SIPF
Società Italiana di Psicofisiologia e Neuroscienze Cognitive

XXIX CONGRESSO NAZIONALE
PALERMO, 30 SETTEMBRE • 2 OTTOBRE 2021
AULA MAGNA VINCENZO LI DONNI
UNIVERSITÀ DEGLI STUDI DI PALERMO
BEYOND THE LOCKDOWN OF THE BRAIN

8.30 – 9.30   SIMPOSIO
EEG BIOMARKERS UNVEIL ABNORMAL NEUROPHYSIOLOGICAL MECHANISMS
IN PATIENTS WITH ALZHEIMER'S AND LEWY BODY DISEASES
CHAIRS: Claudio Babiloni (Roma) – Fabrizio Vecchio (Roma - Noverate, CO)

# EEG functional connectivity in cognitive domains: method and application to Default Mode Networks

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BACKGROUND

The **Default Mode Network (DMN)**, such as other **resting state brain networks, were firstly described in PET and fMRI studies** and replicated many times in literature, as sets of brain regions having highlytime-modulated bloodflow/ metabolic coherent changes interconnected for specific brain functions
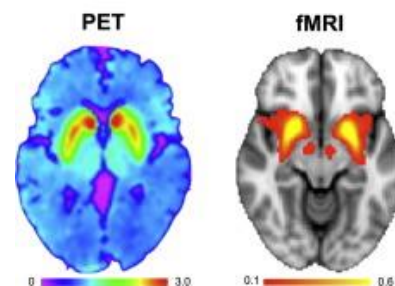
These studies converged on the observation the **DMN is a set of widely distributed brain regions in the parietal, temporal and frontal cortex**. These regions often **show reductions in activity during attention-demanding tasks but increase their activity across multiple forms of complex cognition**, many of which are linked to **memory or abstract thought**.

Default Mode
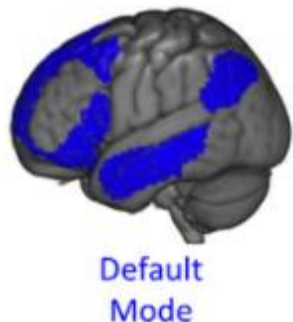
The DMN regions: the posterior cingulate, precuneus, inferior parietal cortex, orbitofrontal cortex, medial prefrontal cortex, ventral anterior cingulate, left dorsolateral prefrontal cortex, left parahippocampus, inferior temporal cortex, nucleus accumbens and the midbrain.

Such cerebral areas are relevant in **self-related information processing, episodic memory** as spontaneous cognition and aspects of consciousness, empathy, and **decision-making.**

DMN is linked with **recollection of autobiographical information**, self-projection in a situation and low-level attentional focus.

APPLICATION TO NEURODEGENERATIVE PROCESSES

Recently, because of the putative association between the **DMN** and **memory**, **cortical activations of the DMN have been investigated to assess** the underlying **physiopathology of AD** and of the **prodromal stage of dementia** known as **Mild Cognitive Impairment (MCI).**

Several papers reported **a preferential evolution according to the type of MCI**. Specifically, **amnesic MCI subjects are more likely to progress in AD** while non amnesic MCI subjects more often evolve to a form of dementia other than AD.

Moreover, **the involvement of executive and linguistic domains beside memory has been found to be a good predictor of evolution in dementia among amnesic MCI.** The progressive association of the different cognitive domains could explain how AD progresses

MCI subjects classification based on their neuropsychological profile, characterized by three subtypes of MCI:

- subjects with pure memory disturbances
- subjects with **impaired memory and language**
- subjects with **deficits in executive functions and processing speed.**

Top view

Bottom view

Default Mode
Network
DMN
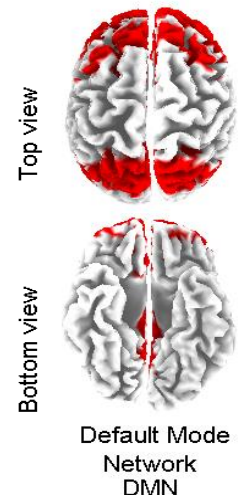
NEW APPROACHES

The relationship among **cognitive domains' impairment**, **DMNs' modulation, and MCI conversion** could be a challenge for possible future models of dementia risk's prediction.

