Flag–ERA JTC 2017-HBP

"CAUSALTOMICS"

Causal connectomics subtending oscillatory spread and information flow in the human brain

TEAM 1 (coordination): Dr. Antoni Valero-Cabré MD, PhD
Institute du Cerveau et la Moelle-Pitié Salpetrière, Paris FRANCE
TEAM 2: Dr. Ioana Mindruta MD PhD
Bucharest University Emergency Hospital, Epilepsy Unit, ROMANIA
TEAM 3: Dr. Alessandro Principe MD, PhD
Hospital del Mar-IMIM Epilepsy Group, Barcelona, SPAIN

Background

1. Brain **oscillatory activity** and interregional **synchrony** have been shown to subtend **network** communication between neural assemblies characterizing different aspects of human cognition.
2. Coding phenomena allow an efficient activation of **neural networks** and a **transfer of information** essential for complex processes subtending **high-level cognition**
3. Oscillatory and synchrony phenomena have been extensively explored in animals and humans using correlational approaches.
4. Nonetheless, **causal** evidence on the physiological features, anatomical constrains and cognitive role played by oscillations and synchrony in the human brain is still lacking.

Postulates & main deliverable

1. The direct manipulation of **neural oscillations** with **rhythmic patterns** of brain **intracranial stimulation** coupled to intracranial EEG has the potential to **causally** characterize **functional** and **structural interactions**, extending our understanding on how brain networks operate.

2. The causal characterization of reliable maps of **natural frequencies**, **oscillatory entrainment** and information flow across brain regions will open novel therapeutic strategies for patients suffering brain diseases, subtended by synchrony impairments.

We aim to build causal connectivity atlases (*causal connectome*) of the human brain that characterize electro-physiological features, structural constraints and connection directionality.

General Aims

GENERAL AIM 1: ENTRAINMENT OF LOCAL & INTEREGIONAL SYNCHRONY WITH INTRACRANIAL STIMULATION

We will use intracranial electroencephalographic (iEEG) recordings to characterize the causal impact of intracranial rhythmic stimulation patterns on ongoing local brain activity and in interconnected brain areas by means of high-resolution iEEG recordings

See Amengual et al Sci Reports 2017 for feasibility

GENERAL AIM 2: MODELING SPREAD OF OSCILLATORY ACTIVITY THROUGH WHITE MATTER TRACTS

We will combine iEEG recordings and diffusion MRI data from each individual patient and by using structural connectomics, functional connectivity measures, we will model how the spread of information across brain sites is constrained by white matter connectivity

See Donos et al Neuroimage 2017 for feasibility

Scientific Work Packages & Methods

Work Package 1

Collecting, anonymizing and databasing iEEG stimulation data and neuroimaging data on a standardized protocol and determining electrode location.

WP Leader: ICM-Paris, assisted by UBH-BUCH & IMIM-BCN

Work Package 2

Analyzing signs of local phase resetting after single pulse stimulation, natural frequencies and entrainment with bursts of intracranial stimulation.

WP Leader: ICM-Paris assisted by UBH-BUCH

Work Package 3

Analyzing network distributed spread of single pulse and burst patterns across brain locations and calculating information transfer measures.

WP Leader: IMIM-BCN assisted by ICM-Paris

Work Package 4

Analyzing DTI data and co-localization of structural and functional connectivity.

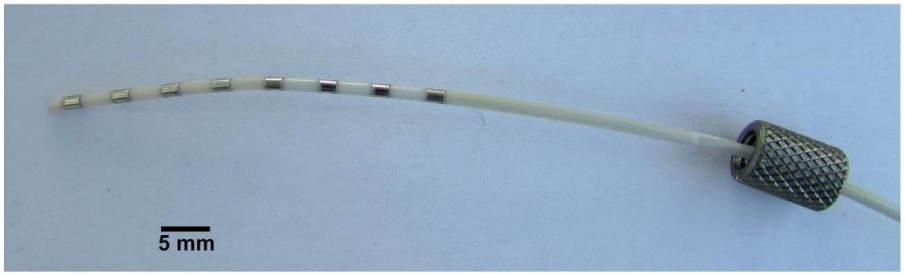
WP Leader: UBH-BUCH assisted by ICM-Paris

