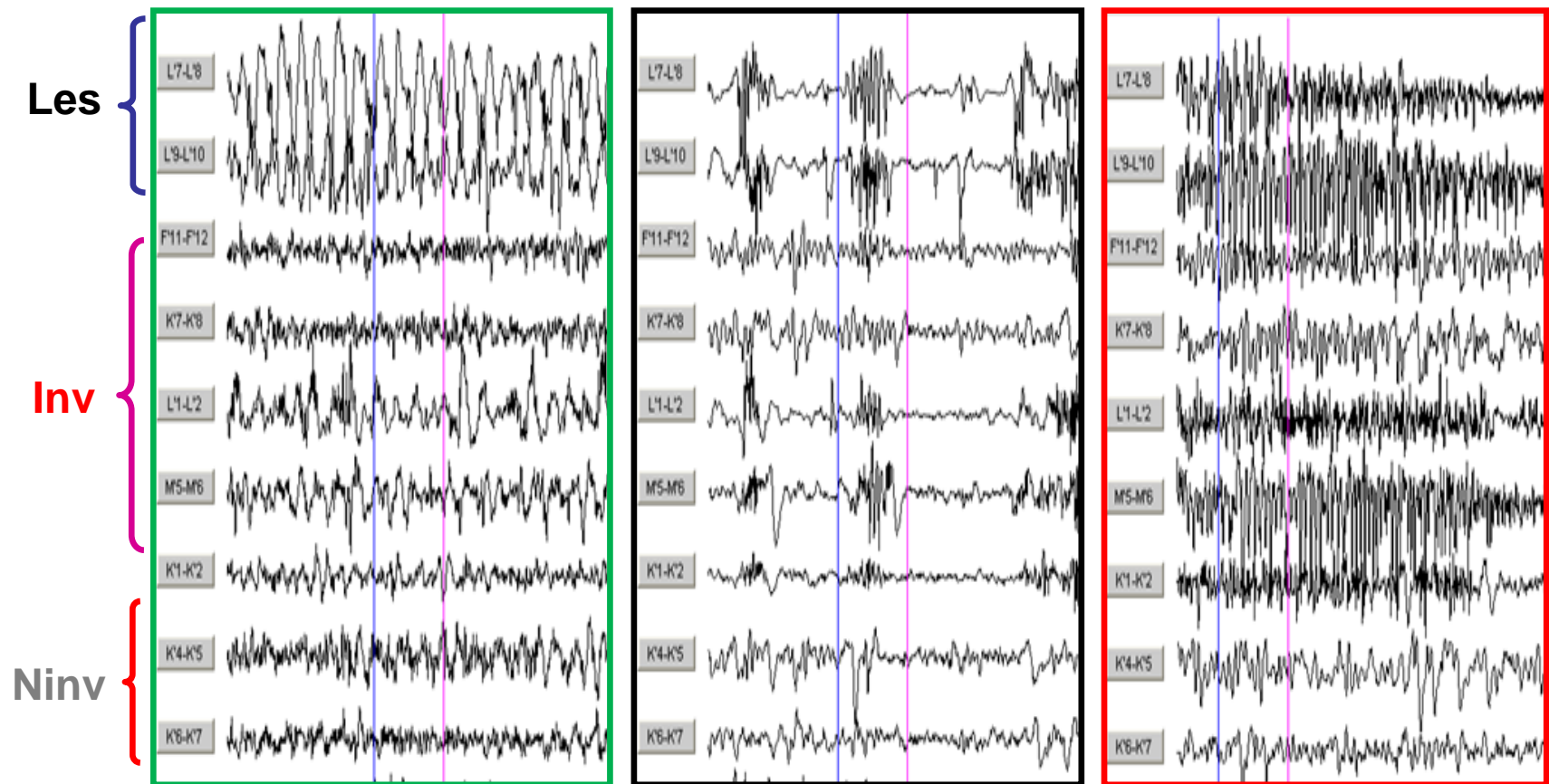
sub-set di 17-24 derivazioni bipolari

- LES: contatti all'interno della FCD
- INV: contatti esterni alla FCD **con** anomalie epilettiformi durante la crisi
- N_INV: contatti esterni alla FCD **senza** anomalie epilettiformi durante la crisi