The **connectivity-based approaches** can map large-scale networks in health and detect the network-level alterations in disease with the **graph theory** solution.

Several studies have demonstrated that the brain has **a Small World (SW) network** architecture, which makes it efficient in a rapid information flow through a sparse connectivity network.

Authors reported **modulation of SW network properties in several frequency bands of M/EEG recordings in AD, which is associated with less efficient information exchange between brain areas, thus supporting the disconnection hypothesis of AD.**
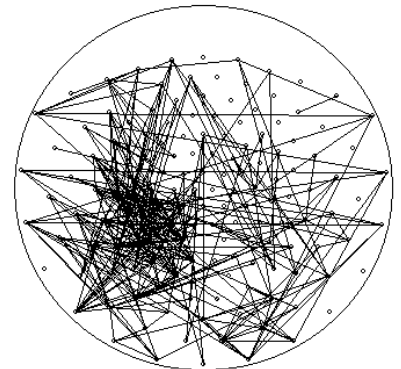
EEG FUNCTIONAL CONNECTIVITY IN MCI SUBJECTS WITH MULTIDOMAIN IMPAIRMENT
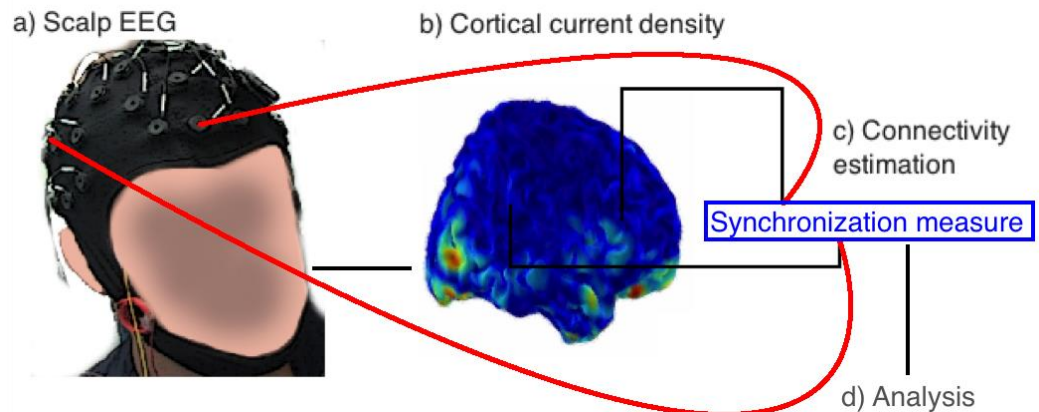
Small World Index in Default Mode Network Predicts Progression from Mild Cognitive Impairment to Dementia

Francesca Miraglia ✉, Fabrizio Vecchio, Camillo Marra, Davide Quaranta, Francesca Alù, Benedetta Peroni, Giuseppe Granata, Elda Judica, Maria Cotelli and Paolo Maria Rossini

EEG was explored because it is a useful tool for the study of the temporal dynamics of ongoing brain activity in the DMN.

a) Scalp EEG
b) Cortical current density
c) Connectivity estimation
Synchronization measure
d) Analysis

Respect to MRI, the EEG has intrinsically a **high temporal resolution** and can provide a relevant picture of summated neural activities.

Finally, it is a **widely available, non invasive and low-cost procedure**

PARTICIPANTS

59 amnesic MCI (aMCI) subjects that met Winblad 2004 and Petersen 2011 criteria (mean age 72.86±0.7SE;mean education 10.24±0.6SE;mean MMSE 25.81±0.26SE).