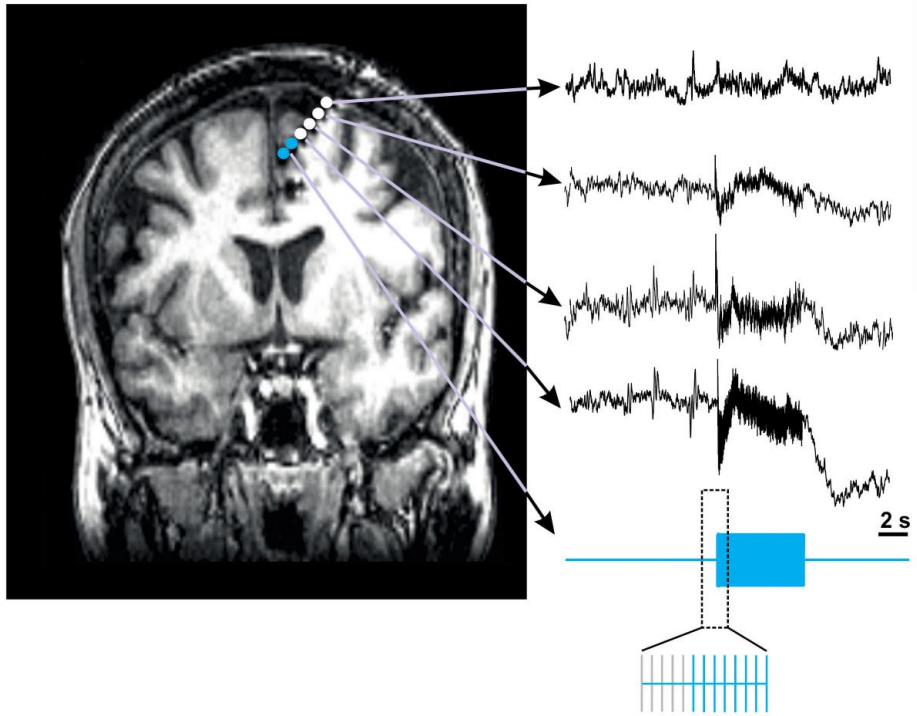
Work Package 5

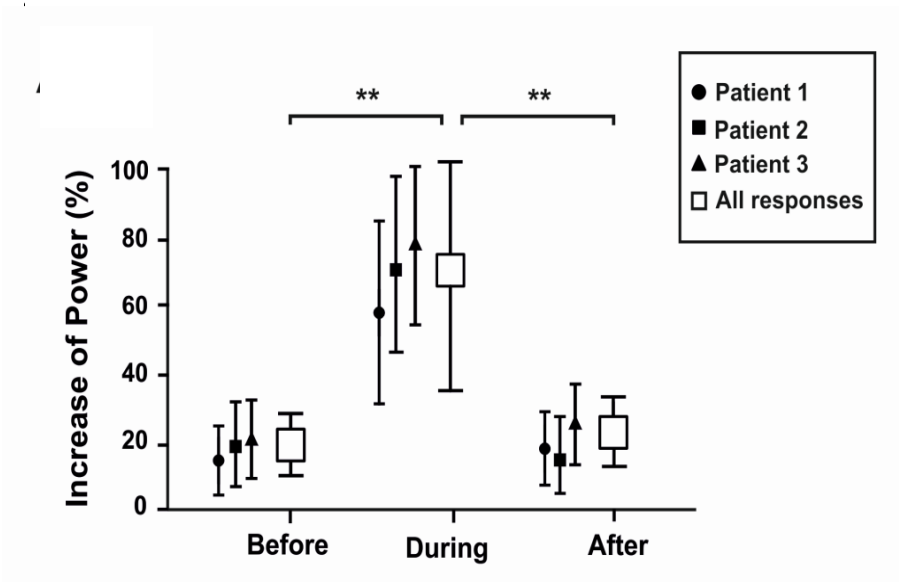
Clinical/cognitive effects of intracortical stimulation in implanted patients.

