

Flag-ERA JTC 2017-HBP

“CAUSALTOMICS”

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

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Objectives

1) ENTRAINMENT OF LOCAL & INTERREGIONAL SYNCHRONY WITH INTRACRANIAL STIMULATION

- **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

2) MODELING SPREAD OF OSCILLATORY ACTIVITY THROUGH WHITE MATTER TRACTS

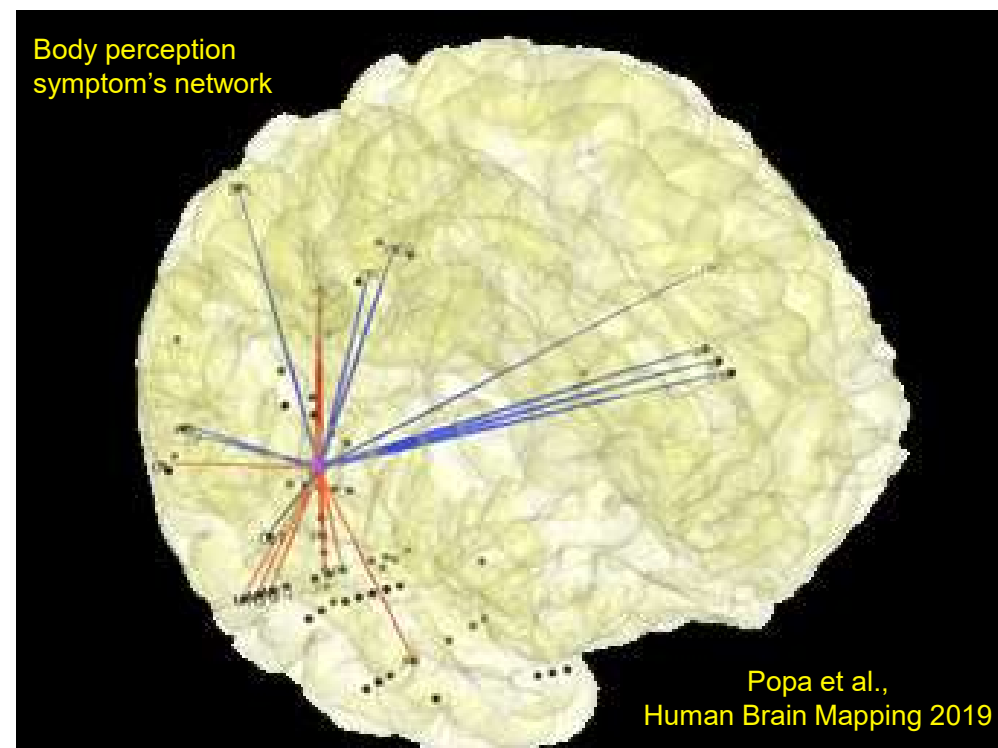
- **combine iEEG recordings and diffusion MRI data** from each individual patient and model how the spread of information across brain sites is constrained by white matter connectivity

SGA 3 expected outcomes:

- OC4 personalized brain models
- OC8 large scale sharing of medical data

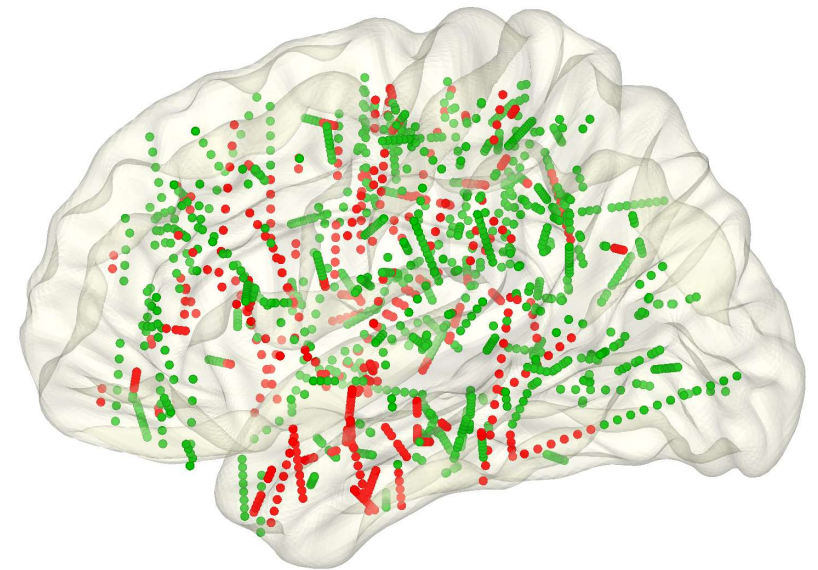
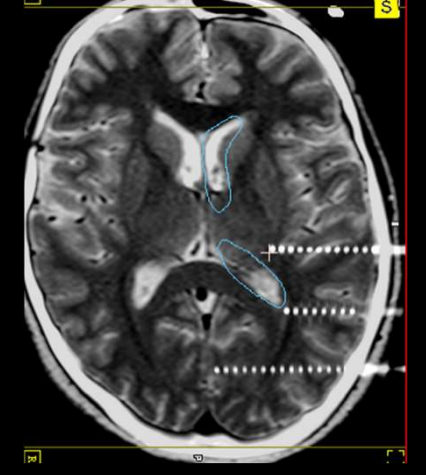
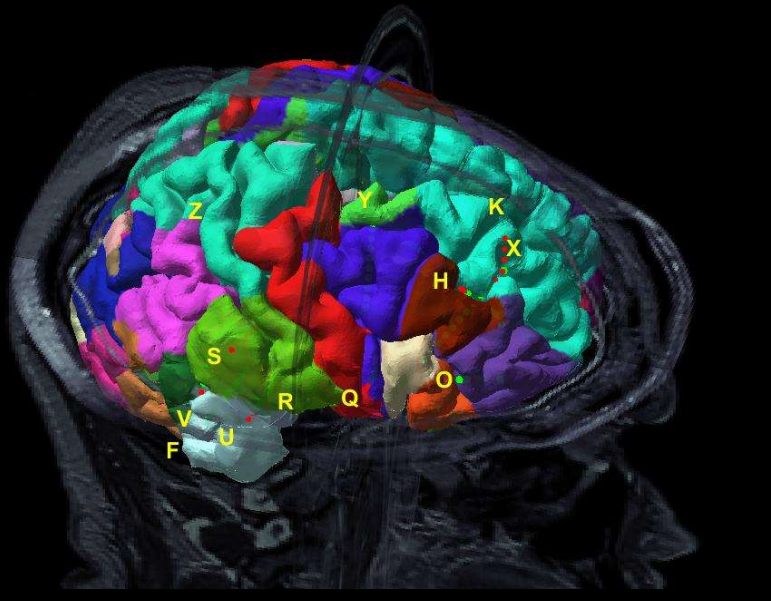
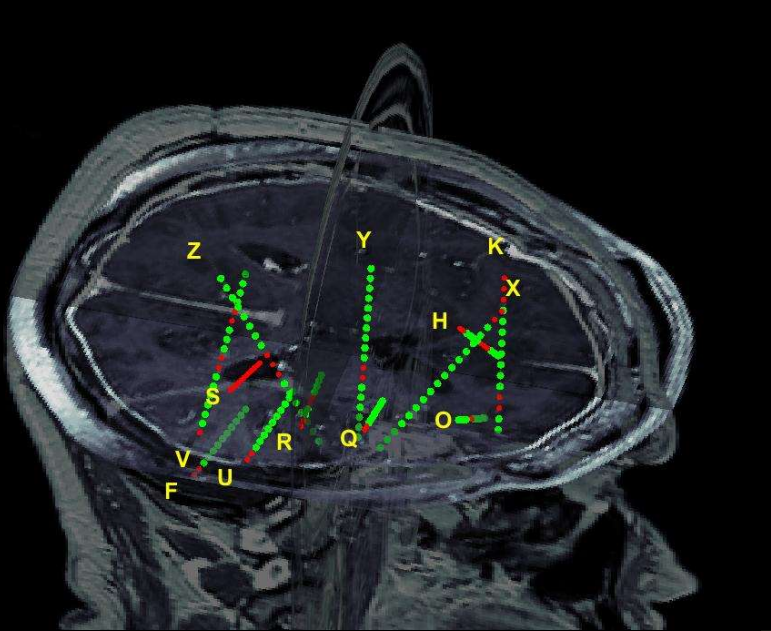
“In Direct Electrical Stimulation, the stimulated point is only an input gate into a large distributed network.”