All subjects were characterized in:
-**MCI** with and without **linguistic domain impairment** in the first analysis;
- in the second analysis all the subjects were further divided in **MCI** with and without **executive domain** impairment **according to the results of executive and linguistic tests.**

The participants were further classified respect to their **clinical evolution after 48 months follow-up:**
- **converted to AD** (30 subjects, mean age 73.1 years *±0.19 SE*)
- **stable MCI** (29 subjects, mean age 72.6 years *±0.17 SE)*

Neuropsychological tests subjects' classification in linguistic and/or executive domain impairment:
Rey's Auditory Verbal Learning task and Rey-Osterreith figure and delayed recall of Rey's figure; Episodic Memory Score; Language: Phonological and semantic fluency; Visuospatial function: copy of Rey's figure. Copy of drawings with and without landmarks; Executive function and behavior: Stroop colour-word test; MFTC (Multiple Features Target Cancellation)

METHODS

- 32 EEG channels data recordings

- 5' Eyes closed resting state condition

- EEG sources connectivity analysis by graph theory (Small World index) in **Default Mode Network** based on fMRI studies (Allen et al., 2011, Agosta et al., 2012)

- **10 BAs for left and right hemisphere**, as evaluated by neuroanatomic Montreal Neurological Institute (MNI) space with correction to Talairach space

| Regions	Brodmann areas
Posterior cingulate cortex/precuneus	23
Inferior parietal lobe IPL (angular gyrus)	39
Pregenual Anterior Cingulate Cortex ACC	10
Dorsolateral Pre frontal cortex PFC/ Middle frontal gyrus	8
Precuneus	7
Inferior Parietal Lobe IPL (supramarginal gyrus)	40
Dorsolateral Pre Frontal cortex PFC	46
Medial temporal cortex	22
Middle cingulate cortex	31
Anterior cingulate cortex	32
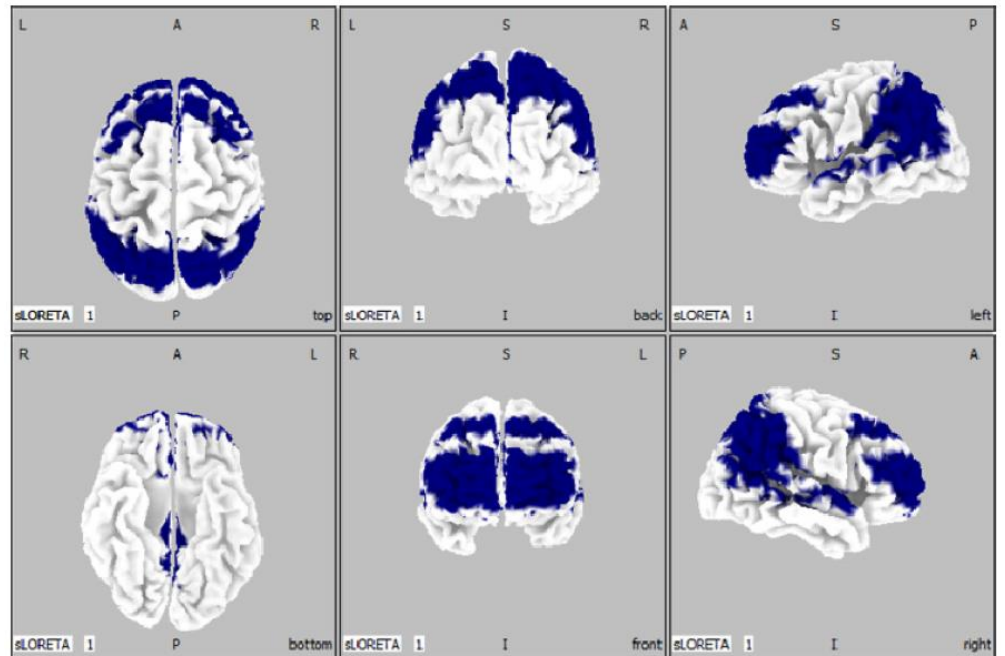
EEG DATA PROCESSING