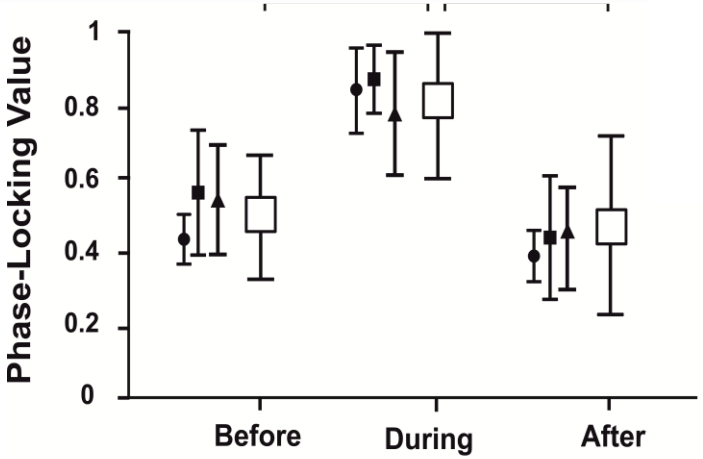
WP Leader: **IMIM-BCN assisted by UBH-BUCH**

WP2: Entraining local oscillations



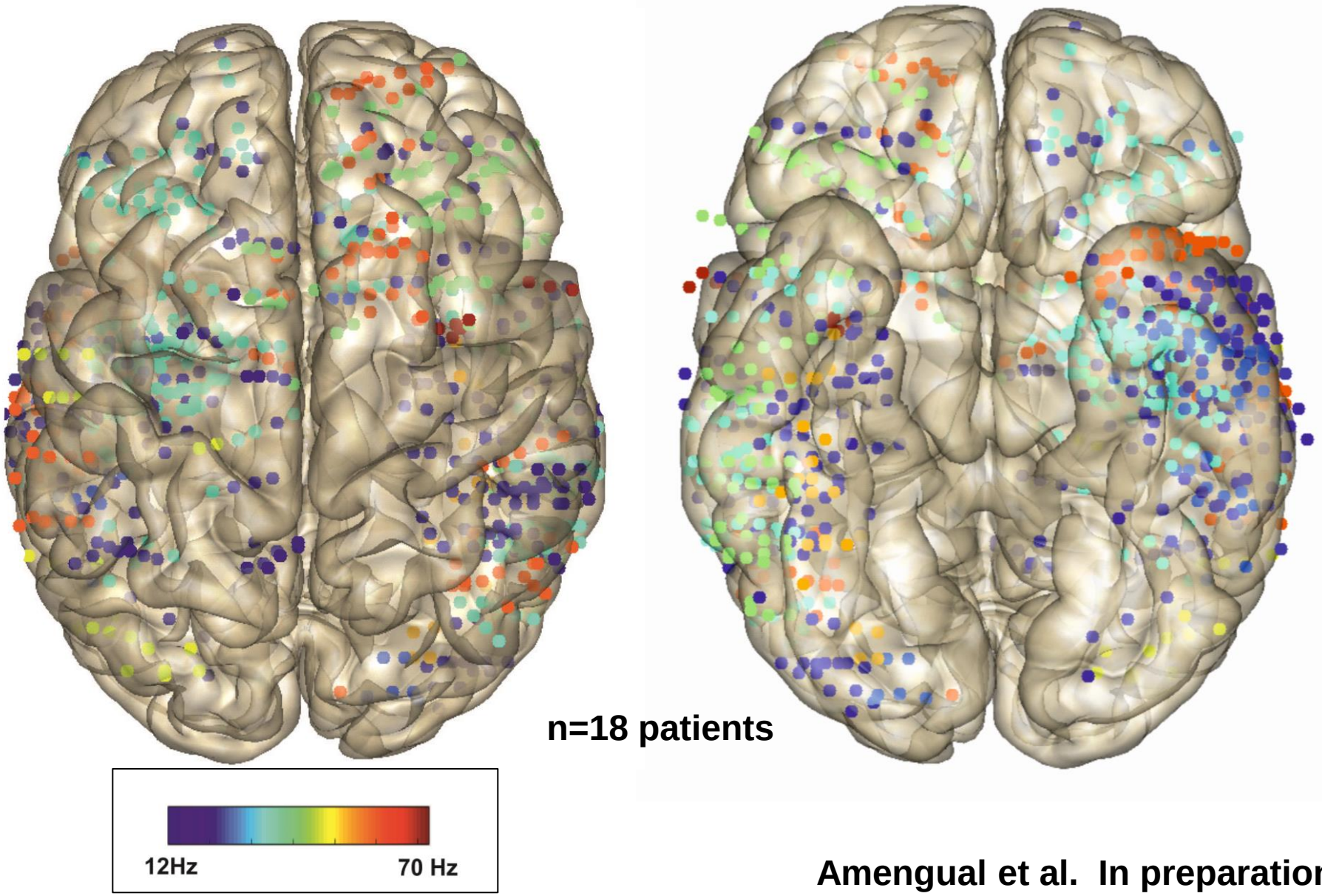






Amengual et al Sci Reports 2017

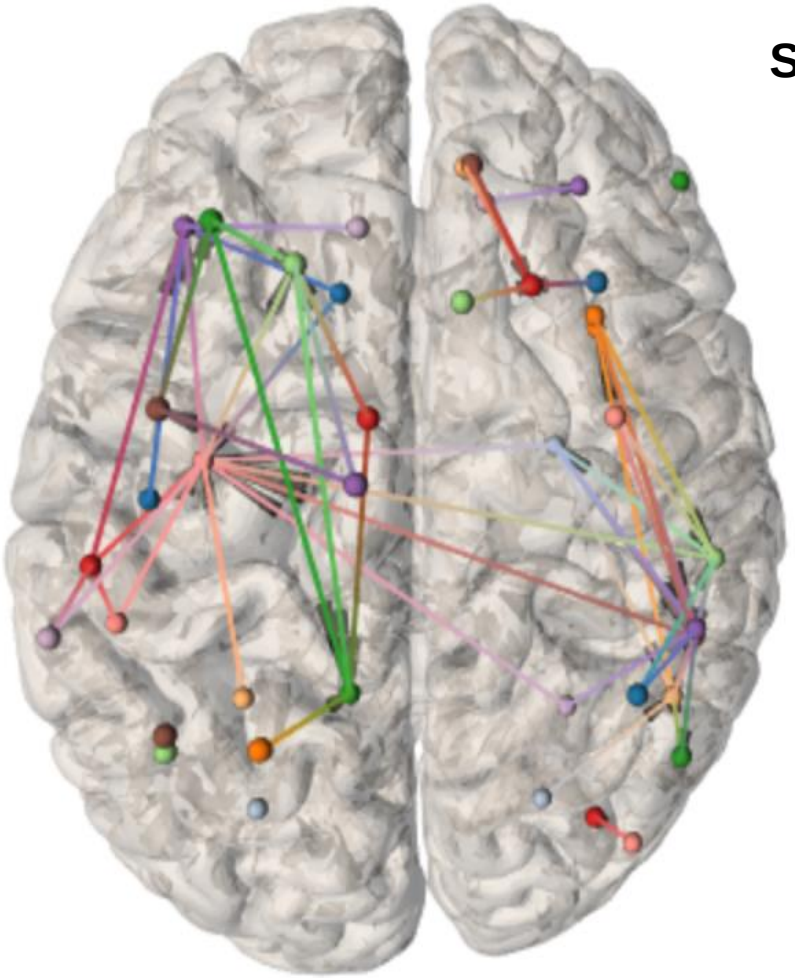
