

# Cortical stimulation and brain mapping in extra- and intra-operative epilepsy surgeries

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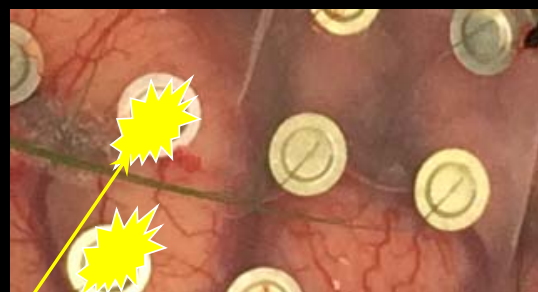
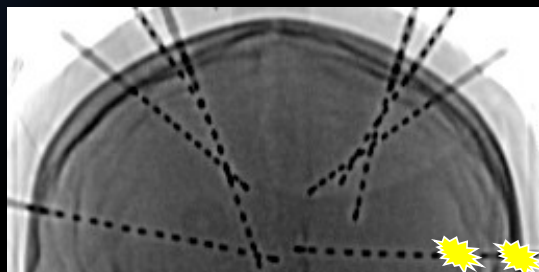
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Stimulation can be delivered to stereo-EEG and subdural grid electrodes.



Electrical stimulator

One can determine if stimulated sites are essential to perform the task, based on the behavioral changes during stimulation.

Stimulus intensity necessary to induce a motor response:

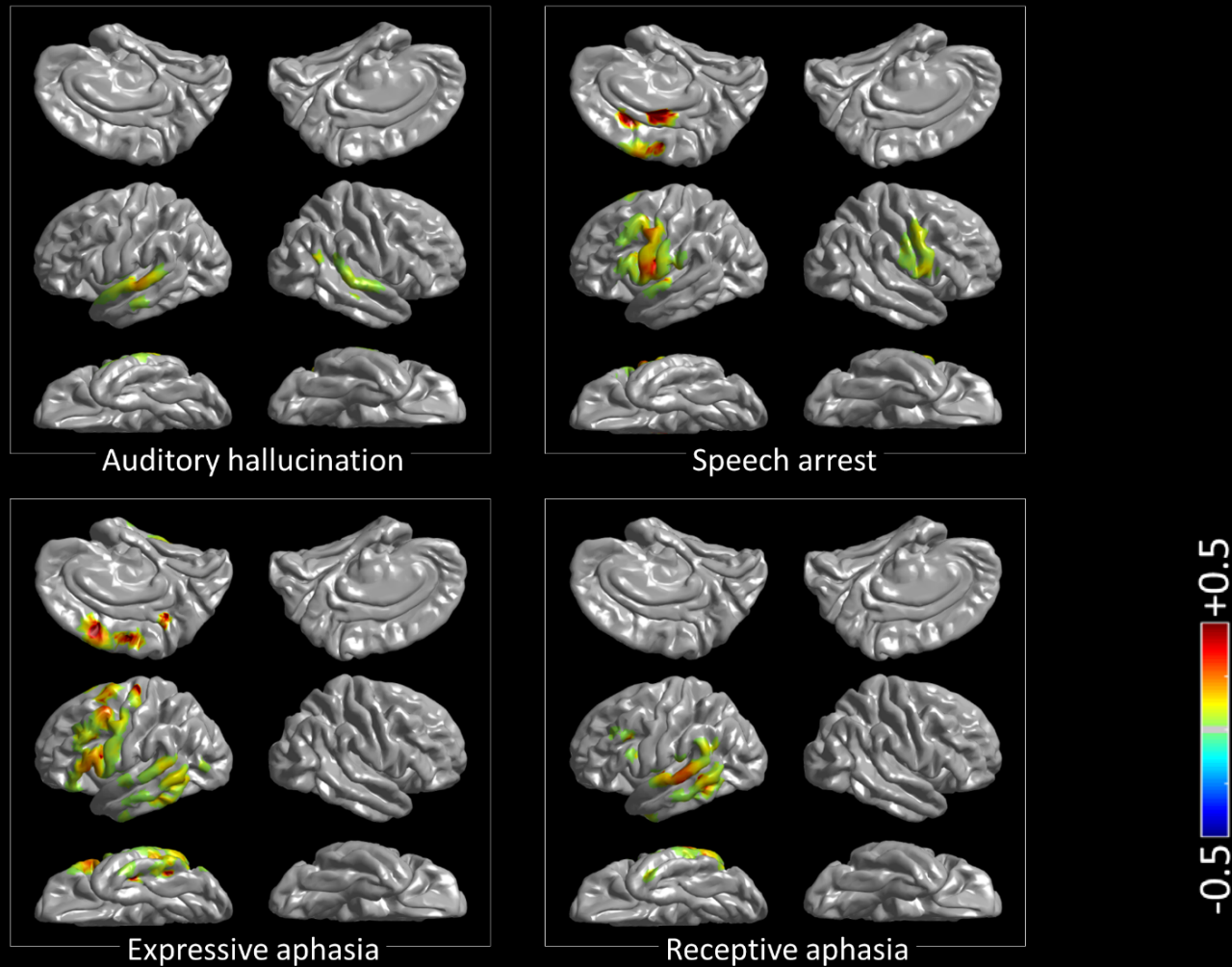
**Stereo-EEG: 3.4 mA** on average

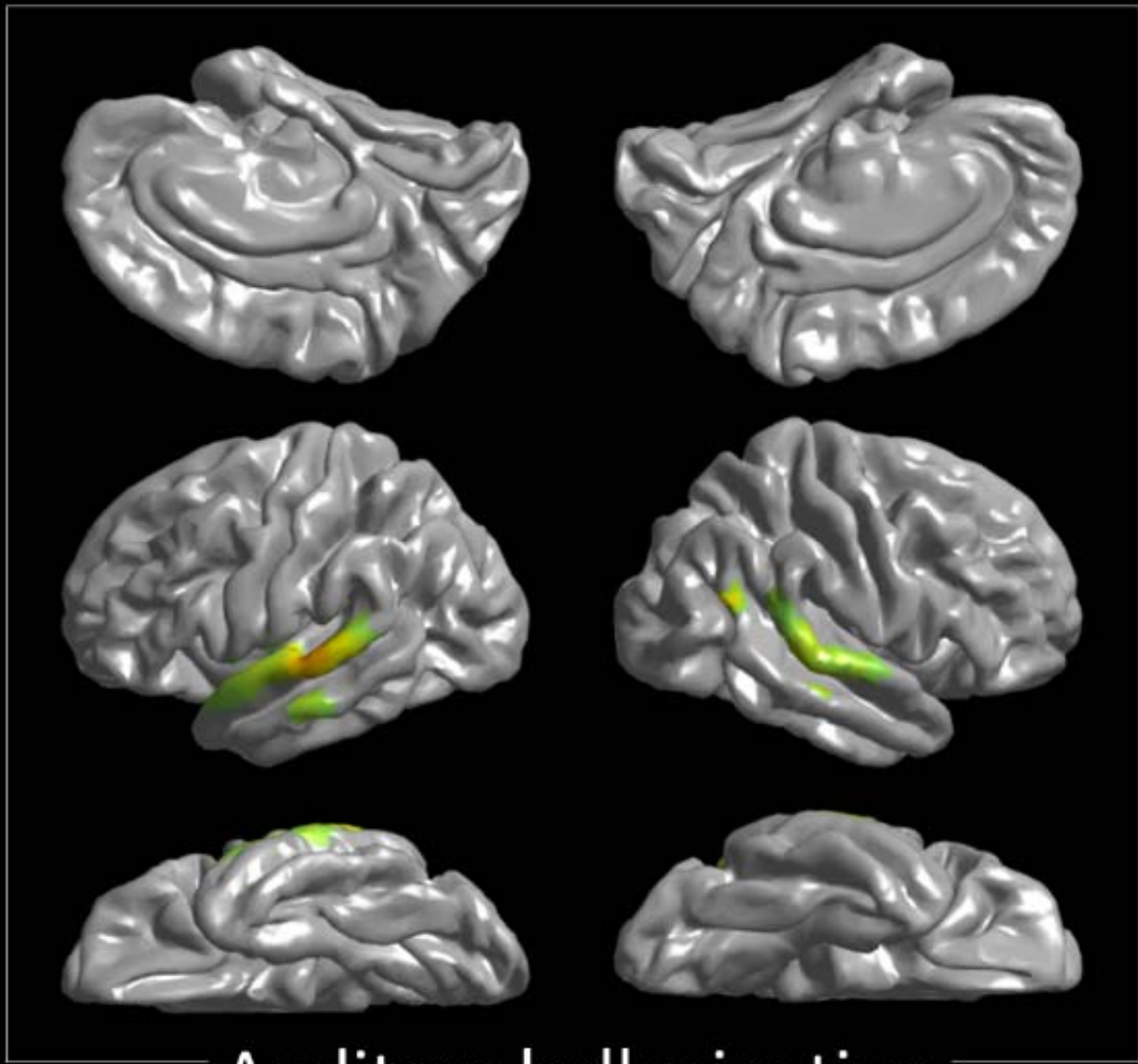
Arya et al. Clin Neurophysiol 2020

**Subdural: 5.4 mA** on average

Zea Vera et al. Clin Neurophysiol 2017

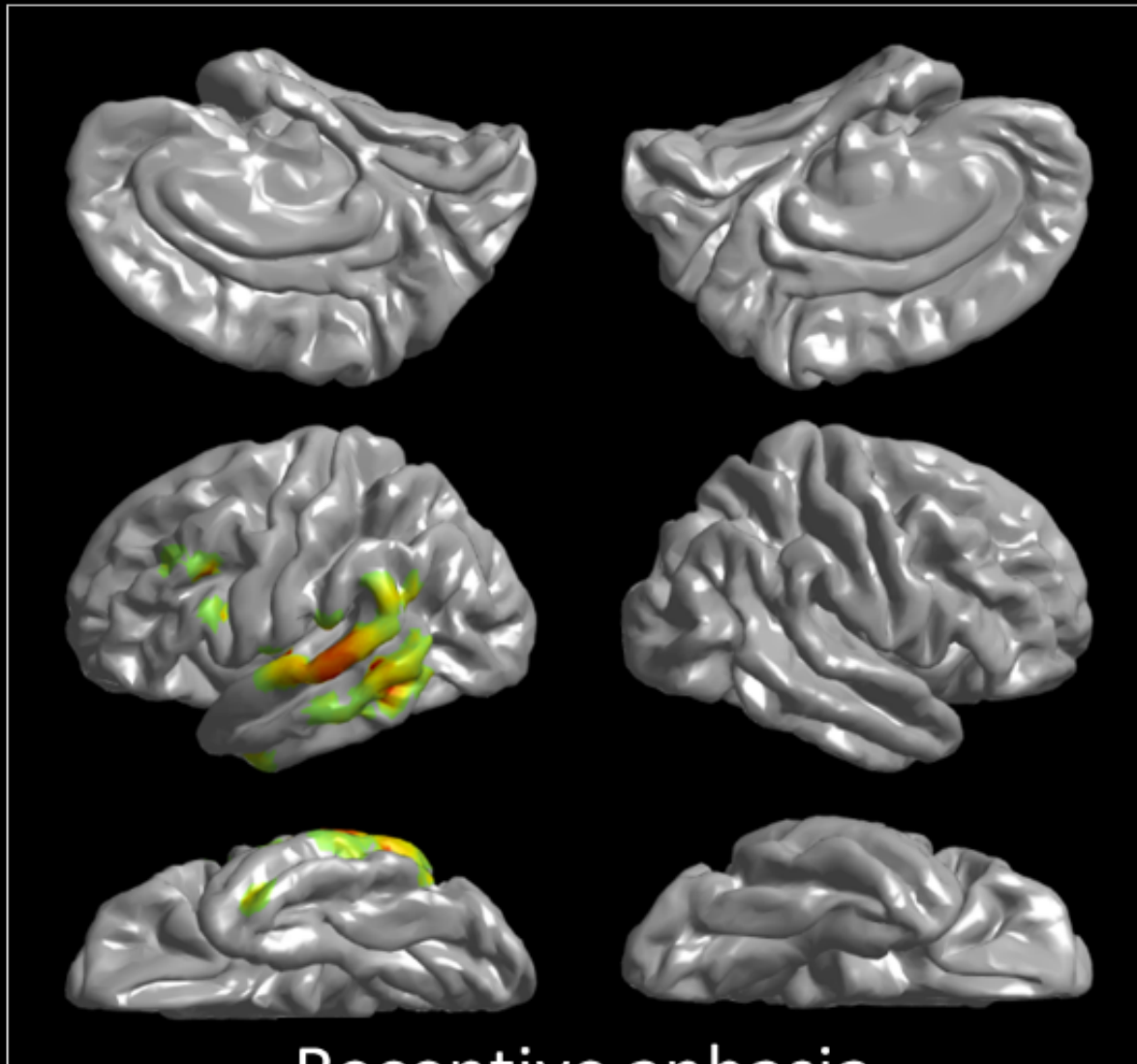
# Whole-brain level 3D probability maps of speech/language based on extraoperative electrical stimulation in 100 patients (Nakai et al., Brain 2017)