Undirected and weighted networks based on **eLORETA connectivity** between Regions Of Interest (ROIs). The **nodes** of the network are **ROIs,** the **edges** of the network are weighted by the **Lagged Linear Connectivity values**.
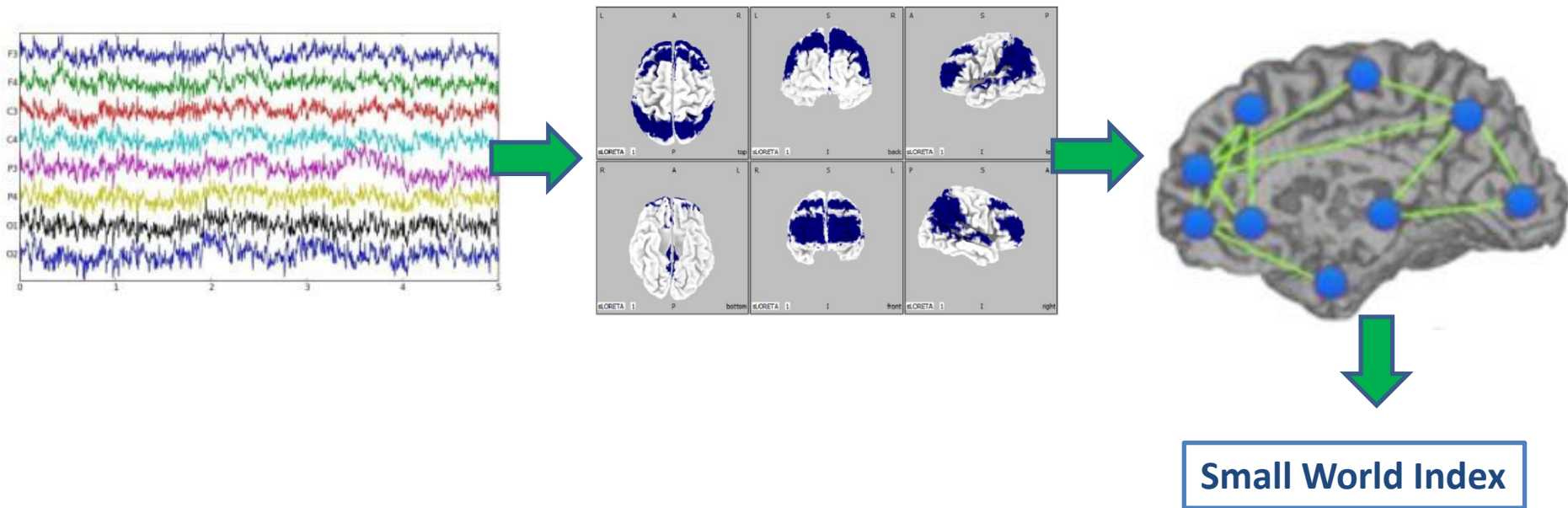
Small World Index

The **Small World Index** (SW) describes the balance between local segregation and global integration of a network. It is defined as the ratio between normalized C and *L - C^w* and *L^w* - with respect to the frequency bands (delta, theta, alpha1, alpha2, beta1, beta2, gamma).