David et al, Front Neurosci 2010



SEEG

- Provides access to virtually any region of the brain
- ~128 contacts used for recording and stimulation

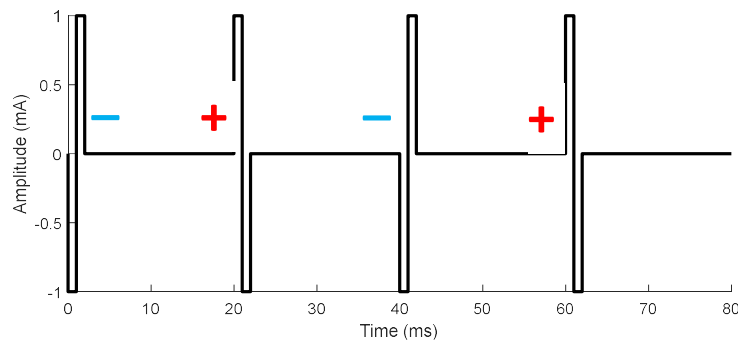


Cortical sampling by SEEG contacts
for all patients included in
CAUSALTOMICS

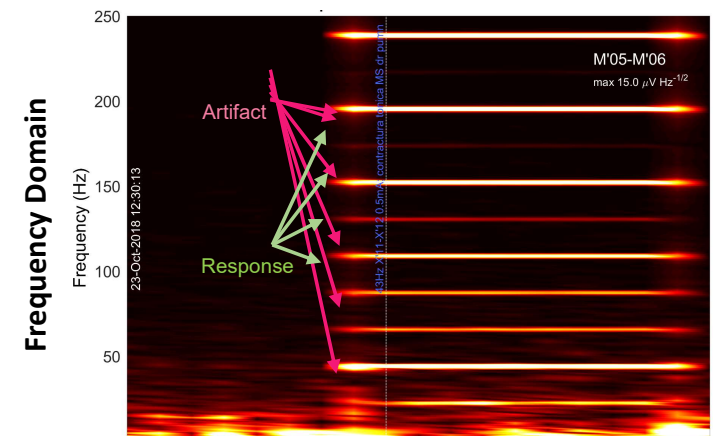
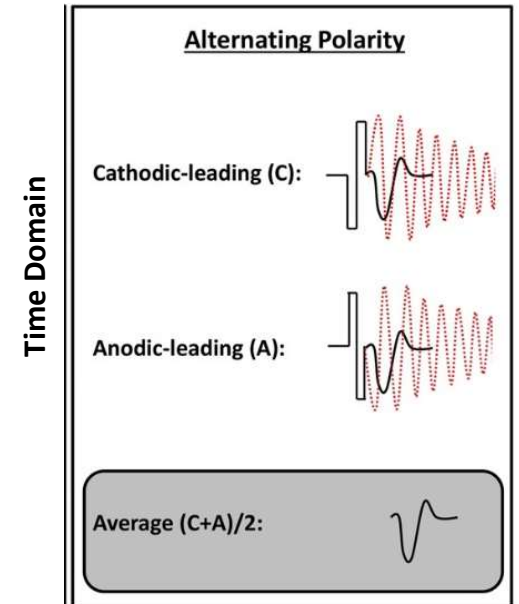
Stimulation protocol

Low frequency - Single pulse electrical stimulation (SPES),
High Frequency Stimulation (HFS) - 50 Hz alternating polarity

- Alternating polarity of HFS pulses, relying on linear artifactual components and nonlinear tissue response allows us to recover the responses during stimulation, while clinical symptoms are evoked



- Will perform an analysis in
 - Time-domain – averaging the responses
 - Spectral domain – filtering of non-overlapping spectral components of responses and artefactual components
 - Complex space