WP2: Mapping Natural Frequencies

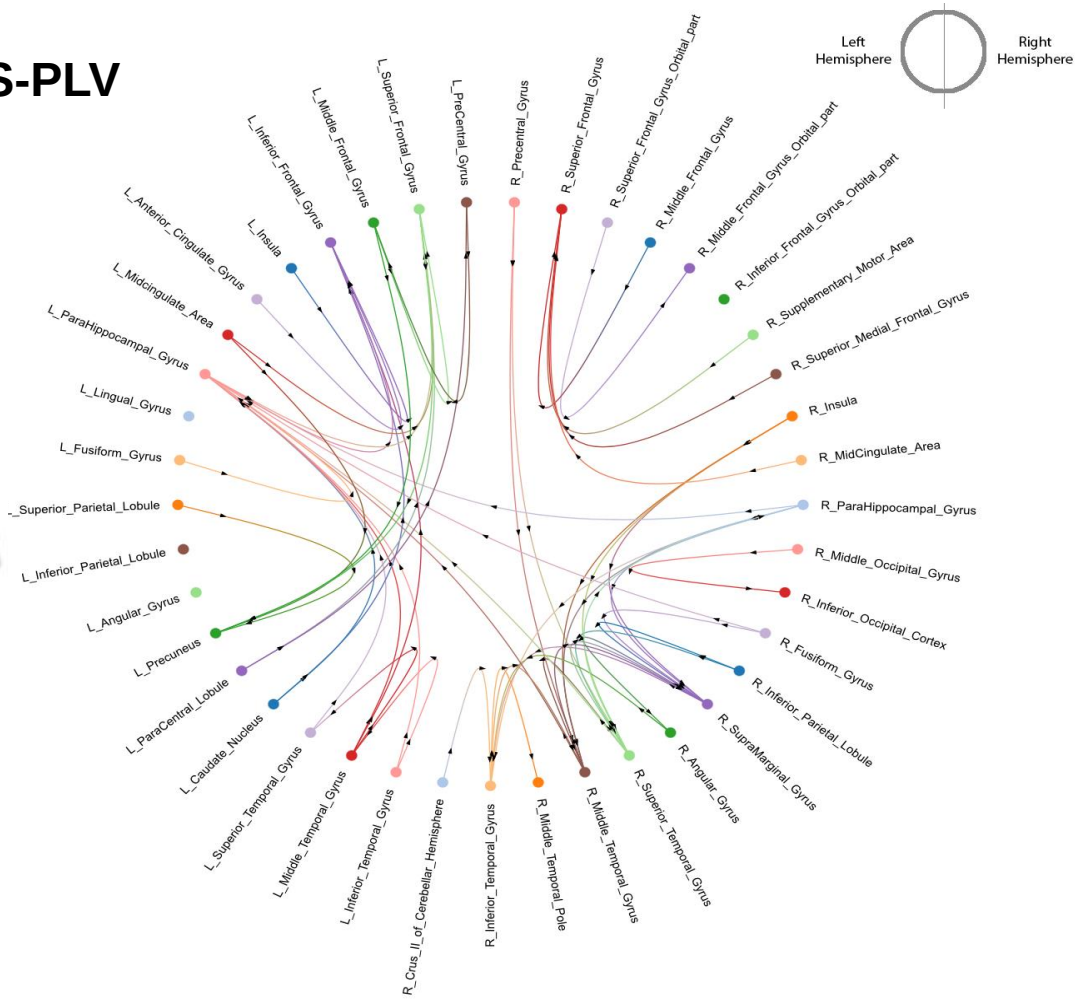


n=18 patients

Amengual et al. In preparation

WP3: Causal Functional Connectivity



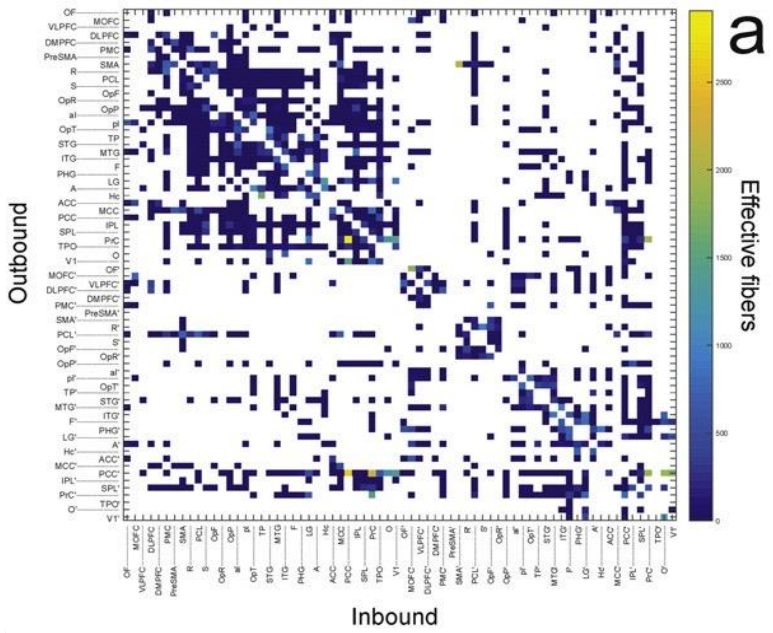


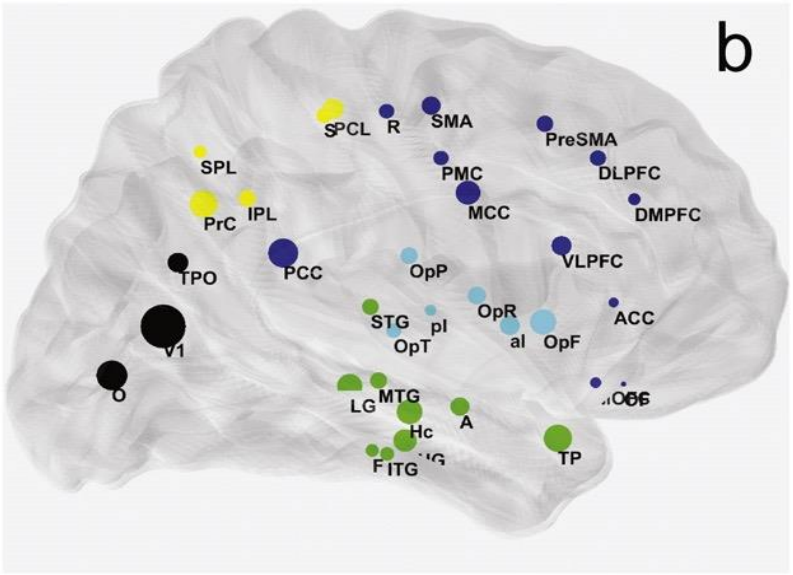