Results I: DMN IN CONVERTED AND STABLE aMCI SUBJECTS WITH <u>LINGUISTIC</u> DOMAIN IMPAIRMENT

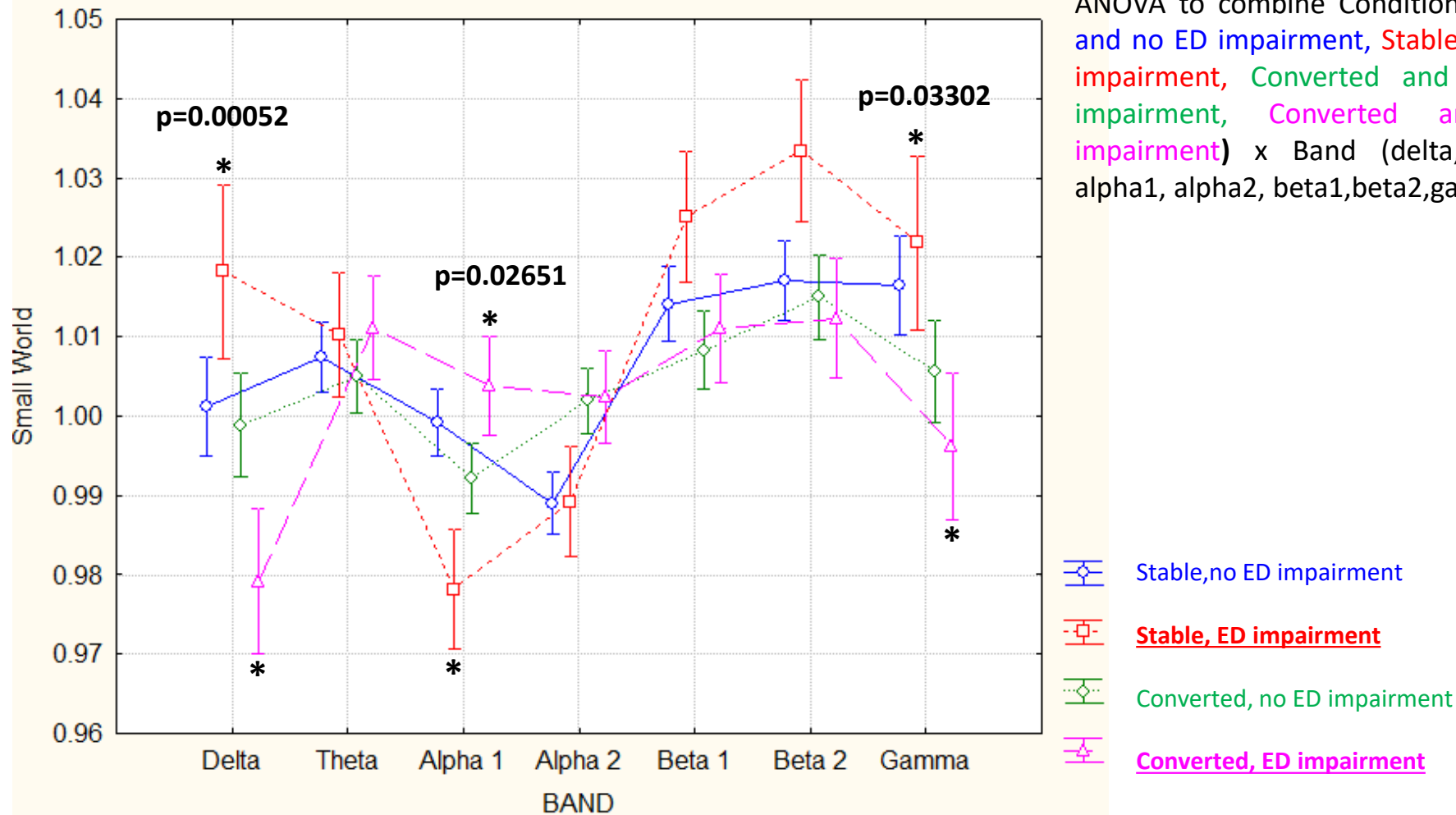Current effect: F(18, 330)=1.7751, p=.02709