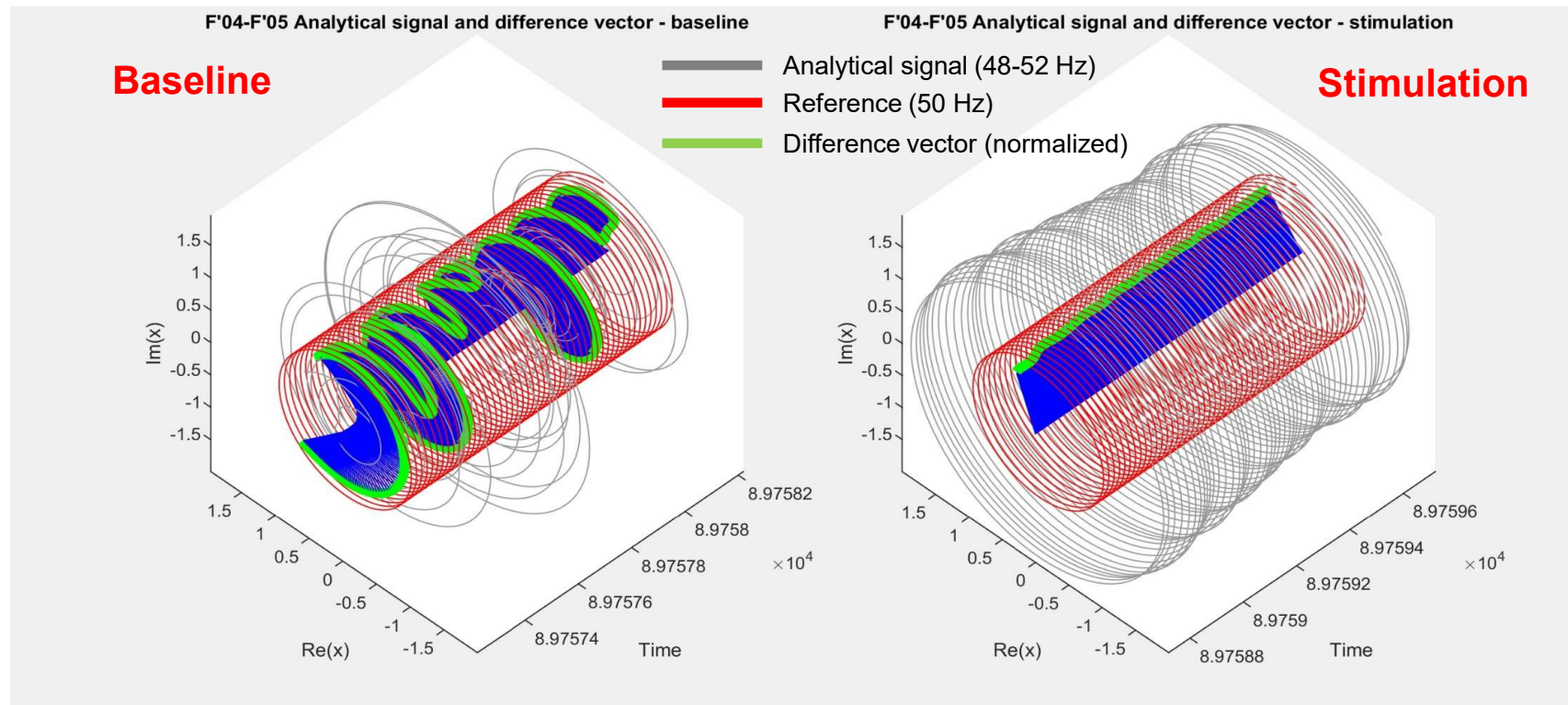
Analysis in complex space

- Analytical signal

- Signal filtered in the 48-52 Hz then represented in the complex – time space by means of the **Hilbert transform**

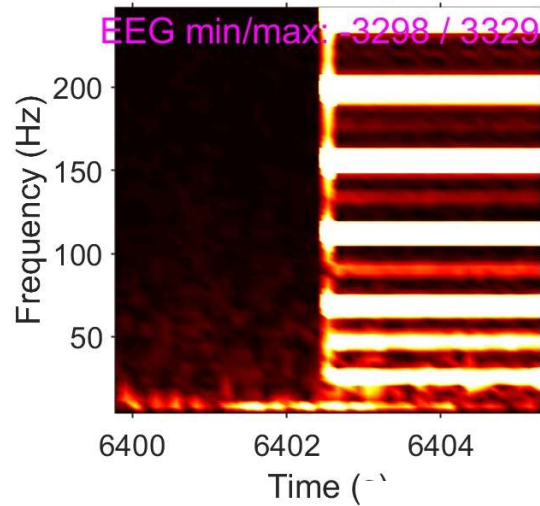
$$H\{x\}(t) = \int_{-\infty}^{\infty} \frac{x(\tau)}{t - \tau} d\tau$$

$$x_a(t) = x(t) + jH\{x\}(t)$$

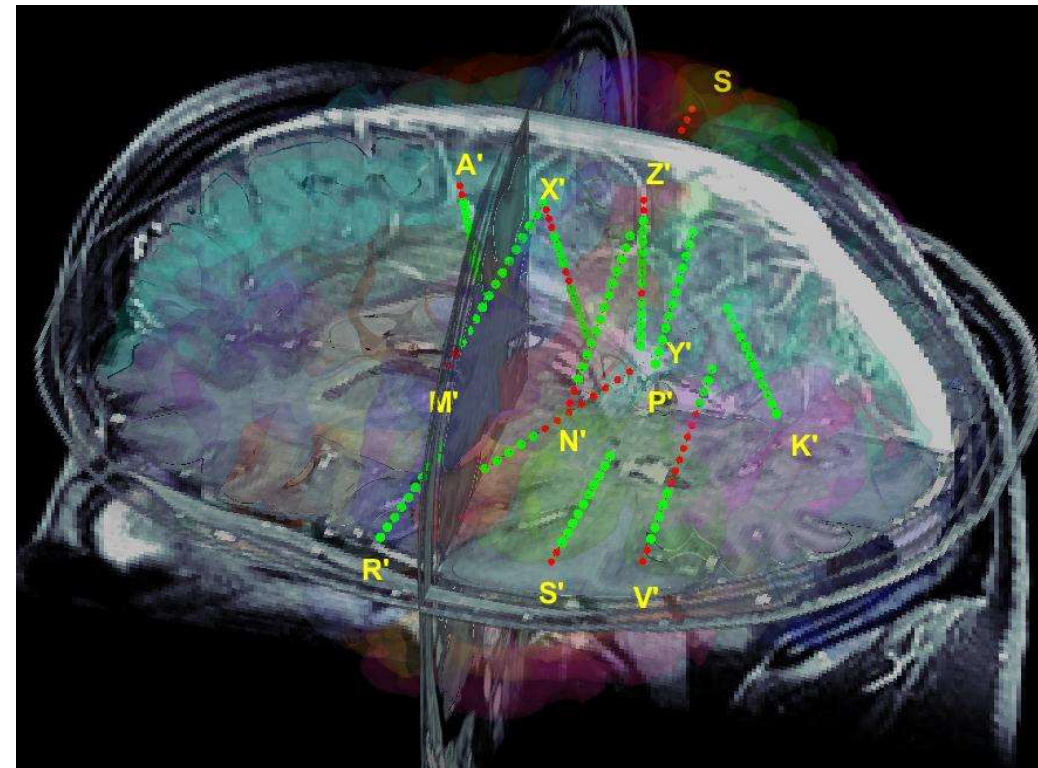
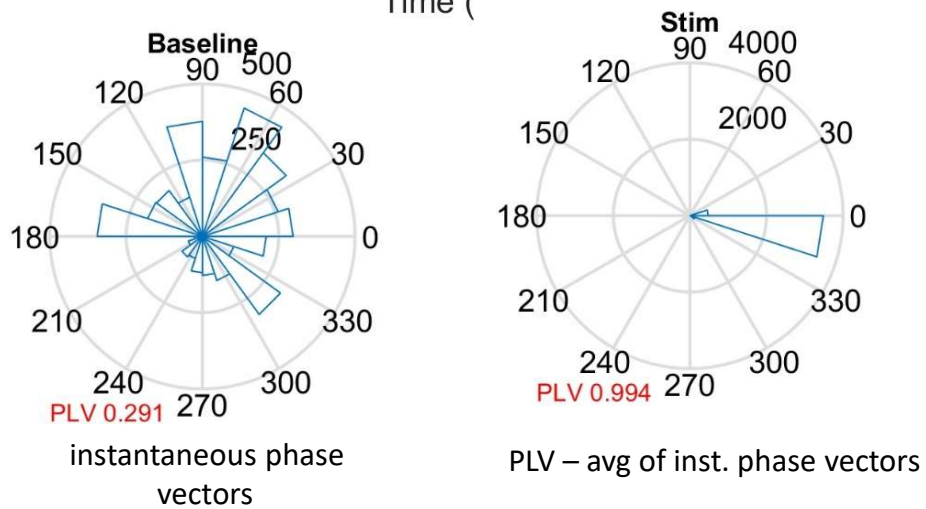