n=18 patients

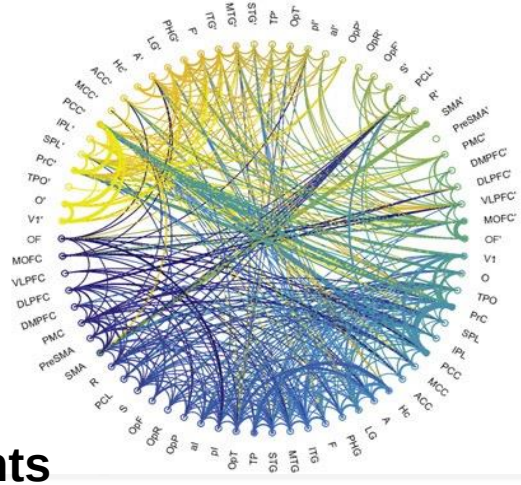
Duarte et al In preparation 2017

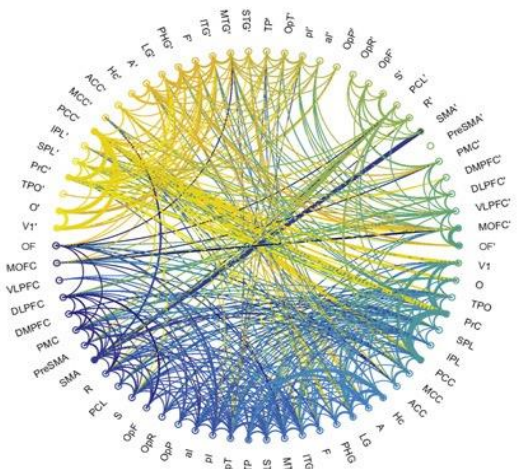
WP4: Effective-Structural connectivity

Effective Connectivity vs. Structural Connecticity