p=0.001275
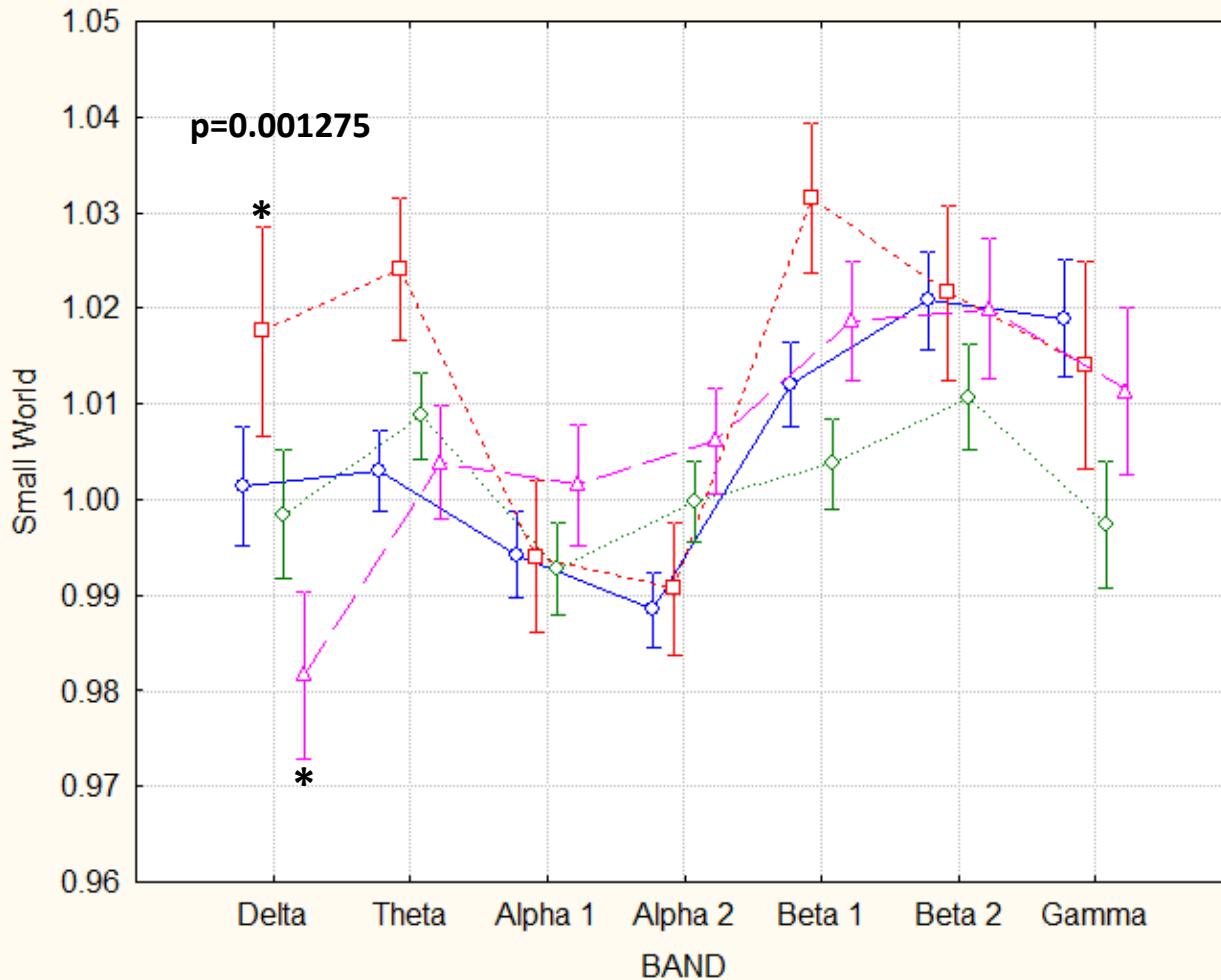
A two-way ANOVA to combine Condition **(**Stable and no LD impairment, Stable and LD impairment, Converted and no LD impairment, Converted and LD impairment**)** x Band (delta, theta, alpha1, alpha2, beta1,beta2,gamma).