Connectivity measure: Phase locking

captures synchrony between brain areas

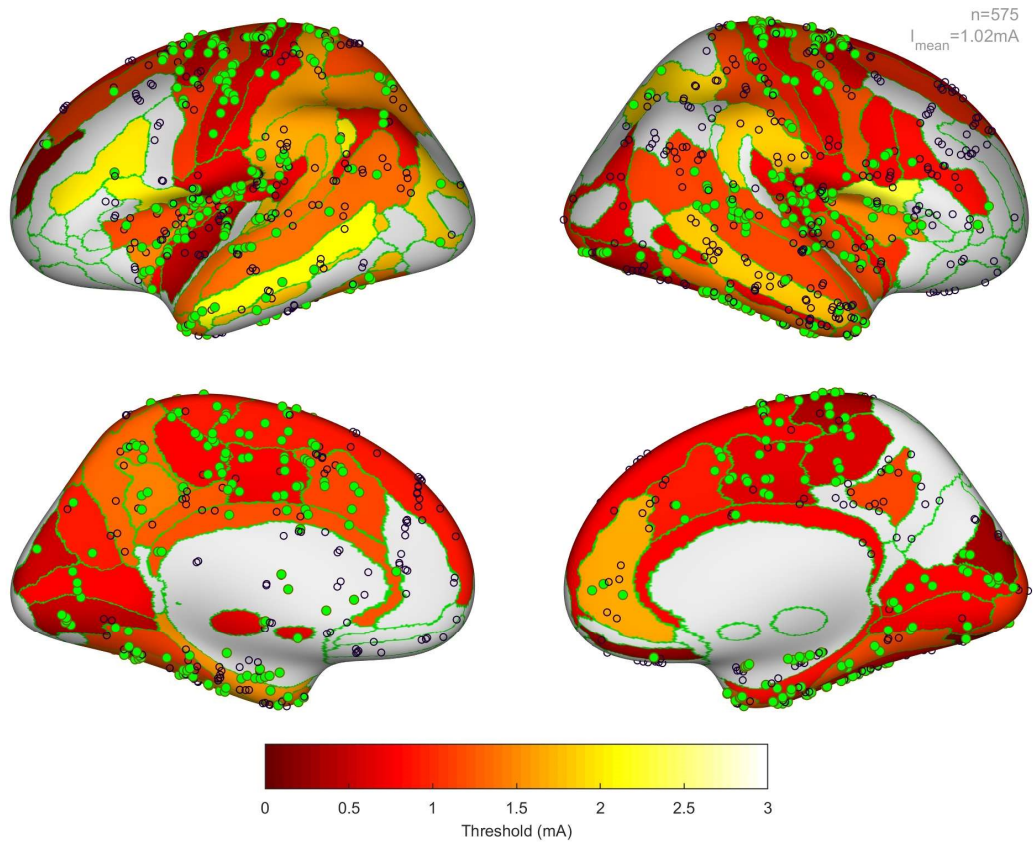


SEEG 80 Stim N'02-N'03 (Rolandic) Resp Z'09-Z'10 (Somatosensory)