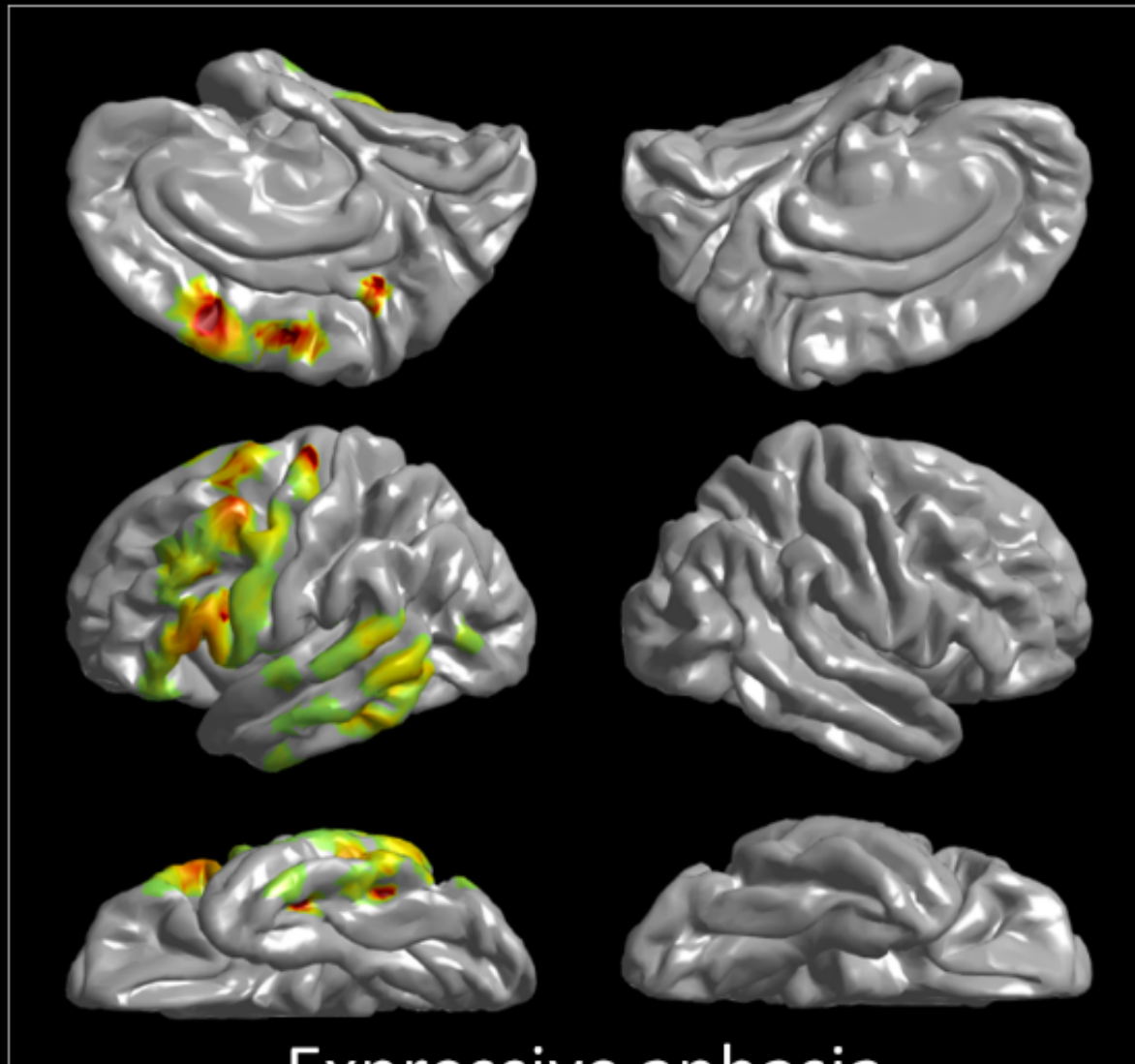
Auditory hallucination

(Nakai et al., Brain 2017)