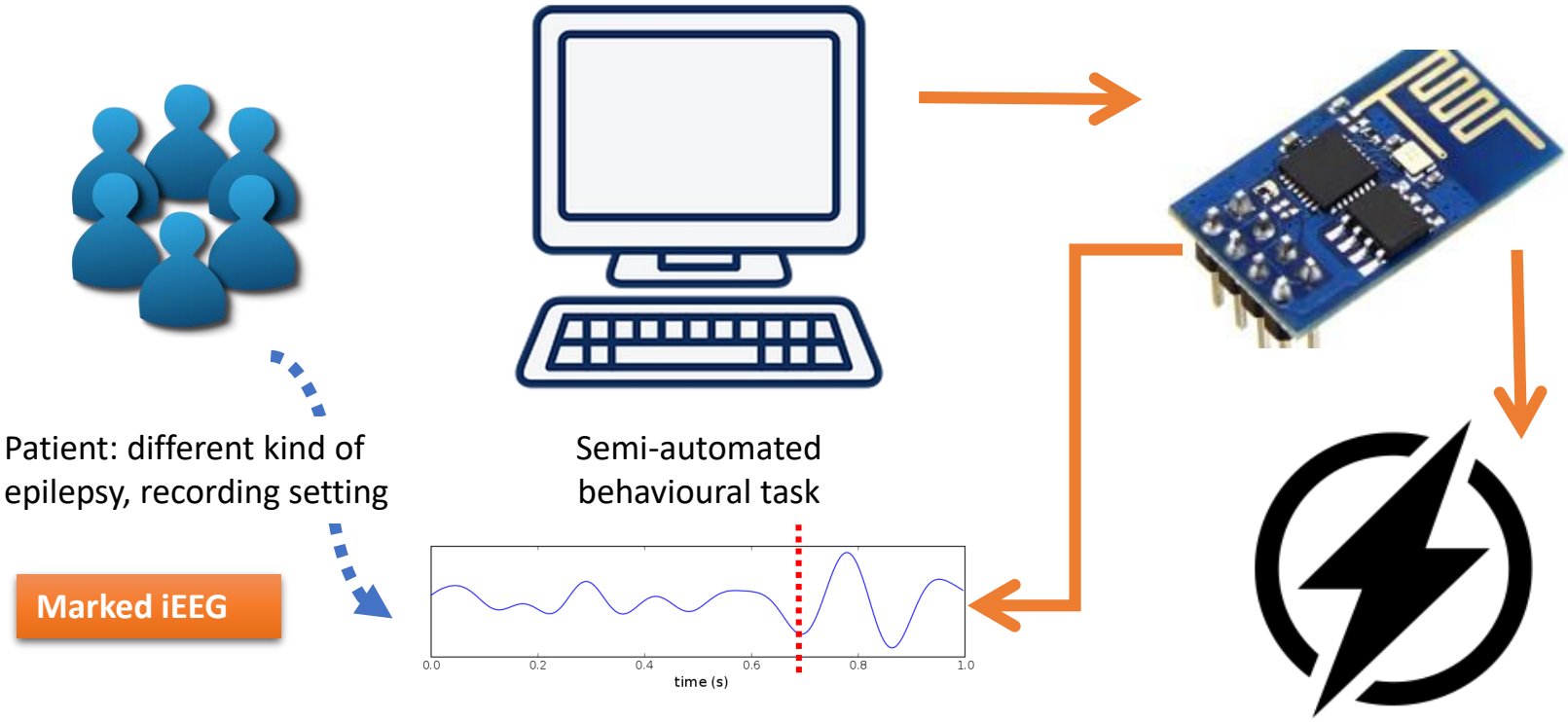


n=24 patients

Donos et al Neuroimage 2016

WP5: Stimulation and cognition

GOAL: acquire objective behavioural and cognitive data synchronized to iEEG and e-stim



Cognitive and e-stim framework: semi-automated tasks challenging different domains (motor, sensitive, language and memory) will be administered to the patient; through a microcontroller we will start e-stim and put markers over the iEEG traces. The clinician will retain control over e-stim.