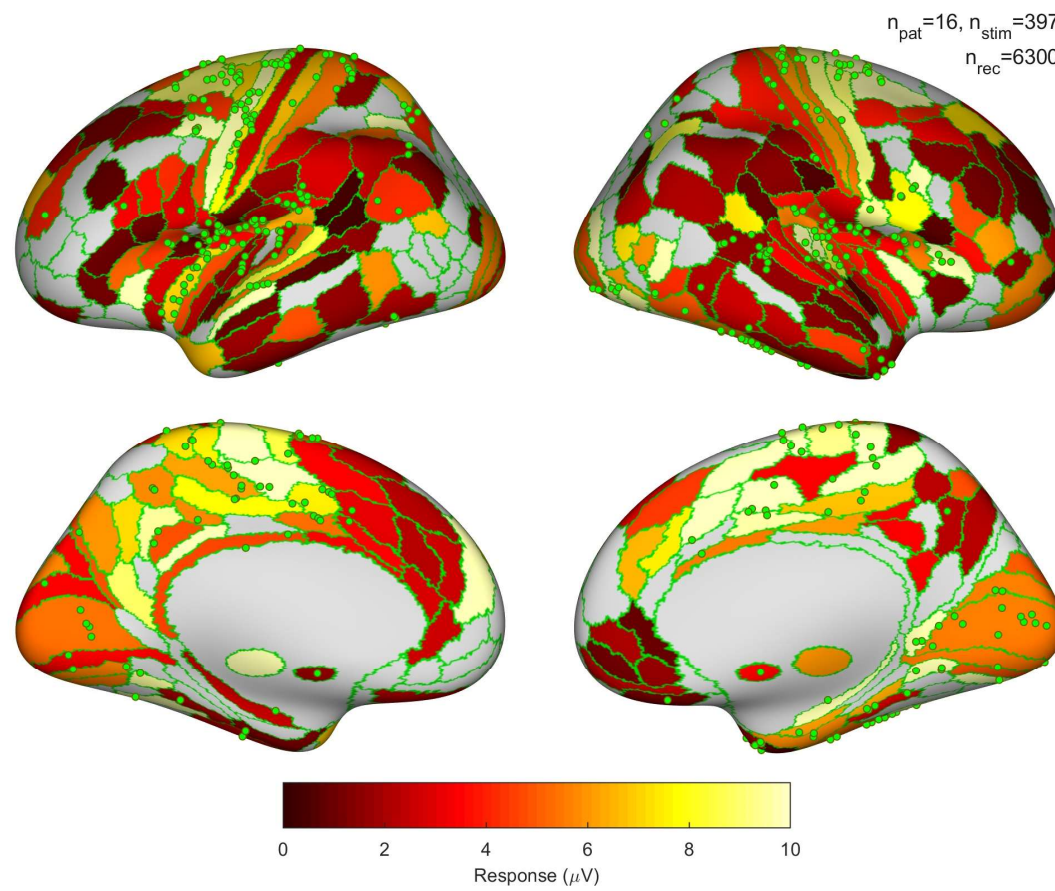


Patients explored (n=27) – clinical response mapping on HFS

Threshold map



Response map



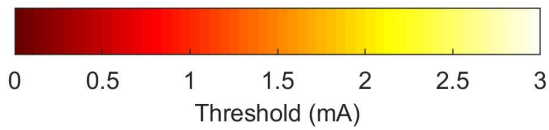
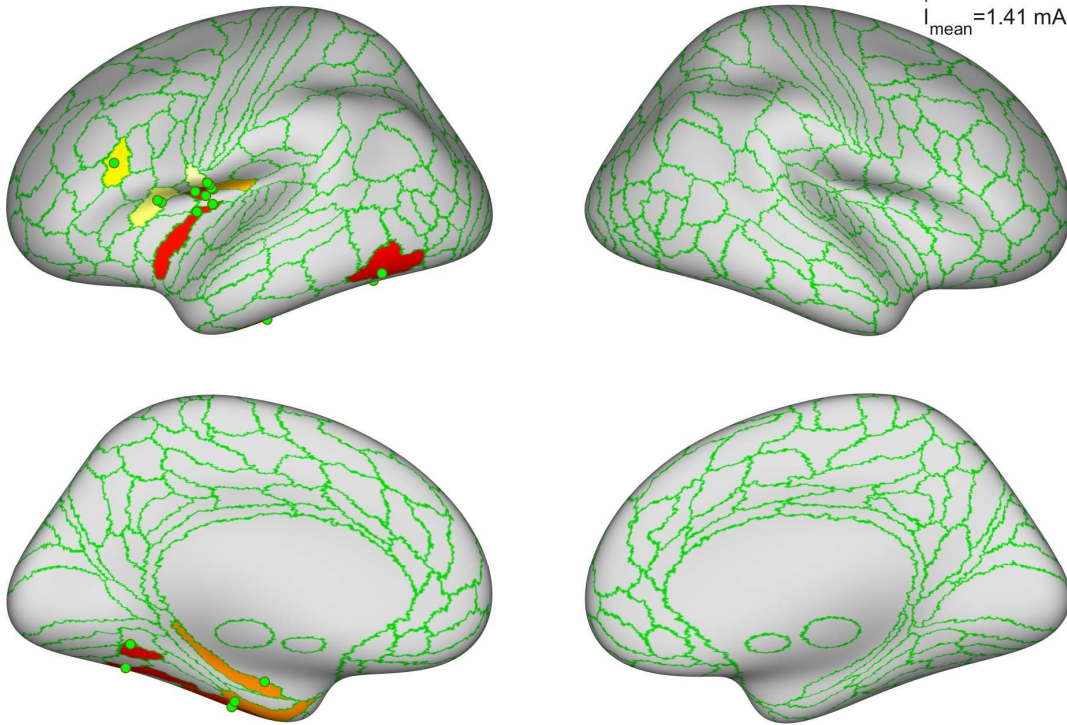
Number patients included: 27

Barborica et al, submitted

Group analysis - language responses

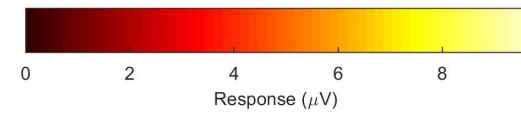
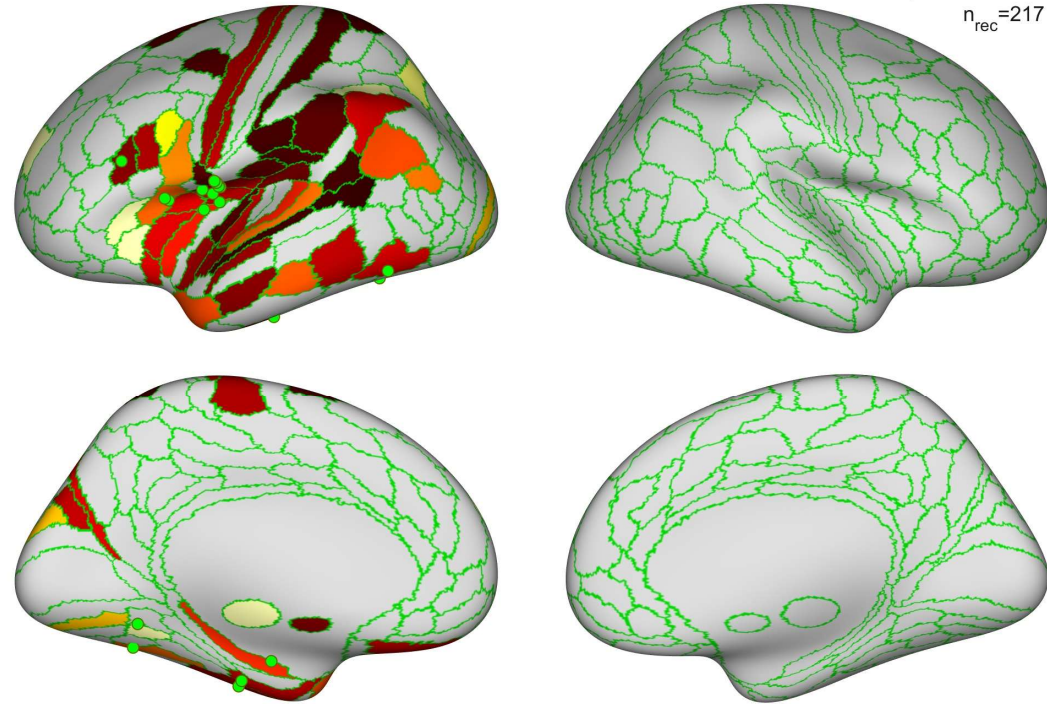
Location of stimulation
Threshold map