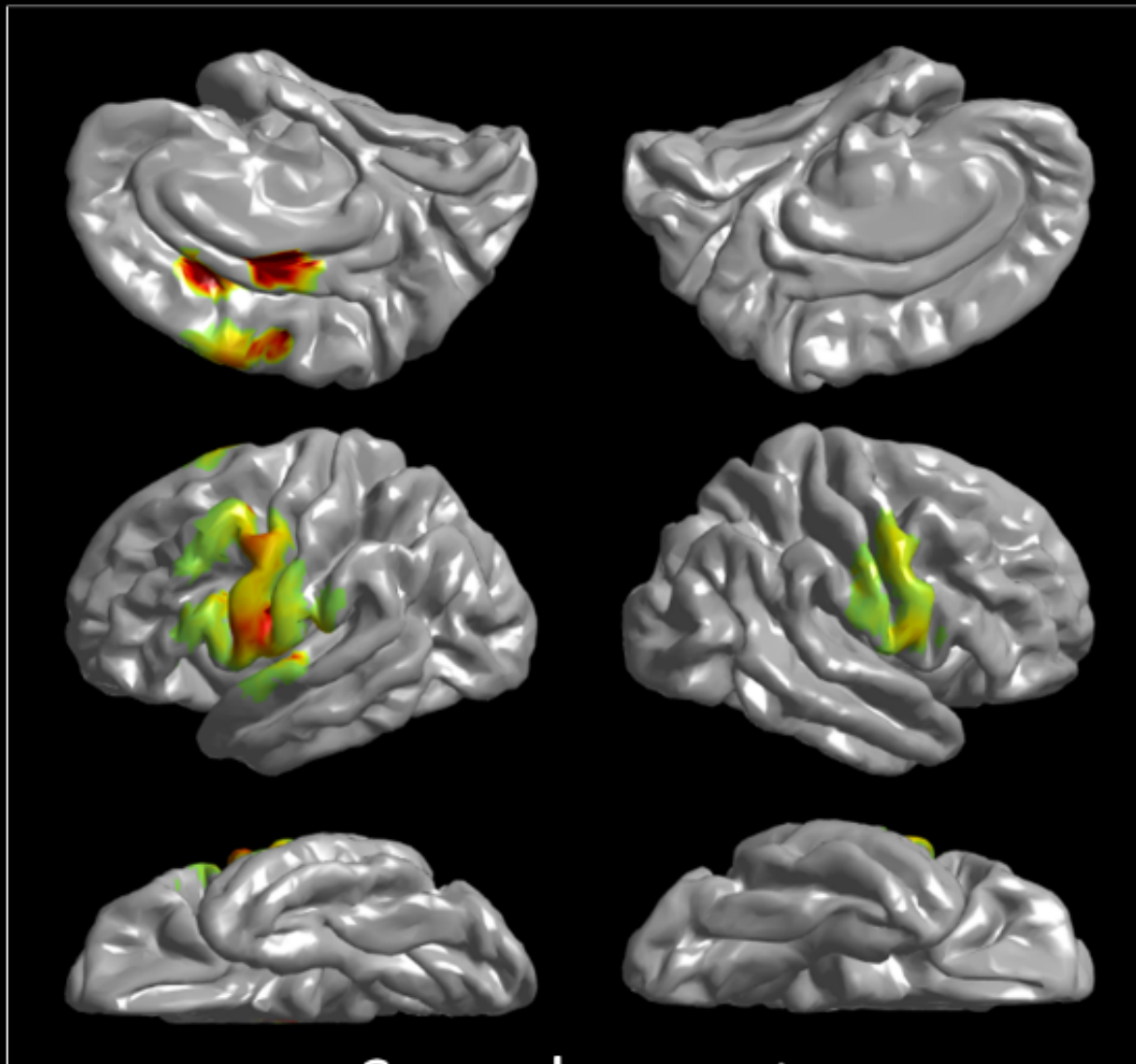
Receptive aphasia

(Nakai et al., Brain 2017)



Expressive aphasia

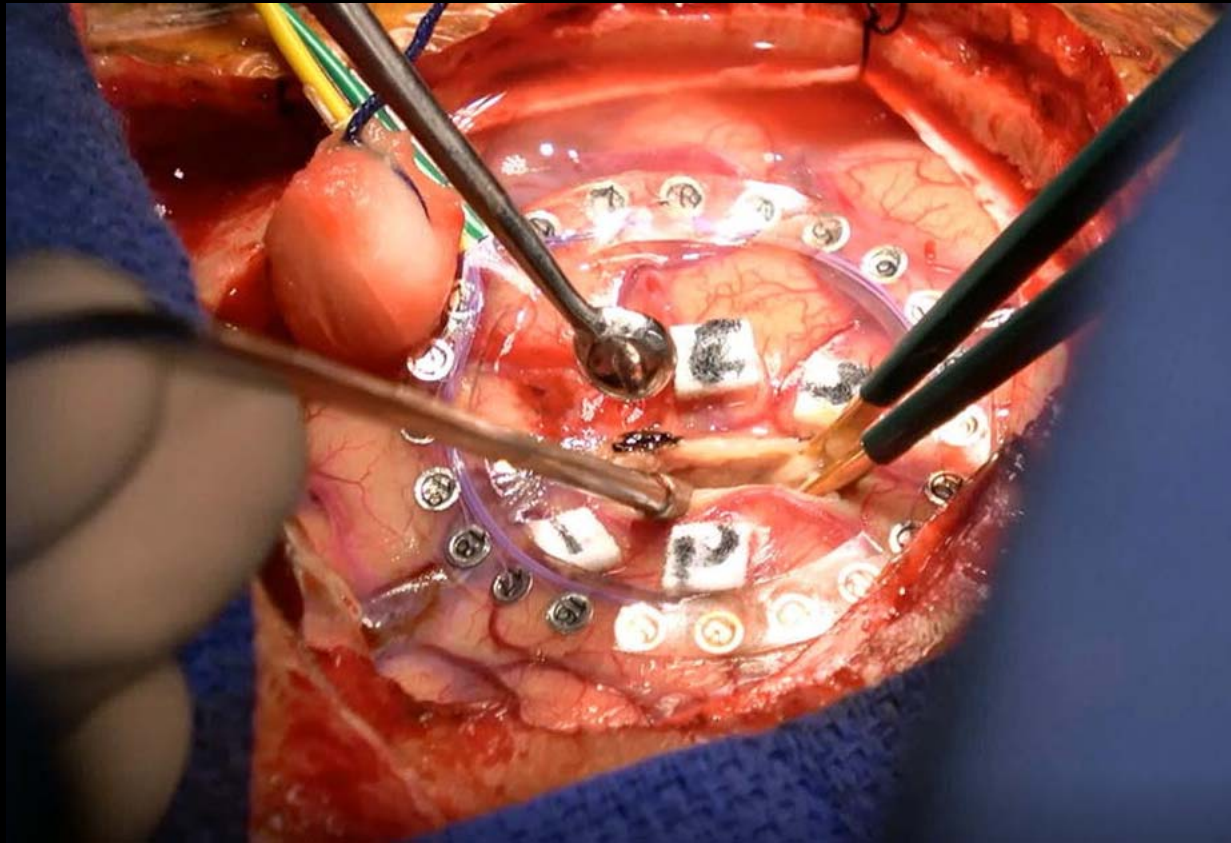
(Nakai et al., Brain 2017)



Speech arrest

(Nakai et al., Brain 2017)

**Intraoperative** stimulation-based language mapping:  
plausible in adults who can tolerate awake craniotomy.



Tatum et al. Clin Neurophysiol 2020



Stimulation of the **left medial temporal lobe** structure:  
for assessment of the **memory** function.

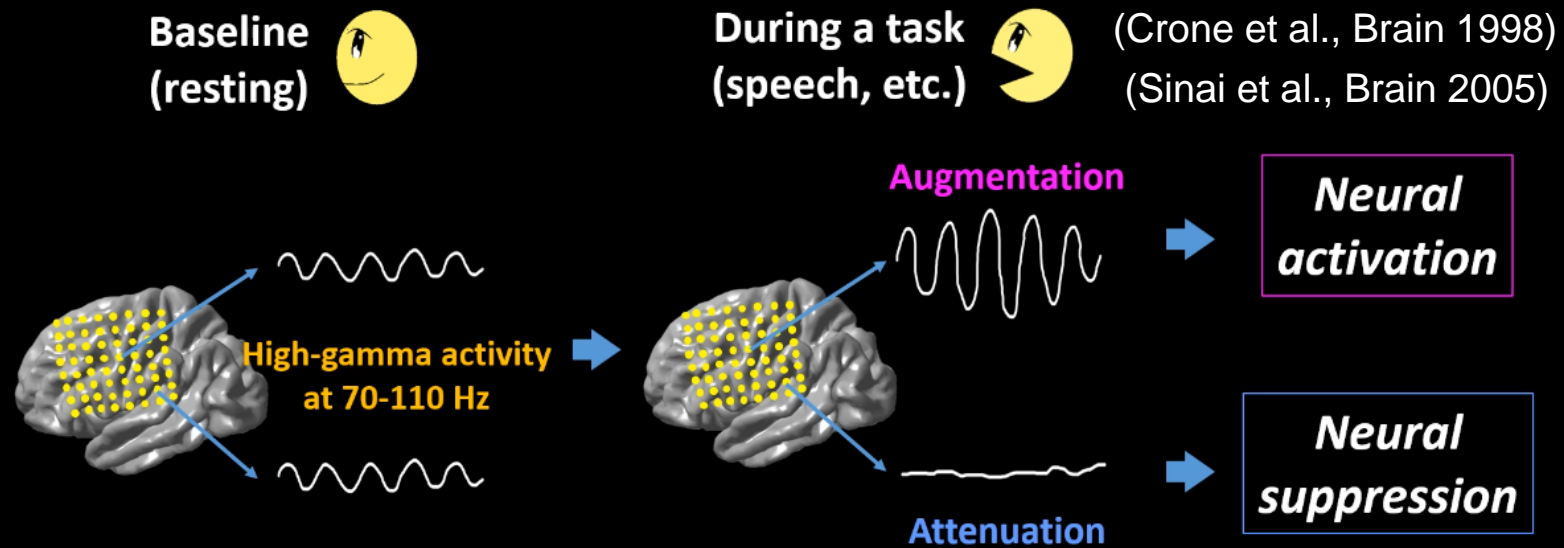
First author	Tani	Lacruz
Publication Year	J Neurosurg 2016	Neuroscience 2010
N of patients	11	12
Frequency (Hz)	50	0.2
Pulse width (ms)	0.2	1
Intensity (mA)	$\leq 6$	4 or 6
Duration (seconds)	5	Not available

