A physiological connectome of the human brain based on intracranial electrical stimulation in patients with epilepsy

Cristian Donos

Mihai Maliia, Ioana Mindruta, Jean Ciurea, Andrei Barborica

1Physics Department, University of Bucharest, Bucharest, Romania
2Neurology Department, University Emergency Hospital, Bucharest, Romania
3Neurology Department, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania
4Neurosurgery Department, Bagdasar-Arseni Hospital, Bucharest, Romania
5FHC Inc, Bowdoin ME, USA

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Presentation Outline:

- Presurgical evaluation using Stereoelectroencephalography (SEEG): The challenge of finding the epileptogenic network
- Single Pulse Electrical Stimulation (SPES)
- Physiological Connectome
- Conclusions
Stereoelectroencephalography (SEEG) is the only recording method that allows to record cerebral activity from the mesial structures!

**SEEG**

- Provides direct access to electrophysiological recordings in the seizure onset zone, when located in deep brain structures
- Allows delineation of the epileptogenic area in 3D volume
- Provides excellent time & space resolution
- HFOs and spikes are well evidenced
Trajectory Planning: Optimizing placement based on a vascular Safety Index

\[ SI = 1 - \max(I(z)) \]

**Safety Index (SI)** – quantifies proximity to the blood vessels

\[ I = \text{Maximum Intensity Projection on digital angiogram} \]

Balanescu et al., Stereotact Funct Neurosurg 2014;92(2):117-25
**Epileptogenic network**

**Epileptogenic Zone:**

"the site of the beginning and of the primary organization of the epileptic seizures" (Munari and Bancaud, 1987)

"the minimum amount of cortex that must be resected (inactivated or completely disconnected) to produce seizure freedom" (Luders et al., 2006)

**Symptomatogenic zone**

"area of cortex which, when activated, produces the initial ictal symptoms or signs"

**Functional deficit**

"area of cortex that is not functioning normally in the interictal period"

**Eloquent Cortex**

**Irritative zone**

"area of cortex which generates interictal spikes"

**Seizure Onset Zone**

"area of cortex that initiates clinical seizures"

**Epileptogenic lesion (if present)**

"macroscopic lesion which is causative of the epileptic seizures because the lesion itself is epileptogenic (e.g. cortical dysplasia) or by secondary hyperexcitability of adjacent cortex"

**Epileptogenic Zone**

"area of cortex that is indispensable for generation of seizures"

After Luders et al 2006 & Kahane, AES 2012
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Single Pulse Electrical Stimulation (SPES)

Responses to single pulse electrical stimulation identify epileptogenesis in the human brain *in vivo*

A. Valentín,¹ M. Anderson,¹ G. Alarcón,¹,² J. J. García Seoane,² R. Selway,¹ C. D. Binnie¹ and C. E. Polkey¹

- Current intensity = 1 ÷ 8 mA
- Pulse width = 0.3 ÷ 1 ms
- Interpulse interval = 10 s
**SPES Protocol Parameters – what to use?**

- **Charge per phase** is the underlying parameter that determines the magnitude of the intra-cranial EEG responses to single pulse electrical stimulation.

Presurgical evaluation using Stereoelectroencephalography (SEEG): The challenge of finding the epileptogenic network

Single Pulse Electrical Stimulation (SPES)

Physiological Connectome

Conclusions
Physiological Connectome

Connectivity types:

1. Structural connectivity – the neuroanatomical network (DTI, postmortem dissections)
2. Functional connectivity – nonlinear dynamics of neurons and neuronal populations result in patterns of statistical dependencies (fMRI, EEG, etc)
3. Effective connectivity – causal interactions (electrical brain stimulation, Granger causality)

**STRUCTURAL + EFFECTIVE → PHYSIOLOGICAL CONNECTOME**

Sporns O. Discovering the Human Connectome, MIT Press, 2012
Structural connectivity

NTU-90: A high angular resolution brain atlas constructed by q-space diffeomorphic reconstruction

Fang-Cheng Yeh a, Wen-Yih Isaac Tseng b,c,*

a Department of Biomedical Engineering, Carnegie Mellon University, Pennsylvania, USA
b Department of Medical Imaging, National Taiwan University Hospital, Taipei, Taiwan
c Center for Optoelectronic Biomedicine, National Taiwan University College of Medicine, Taipei, Taiwan

90 healthy subjects → 45 males , mean age 32.58±12.96 years
→ 45 females, mean age 33.58±12.26 years

Fibers extracted using DSISTudio (http://dsi-studio.labsolver.org).
Effective connectivity

Contact selection criteria:

- Outside the epileptogenic network
- SPES responses are over the 3rd quartile (RMS Q3)
- SPES responses with Spearman’s correlation coefficient $\rho > 0.5$ and $p < 0.05$
Physiological Connectome

Workflow:

- SPES > Q3
  - Patient 1
  - ........
  - SPES > Q3
    - Patient N

- SPES > Q3
- DSI Atlas
- List of Structures
- Effective Connectome
- Structural Connectome
- Physiological Structural – Effective Connectome

Fiber directionality:

- S1
  - Rms = 72 uV
  - DTI = 100 fib
  - Rms = 48 uV

- S2
  - Rms = 72 uV
  - DTI = 60 fib
  - Rms = 48 uV

- S1
  - dDTI = 40 fib
  - Rms = 48 uV

- S2
  - dDTI = 60 fib
  - Rms = 72 uV
**Applications:**
- Epileptogenic network identification by comparing patient’s specific connectome with the physiological connectome.
- Identification of stimulus (seizure?) propagation pathways.
Propagation pathways

Given two structures A and B, the pathfinding algorithm performs a multi-level search in the physiological connectome.

The search priorities (at each level) are:
1. Direct connections between A and B
2. The largest number of fibers connecting A to another structure X which is an intermediate structure along the path from A to B

If pathway not found, the search continues with Y, an intermediate structure with the second largest number of fibers connecting A to Y.

And so on...
Propagation pathways

Path finding: stimulus propagation in spite of 0 direct fibers between A - ACC

A  - Right Amygdala
Hc - Hippocampus
LG - Right Lingual Gyrus
PCC - Right Posterior Cingulate
ACC - Right Anterior Cingulate

Answer: A-> Hc -> LG-> PCC-> ACC
Cingulum Bundle – role in emotion processing (Doucet et al. Hum Brain Mapp 2013)
Propagation pathways

Horizontal part of Longitudinal Superior Fascicle
Role: language articulation, verbal memory [disartria and anartria obtained during intraoperative stimulations] (Duffau et al 2003)

PMC – Pre Motor Cortex
R – Rolandic
IPL – Inferior Parietal Lobule

Path: PMC-> R -> IPL (hLSF)
Propagation pathways

Ventral Stream

Role: object identification and recognition

V1’ – Left Primary Visual Cortex
O’ – Left Lateral Occipital
LG’ – Left Lingual Gyrus
F’ – Left Fusiform Gyrus

Path: V1’ -> O’ -> LG’ -> F’ (Ventral Stream)
Conclusions

Advantages:
✓ Based on DTI Atlases and subclinical stimulations (SPES)
✓ Can be updated by adding more patients
✓ Interactive plots for easy visualization of connections

Limitations:
✗ Spatial sampling of SPES
✗ Subjectivity in choosing the fiber extraction parameters
The Research Team

**Biophysics**
- Dr. Andrei Barborica
- Dr. Cristian Donos

**Neurology**
- Dr. Ioana Mindruta
- Mihai Maliia

**Neurosurgery**
- Dr. Alin Rasina
- Dr. Jan Ciurea

**EEG Technicians**
- Mariana Popa
- Victorita Raiciu