$n_{pat}=4, n_{stim}=17$
 $I_{mean}=1.41$ mA

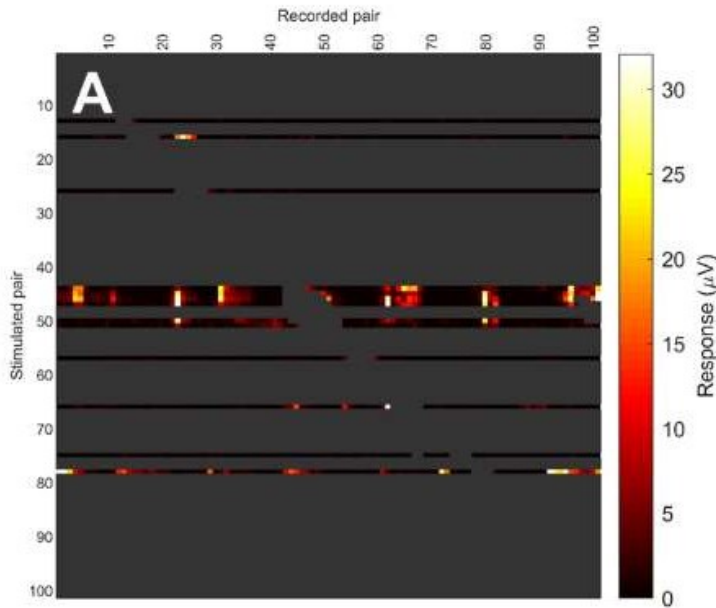


Response map – directed connectivity

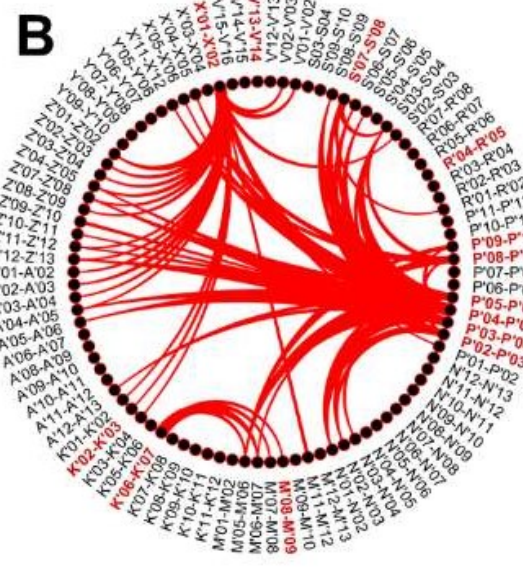
$n_{pat}=4, n_{stim}=17$
 $n_{rec}=217$



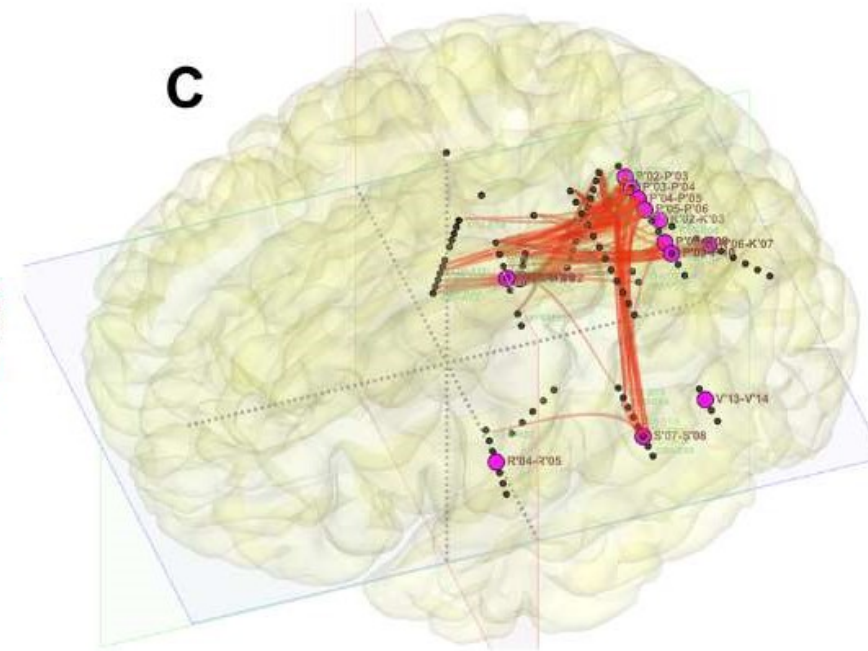
Patient level – somatosensory responses HFS directed connectivity



A) connectivity matrix.



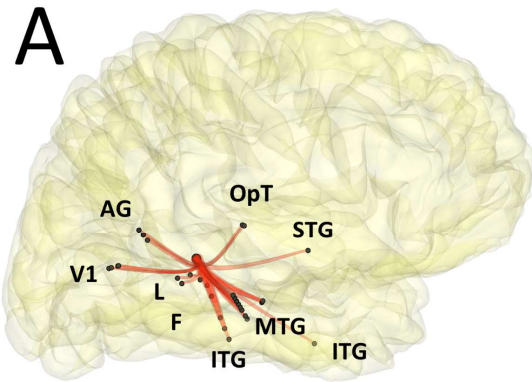
B) circular diagram of the third quartile of the significant connections ($Z\text{-score} > 3$, $p < 0.05$)



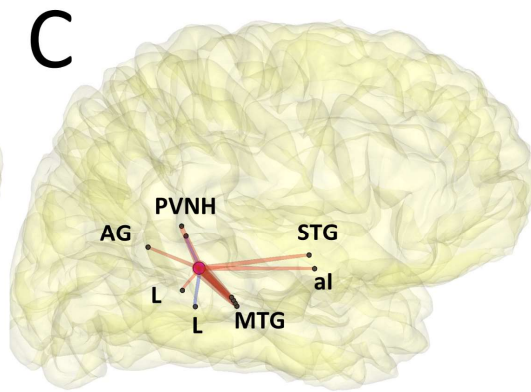
C) 3D representation of the connections in (B).

Patient level analysis

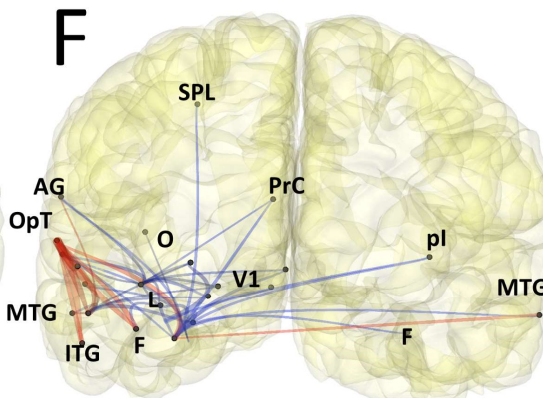
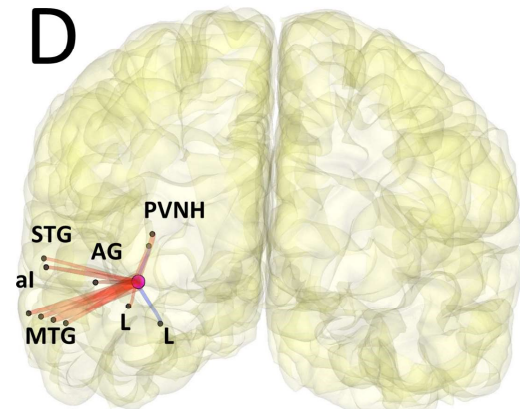
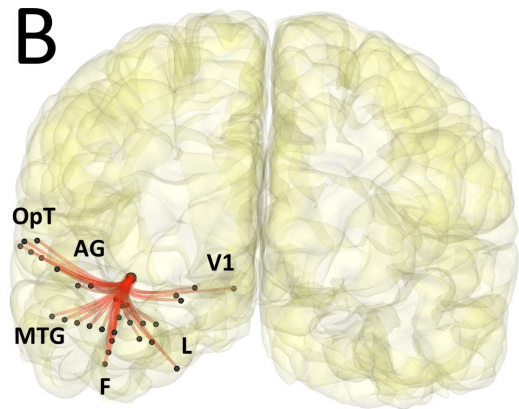
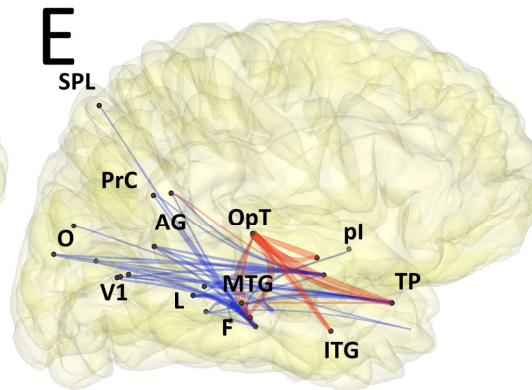
Symptom related
HFS directed connectivity