Picture presentation  
during 5-s stimulation.



Test if a patient can  
recall the object  
several minutes after.

## Principle of brain mapping using high-gamma activity on iEEG



↑ High-gamma amplitude on iEEG

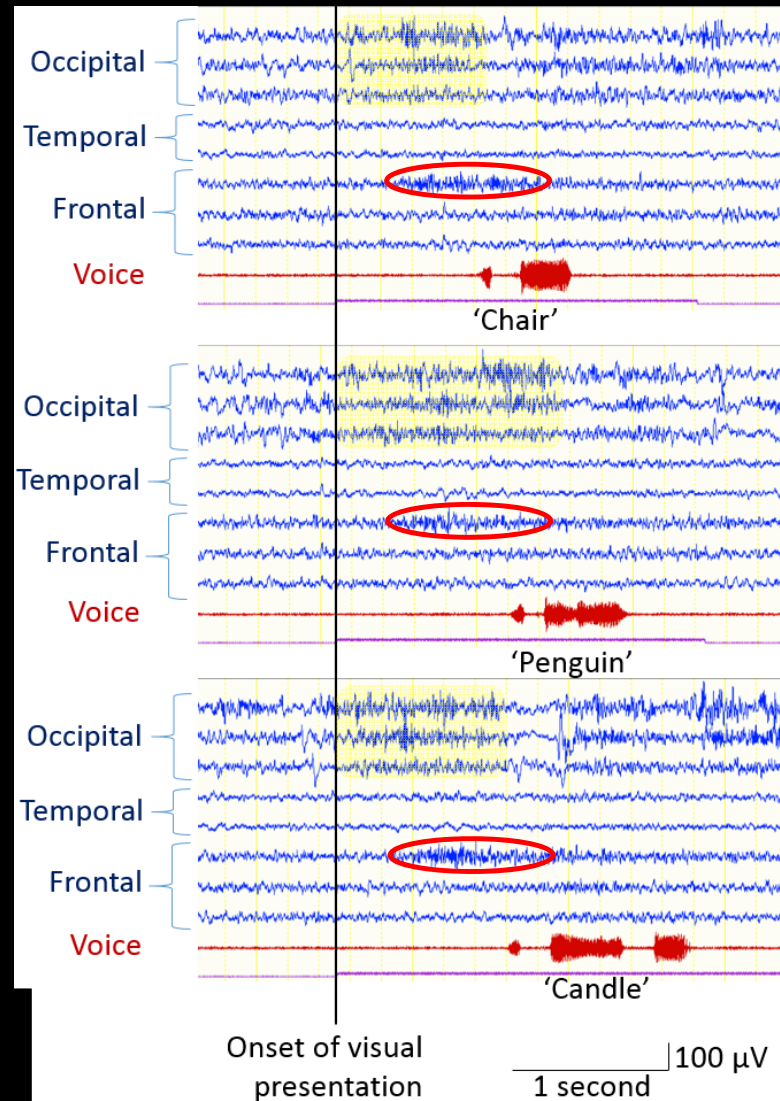
- ↑ Firing on single neuron recording (Ray et al. J Neurosci 2008; Manning et al. J Neurosci 2009)
- ↑ Hemodynamic responses on fMRI (Niessing et al. Science 2005)
- ↑ Glucose metabolism on FDG PET (Nishida et al. NeuroImage 2009)



Assessment of naming-related high-gamma responses (Kambara et al. Clin Neurophysiol 2018)

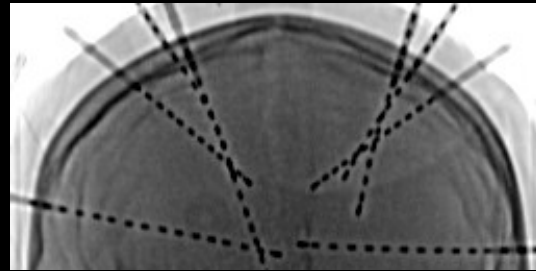
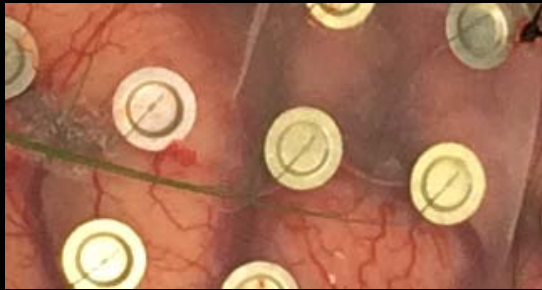
## iEEG traces during picture naming

Even with visual assessment, one would appreciate event-related high-gamma augmentation.

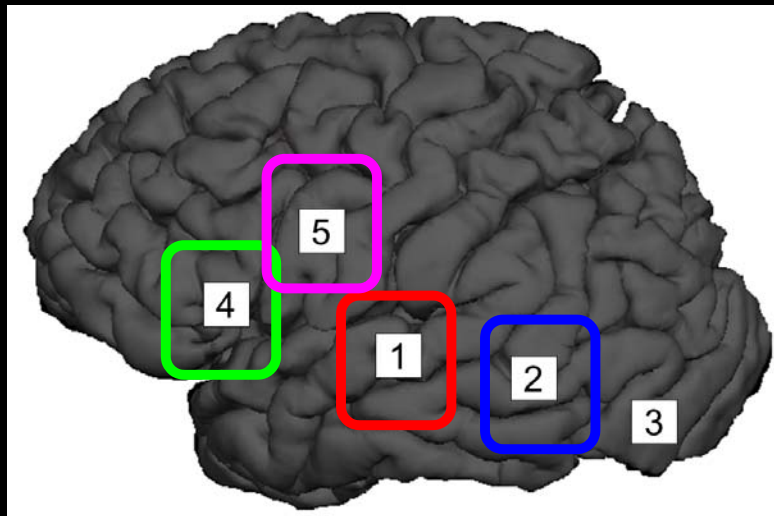


Time constant: 0.03 s  
(Asano & Gotman, Neurology 2016)

One can use either subdural and stereo-EEG electrodes for measurement of event-related high-gamma modulations.