Stable,no LD impairment

Stable, LD impairment

Converted, no LD impairment

Converted, LD impairment

Results In DMN of subjects **who presented impairment in linguistic domain, the small world index decreased in delta band in mci converted subjects respect to mci stable subjects .**

Results II: DMN IN CONVERTED AND STABLE aMCI SUBJECTS WITH <u>EXECUTIVE</u> DOMAIN IMPAIRMENT

Current effect: F(18, 330)=1.8364, p=.02050

The second analysis was a two-way ANOVA to combine Condition (Stable and no ED impairment, Stable and ED impairment, Converted and no ED impairment, Converted and ED impairment) x Band (delta, theta, alpha1, alpha2, beta1,beta2,gamma).

- Stable,no ED impairment
- **Stable, ED impairment**
- Converted, no ED impairment
- **Converted, ED impairment**

Results In DMN of subjects who presented impairment **in executive domain,** the small world index **decreased in delta and gamma band and increased in alpha 1 band in mci converted subjects respect to mci stable subjects .**

CONCLUSIONS

❑ **Both groups of patients with linguistic and executive domains impairment presented the same trend in low EEG frequency bands–delta band-revealing a reduction of SW architecture in subjects who converted to dementia.**

❑ **The alterations in delta, alpha, and gamma bands of MCI subjects with executive domain impairment:**
   ❑ **confirm previuosly evidence** of AD and MCI subjects SW modulation respect to Control Group (Vecchio et al., 2018)
   ❑ **could be considered in line with the hypothesis that the executive domain impairment is interpreted as a higher risk of neurodegenerative mechanisms in act** compared to the linguistic domain.

❑ The **SW index delta- alpha reciprocal inhibition** might **reflect a process of progressive disconnection of the aging brain** that could appear as **a loss communication efficiency in the brain in the executive domains.**

❑ Several previous studies revealed that **alpha and gamma bands are involved in attention and memory processes, such as in memory tasks including episodic, encoding, retrieval and in elevated recognition memory performance**, and that alpha and gamma band selective involvement could be considered an **important marker for cognitive decline.**

FUTURE PERSPECTIVES

❑ The combination of **Neuropsychological and Neurophysiological** investigations could represent an **interesting method to distinguish among MCI subjects presenting with specific cognitive patterns,** specifically between those subjects that remain in a **stable condition** and those subjects prone to **convert to overt dementia**.

❑ This aspect could encourage further studies to confirm our results and to **find** possible **biomarkers of MCI progression**.

Thanks for your Attention!

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Inclusion criteria

The age of the subjects was between 50 and 85 years; for each subject, Mini Mental State Examination

score was corrected by age and education and its value was equal or superior to 24/30; Clinical Dementia Rating (CDR) global score was 0.5.

All MCI subjects were administered the following tests exploring memory functions: Rey's Auditory Verbal Learning task and Rey-Osterreith figure and delayed recall of Rey's figure; Episodic Memory Score; Language: Phonological and semantic fluency; Visuospatial function: copy of Rey's figure. Copy of drawings with and without landmarks; Executive function and behavior: Stroop colour-word test; MFTC.

Every six months the subjects underwent a full neuropsychological assessment and a neurological

examination. Based on test performances and clinical examination, the neurologist established whether the subject has progressed to dementia.

Exclusion criteria

Subjects with history of cerebrovascular disease,alcohol abuse, severe medical disorders associated

to cognitive impairment were excluded; subjects in chronic treatment with psychotropic drugs or with

neuroimaging evidences of other potential causes of cognitive decline were ruled out from the study.