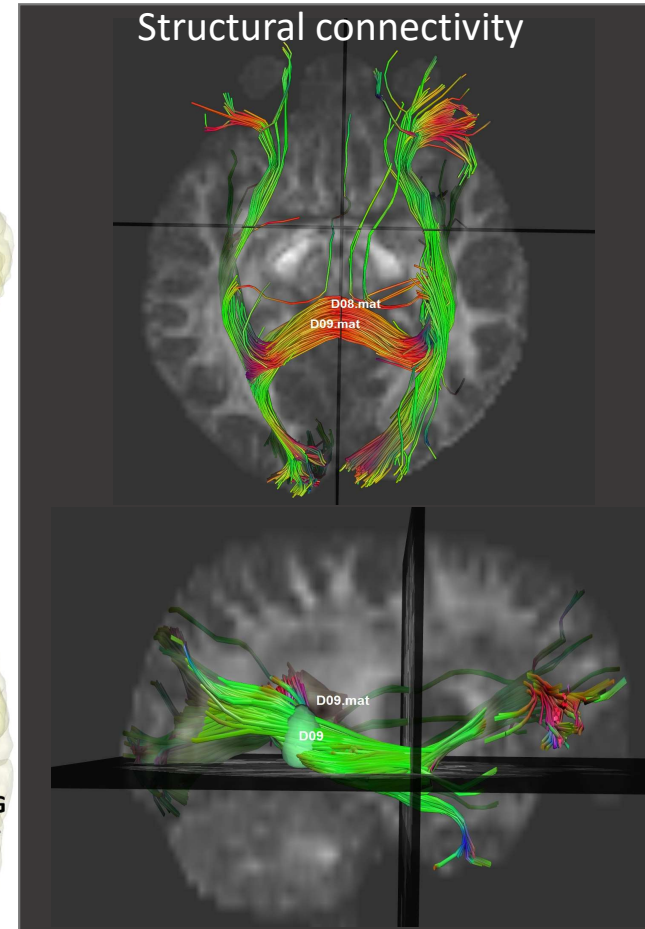
Resting state
CCEP directed connectivity



Symptom related
Functional connectivity
*Non-linear regression analysis
of spontaneous icEEG signal (h^2)*



Structural connectivity



Structure level analysis – subregional cingulum stimulation

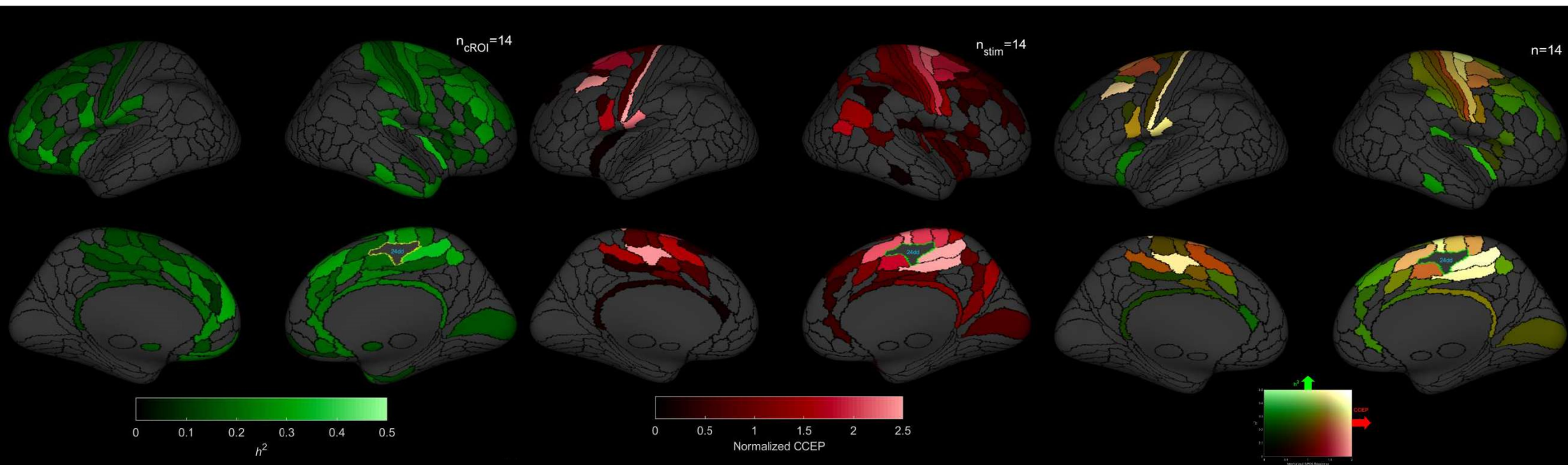
Functional connectivity

Non-linear regression analysis
of spontaneous icEEG signal (h^2)