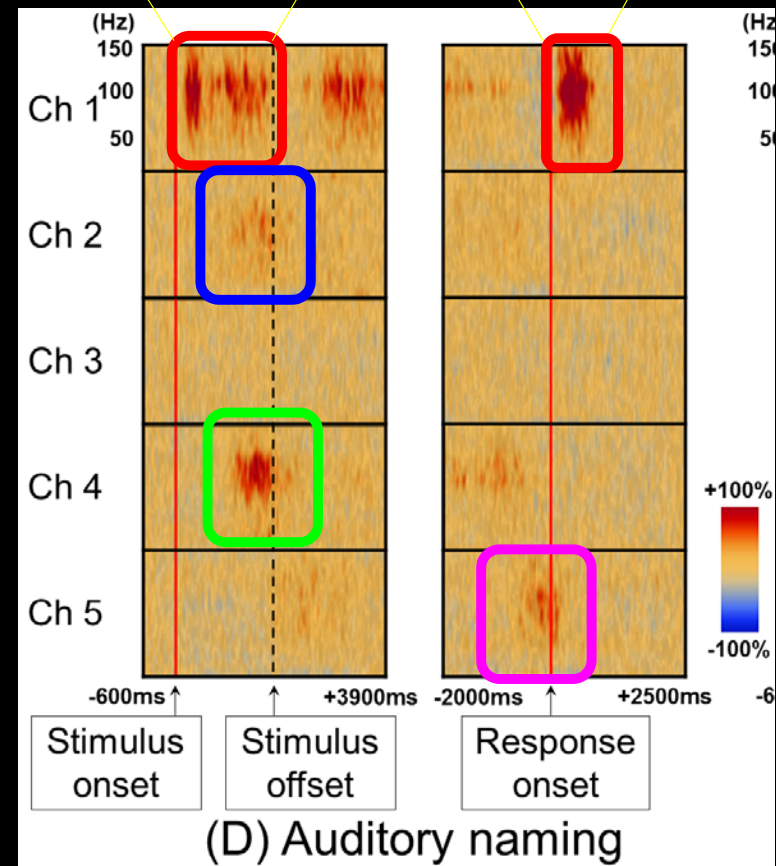
Auditory naming-related high-gamma augmentation in a 12-year-old boy.



(Kambara et al., Clin Neurophysiol 2018)

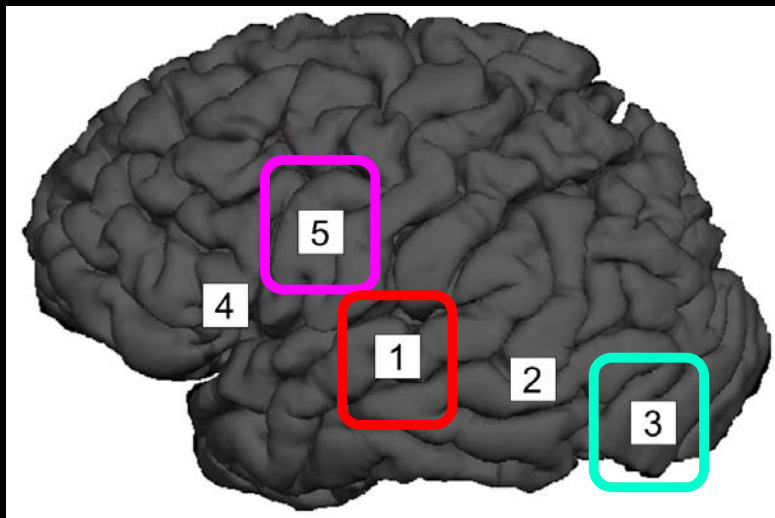
*'What flies in the sky?'*

*'Bird'*

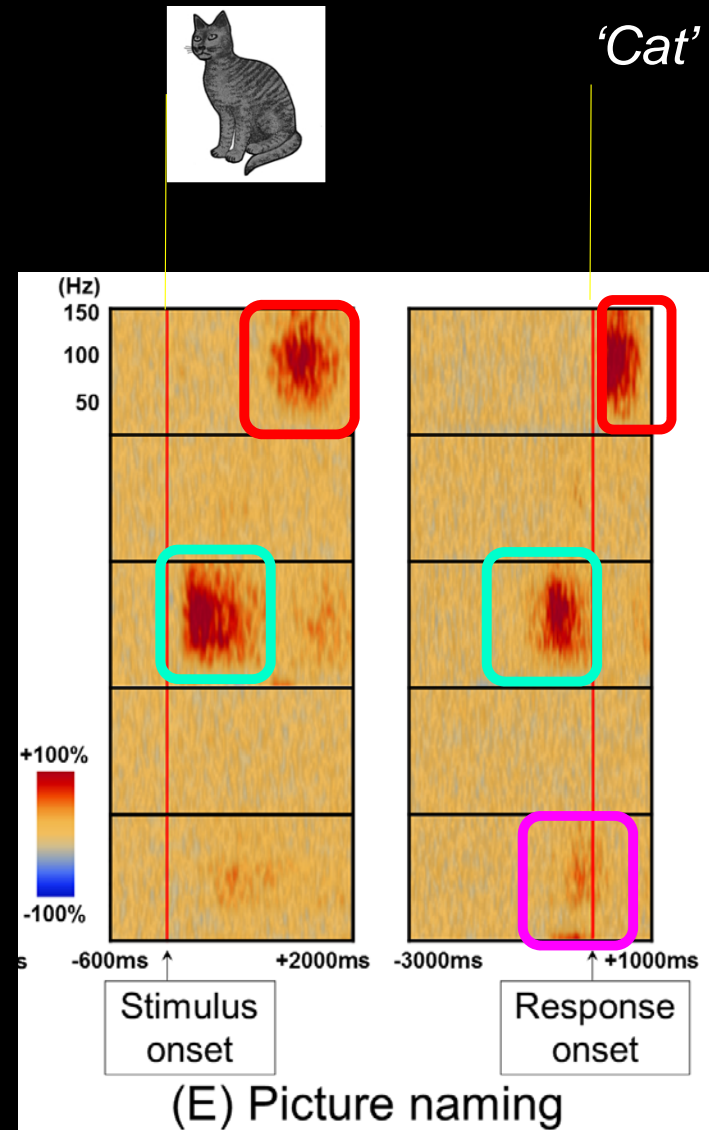


(D) Auditory naming

Picture naming-related  
high-gamma augmentation  
in a 12-year-old boy.