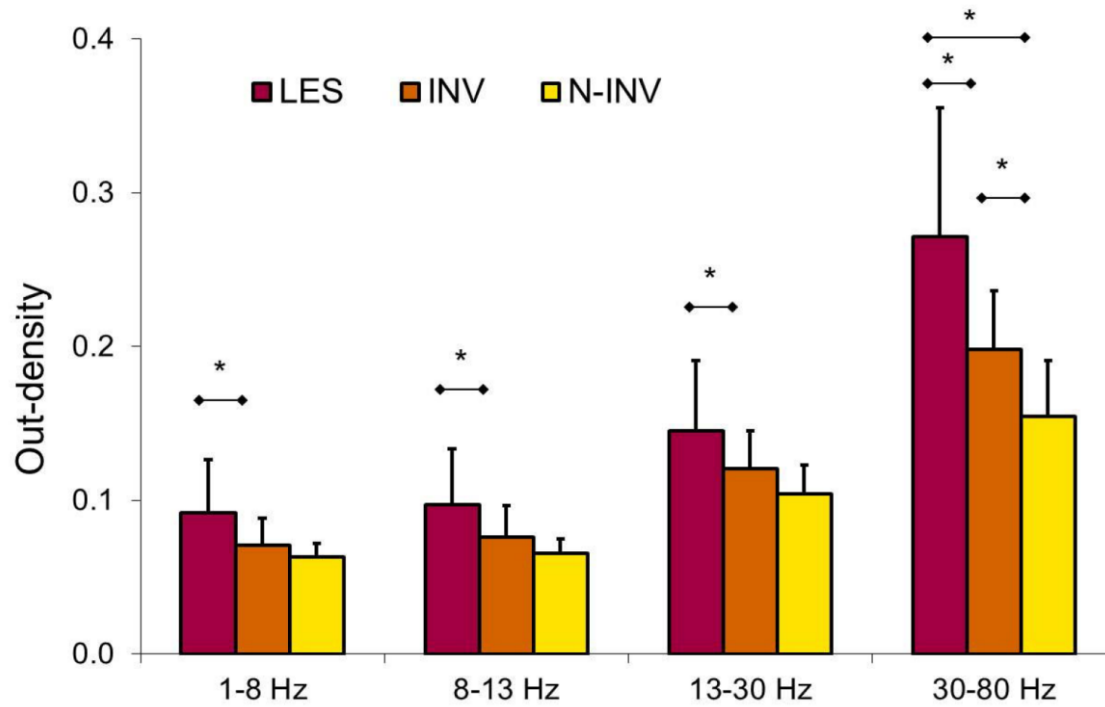
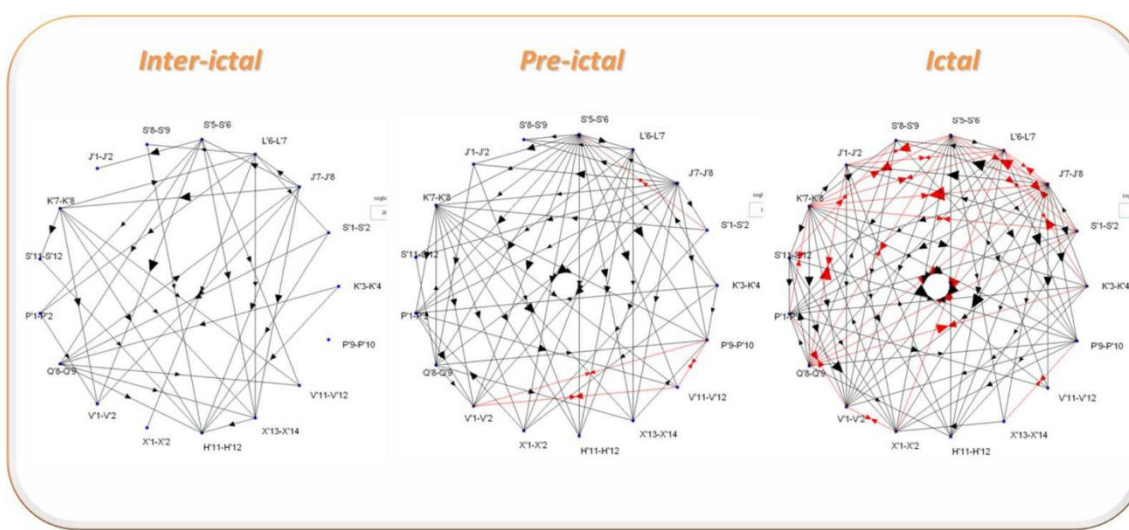
INTER-ICTAL

