Connectivity in epilepsy: Characterization of pathological networks on EEG, MEG and intracerebral EEG

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Course « EEG and MEG connectivity: Basic principles, state-of-the-art methods, and emerging vistas"
Epilepsy

- Approximately 50 million people have epilepsy, making it one of the most common neurological disease (Source WHO)

- Epilepsy is characterized by recurrent seizures, which are pathological hyper-synchronization of brain networks

- In 1/3 of patients, pharmacological treatment cannot stop seizures, and epilepsy surgery can be considered

  => Requires to map precisely the extent of the epileptogenic zone
Presurgical evaluation

The goal of presurgical evaluation is to map the tissues to be resected (i.e., the epileptogenic zone)

• Phase 1: non invasive measures
  Electrophysiology, imaging (MRI, PET, SPECT), video-EEG

• Phase 2: intracerebral EEG
  10 to 15 electrodes, targeting deep structures, with 5 to 15 contacts each
The hallmark of epilepsy is the ‘fast discharge’ as visible on intracerebral EEG. But other patterns of seizure start may exist (Lagarde et al Epilepsia 2016).
Interictal discharges

Interictal spikes

High frequency oscillations

Anywave software meg.univ-amu.fr

Urrestarazu et al 2007
Why study MEG/EEG/SEEG epileptic networks?

- Electrophysiology has the temporal dimension to track propagation at the millisecond time scale

- Large networks can be involved early at the seizure onset => importance of quantification for delining the tissues to be resected (local measures)

- Connectivity is a promising venue as new biomarkers of epileptogenic tissues (global measures (graph measures))

Bartolomei et al 2001

Adebimpe et al 2016
INTRACEREBRAL NETWORKS
Epileptogenicity (local) indices

Bartolomei et al 2008

David et al 2008

See also Gnatkovsky et al Epilepsia 2011

The indices take into account the increase of energy in the high frequency (gamma band) and the time of involvement in the seizure.
Connectivity measures

= measure the level of coupling between distant areas

Coherence (correlation in frequency domain)
Gotman 1983 (measure of directionality!)
See also Gotman and Levtova 1993

Other connectivity measures:
Granger causality phase locking index

Wendling et al 2001: non linear correlation (h2)
See also Pijn et al 1989
Time-varying connectivity graphs (« dynamic connectivity ») results in complex patterns:

Graph measures summarize graph properties. Simplest (local) measures:

IN and OUT degrees (number of ingoing and outgoing arrows at a given node)
IN and OUT strength (sum of ingoing/outgoing connectivity values)

For other local measures see Amini et al Physiol Meas 2010
Seizure start is (typically) a period of decrease of synchrony!

Wendling et al. Brain 2003

→ Importance to investigate « after discharge », preictal and interictal periods
Ictal SEEG

Van Mierlo et al 2013
Interictal Networks

Step 1 and 2: detection of mono-IIS and formation of multi-IIS

Co-occurrence boolean matrix: $B = \begin{bmatrix} 1 & 0 & 1 & 1 & 0 & 1 & 0 & 1 & \ldots & 1 \\ 1 & 1 & 1 & 1 & 0 & 1 & 1 & 1 & \ldots & 1 \\ 0 & 1 & 1 & 1 & 0 & 1 & 1 & 1 & \ldots & 1 \\ 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & \ldots & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & \ldots & 0 \end{bmatrix}$

Step 3: extraction and visualisation of SCAS

C1: search of frequent sets ($\lambda=0.1$) and
C2: search of significant sets ($\beta=99.9\%$) and
C3: search of maximal sets ($\eta=0.25$)

Graphical representation of SCAS

Bourien et al 2005
Preictal networks

Courtens et al Brain Connect 2016
Preictal networks: impact of frequency band

Courtens et al Brain Connect 2016
SURFACE (MEG, EEG) NETWORKS
Connectivity at source level: EEG

Dynamic directed interictal connectivity in left and right temporal lobe epilepsy

Coito et al. Epilepsia 2015

Connectivity method: weighted partial directed coherence

Display of Spikes networks + node in/outflow

Coito et al. Epilepsia 2015
Connectivity at source level: EEG (2)

Connectivity method: non linear correlation $h^2$

Test with both simulated and real data

Hassan et al Brain Topogr 2017
MEG connectivity at source level

Dai et al. Brain Topogr 2012

One does not need visible spikes!

Epileptic focus localization based on resting state interictal MEG recordings is feasible irrespective of the presence or absence of spikes

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Krishnan et al Clin Neurophysiol2015

See also Jmail et al Brain Topogr 2016

Spike-free connectivity changes: Monto et al Cereb Cortex 2007, Bettus et al Epilepsy res2008
ICA-based MEG connectivity

MEG

ICA

Directed co-occurrence graphs

ICA1

ICA7

Source localization on components

Malinowska et al Hum Brain Mapp 2014

See also Mullen et al 2011!
MEG ICA networks

Malinowska et al, Hum Brain Mapp 2014

-> very good concordance between MEG and SEEG leaders
MEG ICA networks

Malinowska et al, Hum Brain Mapp 2014

-> only part of network can be retrieved (sensitivity must be assessed!)
Limitations of separate recordings

• Separate MEEG/SEEG recordings may not record the exact same activity (fluctuations across brain states)

• Separate recordings do not allow using single trial fluctuations as source of information (as in simultaneous EEG-fMRI)

=> The next step is to record them simultaneously!
SIMULTANEOUS RECORDINGS
Feasibility and setup

Dubarry et al, NIMG 2014

Badier et al J Physiol Meas in press
Example of networks
MEG can expand SEEG view

SEEG-triggered spike average permit to localise a region outside of SEEG implantation
PITFALLS
Source Leakage


Brookes et al 2012
Overlap spikes/oscillations

Filtering sharp spikes or artefacts produces oscillations => there can be a contribution of transients to higher frequency bands (gamma, ripples, even fast ripples)

Benar et al 2010
Solutions to «false ripples»?

«Despiking»

Time-frequency or time-scale analysis

Jmail et al J Physiol Meas 2017

Difficult! See Jmail et al J Neurosci Meth 2011

Lina et al IEEE Trans Biomed Eng 2014

See also Roehri et al 2016, 2017 (whitening procedure)
CONCLUSIONS AND FUTURE DIRECTIONS
• Connectivity can be considered as a new marker in EEG/MEG analysis

• Confirmed by intracerebral EEG recordings

• New venues:
  – Simultaneous recordings for characterizing sensitivity of MEG/EEG
  – Joint analysis of simultaneous recordings (both local and global view)
  – Computational modelling for understanding signals and for parameter estimation
THANK YOU FOR YOUR ATTENTION!