Results I: DMN IN CONVERTED AND STABLE aMCI SUBJECTS

Current effect: F(6, 342)=2.5014, p=.02209

p=0.031926
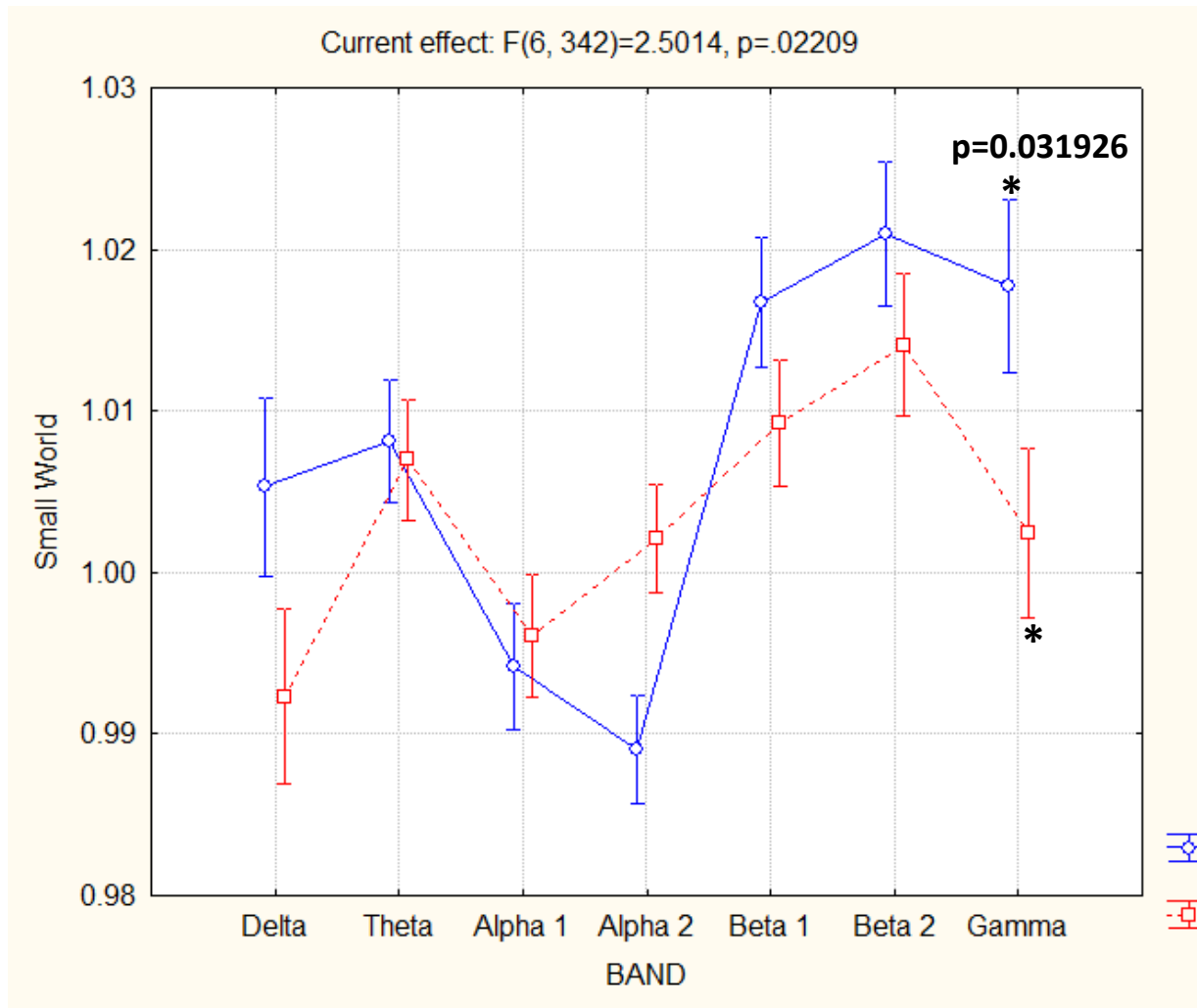
Two-way ANOVA to compare SW index in DMN in Stable and Converted aMCI subjects

All the EEG data were recorded in the baseline, while the conversion was evaluated during follow up visits.

Stable

Converted

Results In DMN, the SW index significantly **decreased in low gamma band** in converted MCI subject compared to stable MCI subjects, in the EEG evaluated at the baseline.