Teams involved

TEAM 1 (coordination): ICM-PARIS, France
Dr. Antoni Valero-Cabré, MD PhD
Neurophysiologist & Cognitive Neuroscientist
CNRS UMR, 7225 & INSERM U1127
& Hôpital de la Pitié-Salpêtrière
10-12 implanted patients/year

TEAM 2: UBH-BUCH, ROMANIA
Dr. Ioana Mindruta MD PhD
Clinical Neurologist & Epileptologist
Bucharest University Emergency Hospital
Epilepsy Unit
12-15 implanted patients/year

TEAM 3: IMIM-BCN
Dr. Alessandro Principe MD,PhD
Clinical Neuro-physiologist & Epileptologist
Institut Hospital del Mar-IMIM, Epilepsy Group
12-15 implanted patients/year

Dr. Claude Adam MD PhD
Clinical Neurophysiologist
Dr. Mario Chavez PhD
Physicist/Engineer
Dr. Katia Lehongre PhD
Neuroengineer/Physiologist

Dr. Andrei Barborica PhD
Physicist and neurophysiologist
Dr. Cristian Donos PhD
Physicist, & Clinical Neurophysiologist

Dr. Rocamora MD PhD,
Neurologist & Epileptologist
Dr. Adrià Tauste Campo PhD
Computational neuroscientist
Dr. Ignacio Delgado-Martínez
Neurophysiologist MD, PhD

Help from HBP technical platforms

We have identified 4 specific tasks for which input and help form HBP flagship core and associated members will be instrumental:

- **CASUALTOMICS WP1**: Open access *databasing* and indexing strategies for iEEG and MRI data produced by the consortium
- **CASUALTOMICS WP4**: White matter high-resolution human atlases for co/registration with iEEG effective connectivity maps
- **CASUALTOMICS WP3&4** Computational approaches to *co-register/compare* functional connectivity/structural connectivity maps
- **CASUALTOMICS WP3&4** Computational approaches to combine individual human effective/structural maps in brain space conveying such patterns.

Involving the following HBP technical platforms

- **SP5 Neuroinformatics Platform: Gathering, organizing & making available brain data**
- **SP7 High Performance Analytics and Computing Platform**
- **SP6 Brain Simulation Platform: Developing data-driven reconstructions and simulation capabilities**

Contribution to HBP subprojects

HBP Subproject SP2 Human Brain Organization: Understanding the structure of the human brain, and its electrical and chemical functions.

- CAUSALTOMICS (WP 2,3&4) can contribute (HBP SP2 WP 2.2 & 2.5) causal high-spatial resolution iEEG recordings combined with functional and structural connectivity datasets maps of regional natural frequencies
- Maps exploring causally the ability to entrain and spread behaviorally relevant oscillatory activity and synchrony across human brain regions as a function of structural connectivity maps.

HBP Subproject SP3 Systems and Cognitive Neuroscience: Understanding how the brain performs its systems-level and cognitive functional activities.

- CAUSALTOMICS (WP 3,4 &5) can contribute (HBP SP3 WP 2.1 & 3.2) causal evidence on the anatomical and electrophysiological variables that either constrain or facilitate the flow of information across structural brain networks
- Provide causal prove of the relation of the frequency/phase of these oscillations with specific cognitive/behavioral correlates while analyzing the underlying influence of white matter connectivity physically which conveying such patterns.

Thanks for your attention

Coordinator:

Dr. Antoni Valero-Cabré MD PhD

Cerebral Dynamics, Plasticity and Rehabilitation Group *FrontLab*, Institut du Cerveau et la Moelle, CNRS UMR 7225; INSERM UMR 1127 & Hôpital de la Pitié-Salpêtrière, Paris, FRANCE

E-Mail contact:

avalerocabre@gmail.com

antoni.valerocabre@icm-institute.org