(Kambara et al., Clin Neurophysiol 2018)



(E) Picture naming

Meta-analysis of 15 studies (Arya et al., Epilepsy Behav 2018):

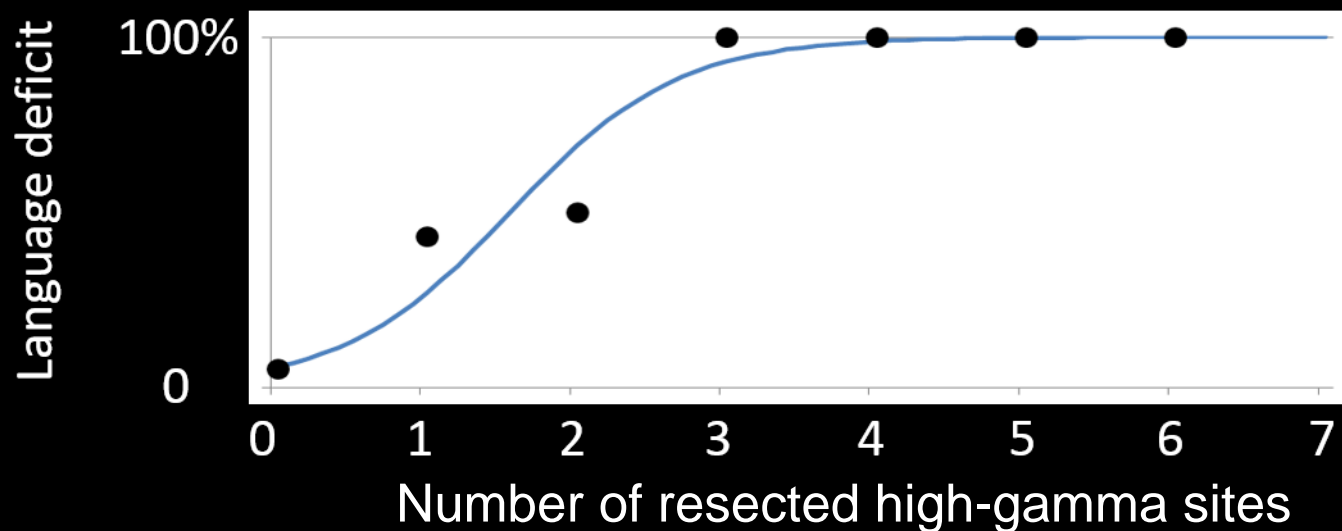
Event-related high-gamma mapping is capable of predicting language areas defined by electrical stimulation mapping.

Diagnostic odds ratio: 6.4.



Naming-related high-gamma activity predicted acute language deficits requiring speech therapy.  
(Kojima et al., Clin Neurophysiol 2013)

New post-surgical language deficits: 15/77 patients



Odds Ratio: 6.0

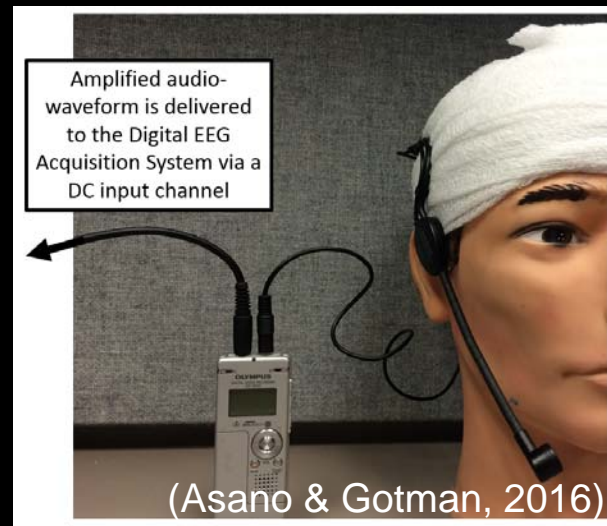
## Advantage of event-related high-gamma mapping:

- Signal fidelity >100 times better than scalp recording (Ball et al. NeuroImage 2009)
- Temporal resolution of tens of ms
- Spatial resolution of 5-10 mm
- Sampling from deep regions
  
- Small start-up funding

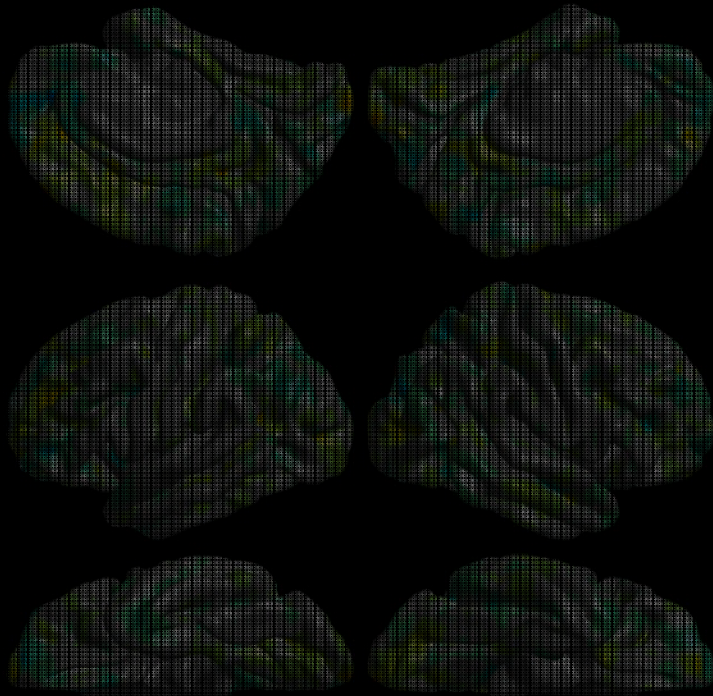
↓ EMG artifacts  
Patient can loudly talk  
during a task.