CCEP directed connectivity

triggered by single pulse electrical
stimulation

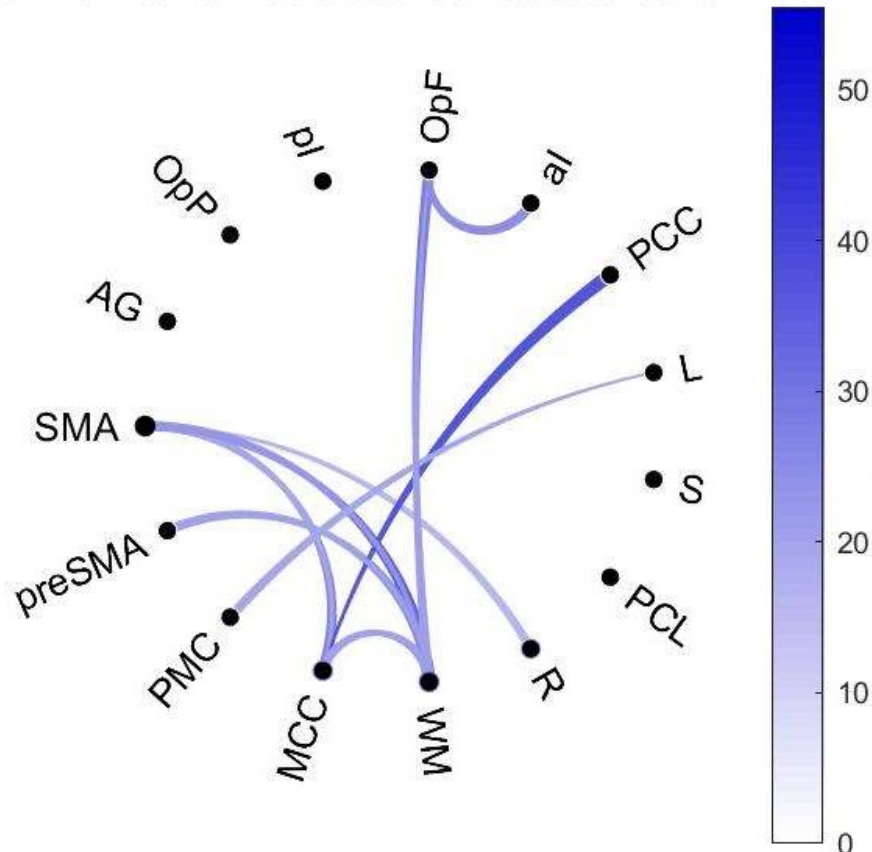
Combined connectivity



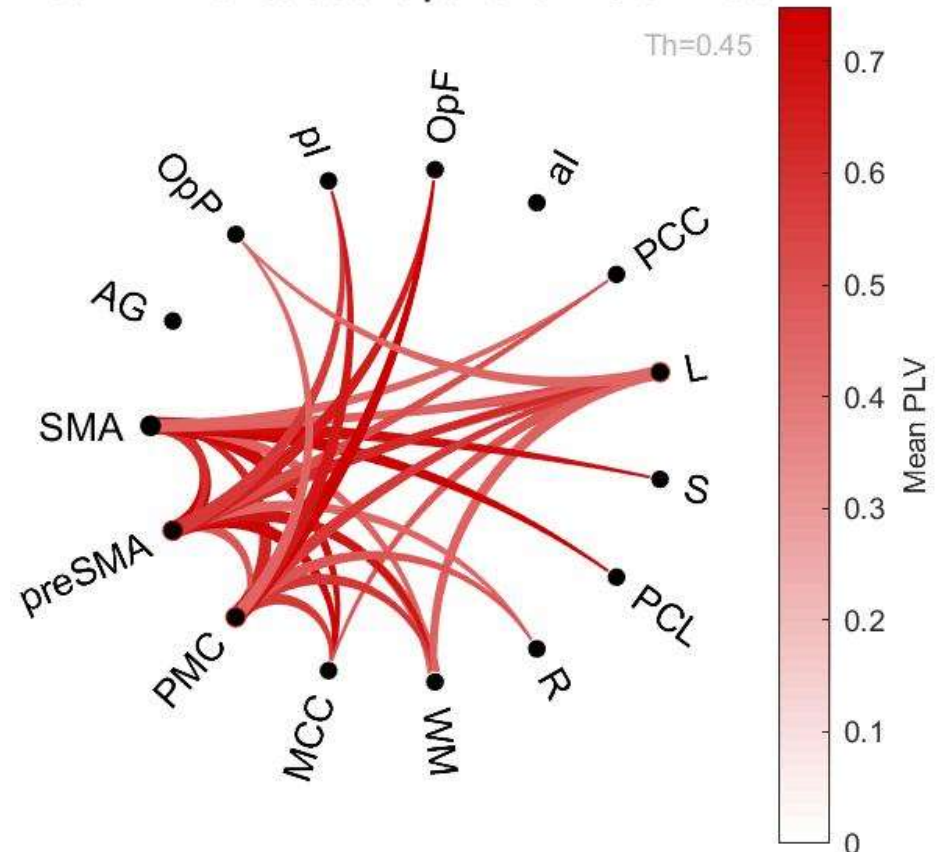
Functional and anatomical connectivity for physiological responses

phase locking value (PLV) vs. number of fibers

Mean number of fibers between structures -SEEG 97



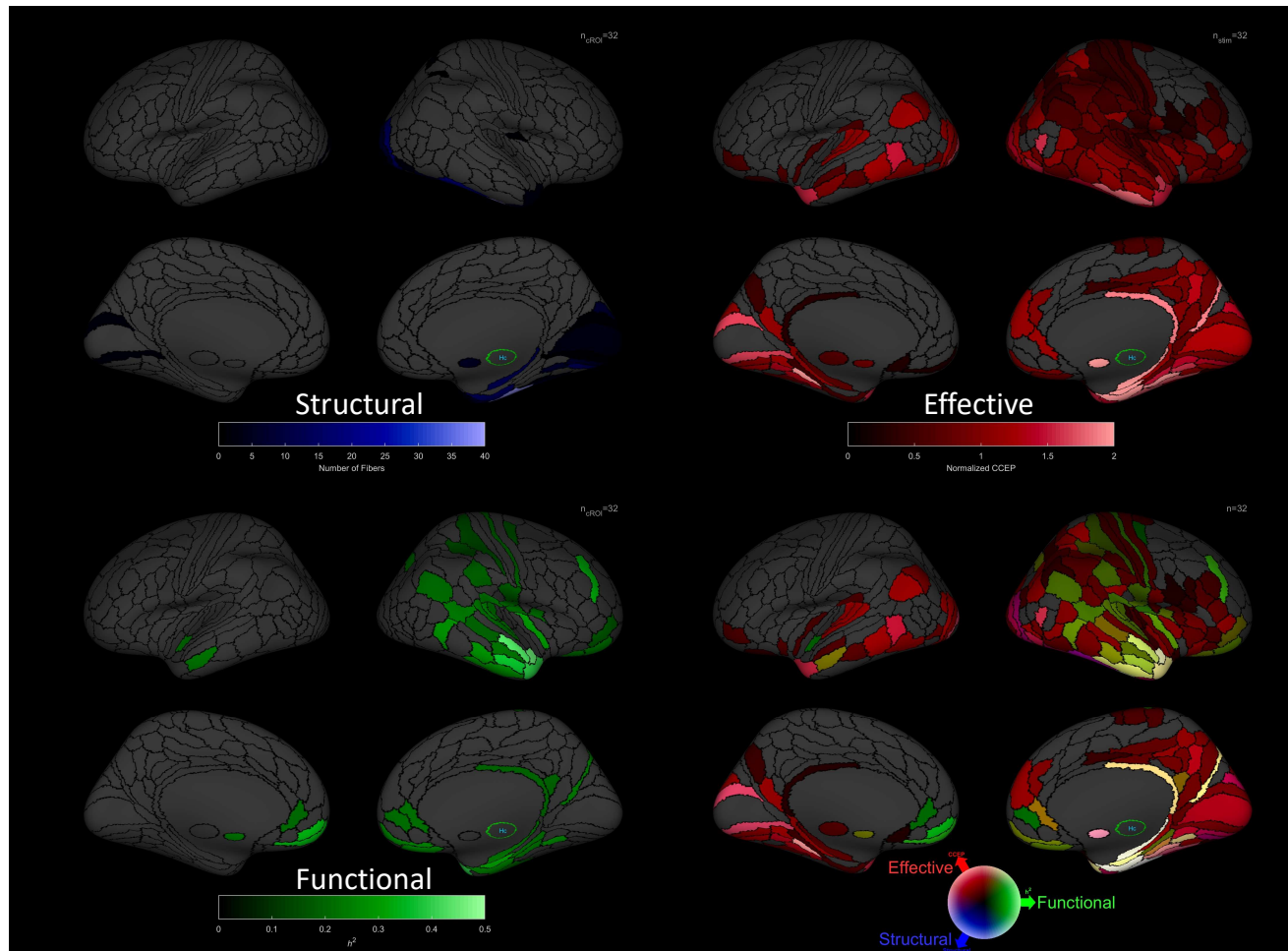
Mean PLV for structure pairs -SEEG 97-motor



SMA=supplementary motor area, preSMA=pre-supplementary motor area, PMC=premotor cortex, MCC=middle cingulate cortex, WM=white matter R=Rolandic, PCL=paracentral lobule, S=sensory cortex, L=lesion, PCC=posterior cingulate cortex, al=anterior insula, OpF=frontal operculum, pl=posterior insula OpP=parietal operculum, AG=angular gyrus

Open-access connectivity atlas

- Connectivity atlas: <http://epi.fizica.unibuc.ro/atlas/>



Responsible research and innovation

- Open access to connectivity database and research publications
- Better surgical decision
- No additional stimulation time, no additional hospitalization time
- Results are based on data post-processing after patients' discharge
- Prediction of post-surgical cognitive deficit
- Completely anonymized data
- Gender equality
- Local and regional meetings