PRE-ICTAL

ICTAL

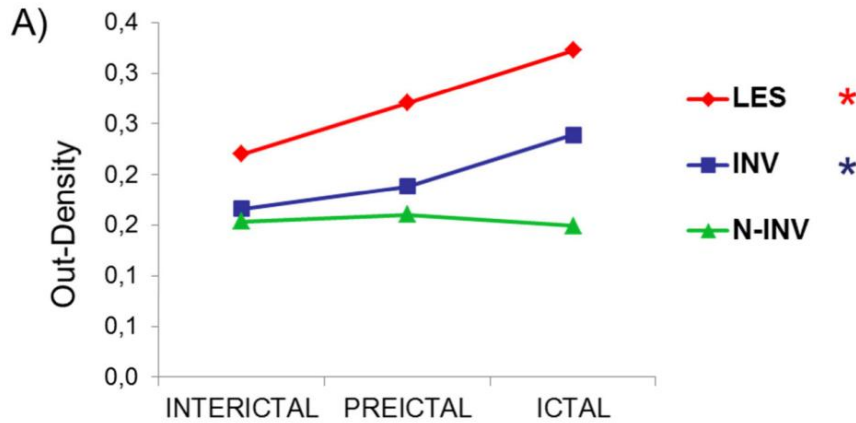


100 μ V



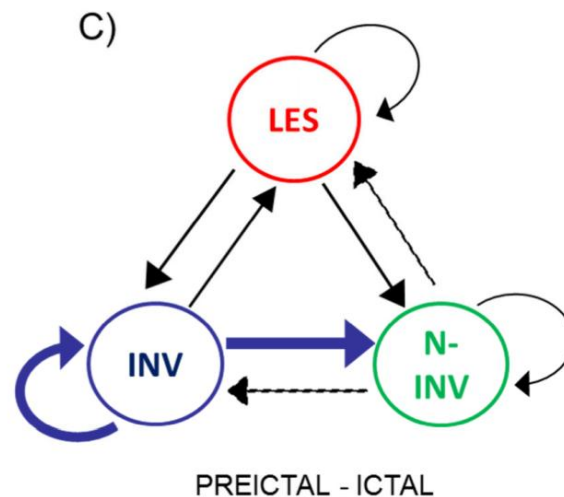
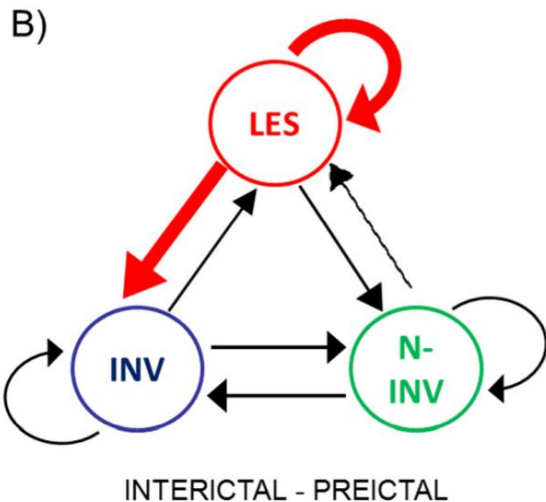
- Epileptogenic area showed abnormal out-going connectivity
- The main significant changes occurred in the gamma band.

Temporal Dynamic changes



FDC plays a leading role in generating and propagating ictal EEG activity by acting as a hub.

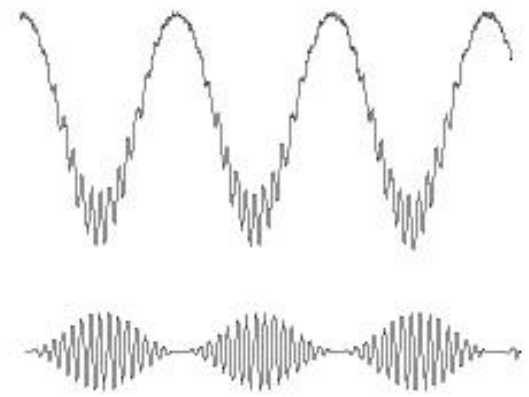
The other cortical regions involved in the ictal activity essentially act as “secondary” generators.



significant (colored arrows) and non-significant (black arrows) increases between two temporal conditions

However,
not only examining brain activity in each single frequency band, but also the relation and interaction between oscillations in different bands, can be informative in understanding brain function.

This concept (cross-frequency coupling CFC) is increasingly received interest especially in the field of cognitive neuroscience.



Grazie