Rapid temporal dynamics  
3D space  
Whole brain level

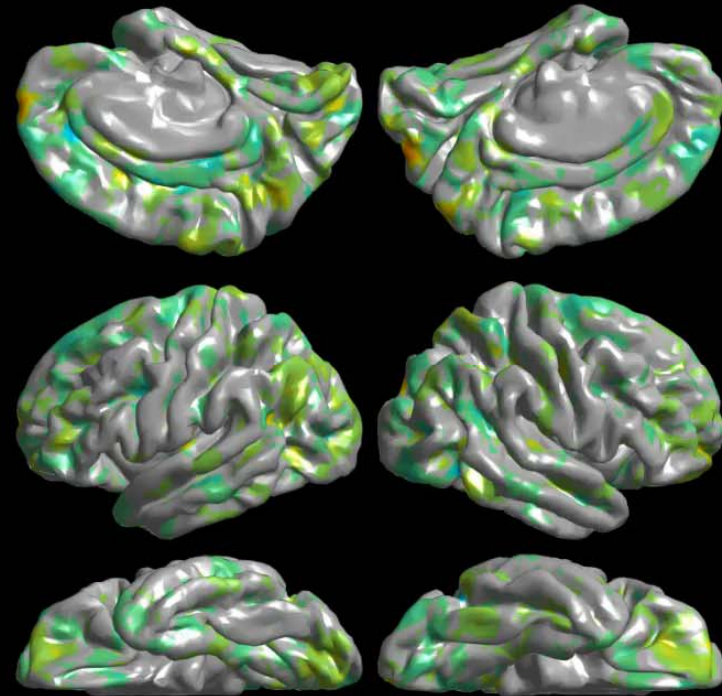
4D functional  
atlas



Picture naming



Auditory naming



-30 ms

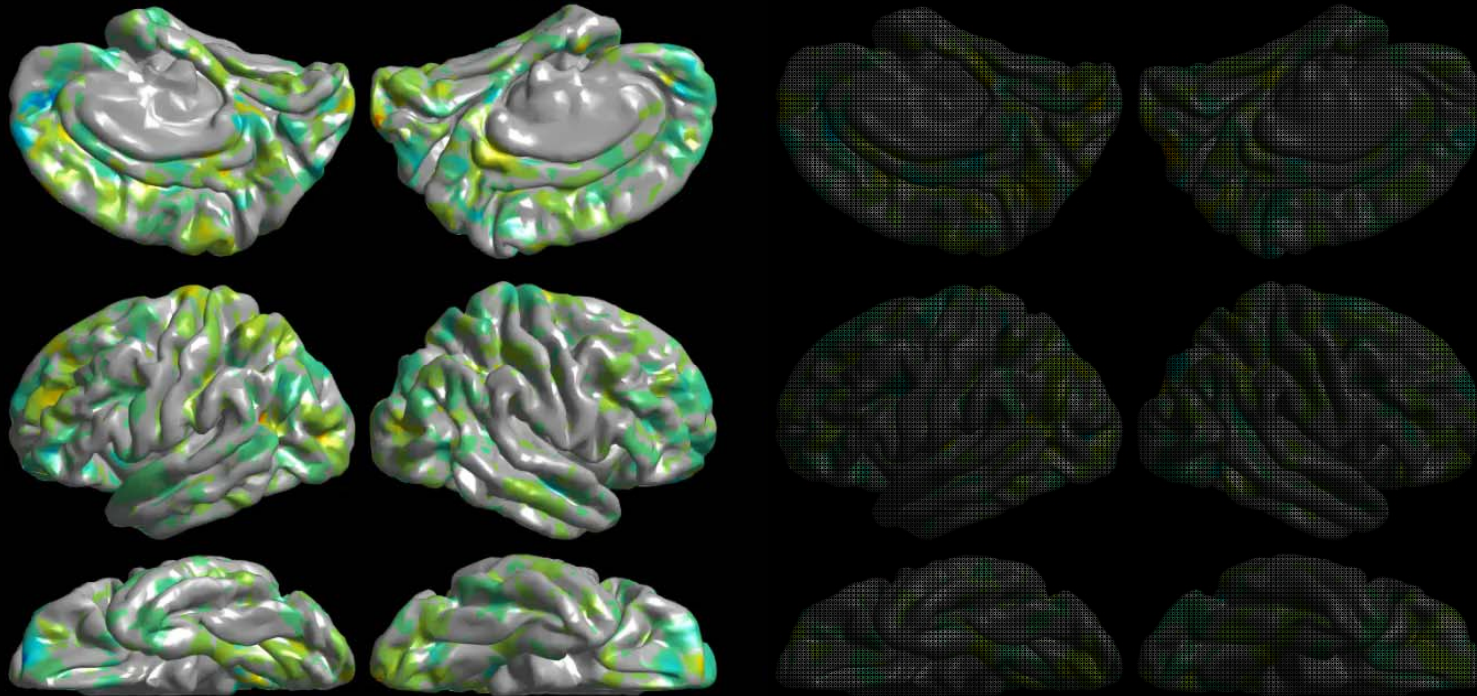
Amplitude change



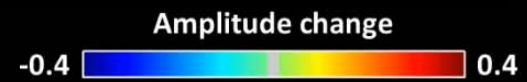
Whole-brain level 4D atlas of auditory language function  
(Nakai et al., Brain 2017)

Picture naming

Auditory naming



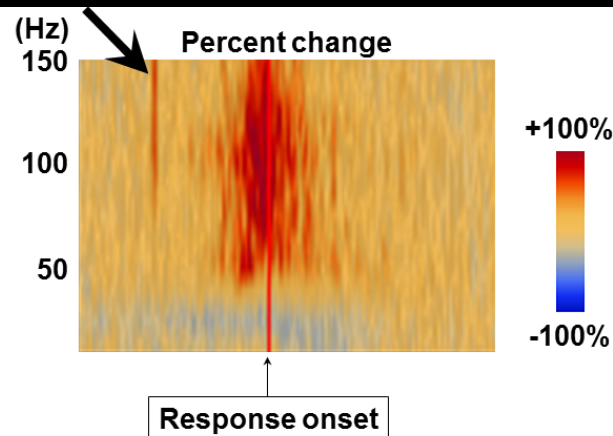
-50 ms



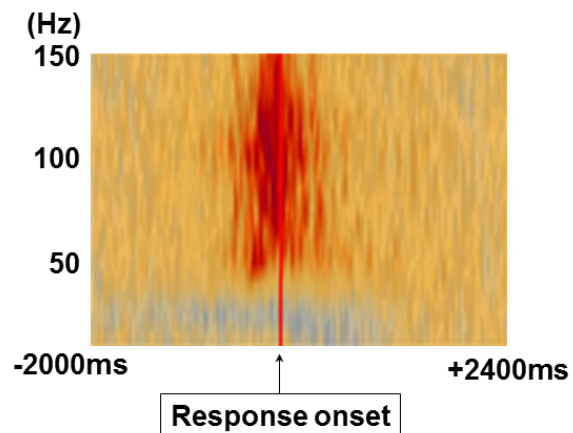
Whole-brain level 4D atlas of visual language function  
(Nakai et al., Epilepsia 2019)

# Unwanted effect of interictal spikes on high-gamma mapping

(Kambara et al., Clin Neurophysiol 2018)

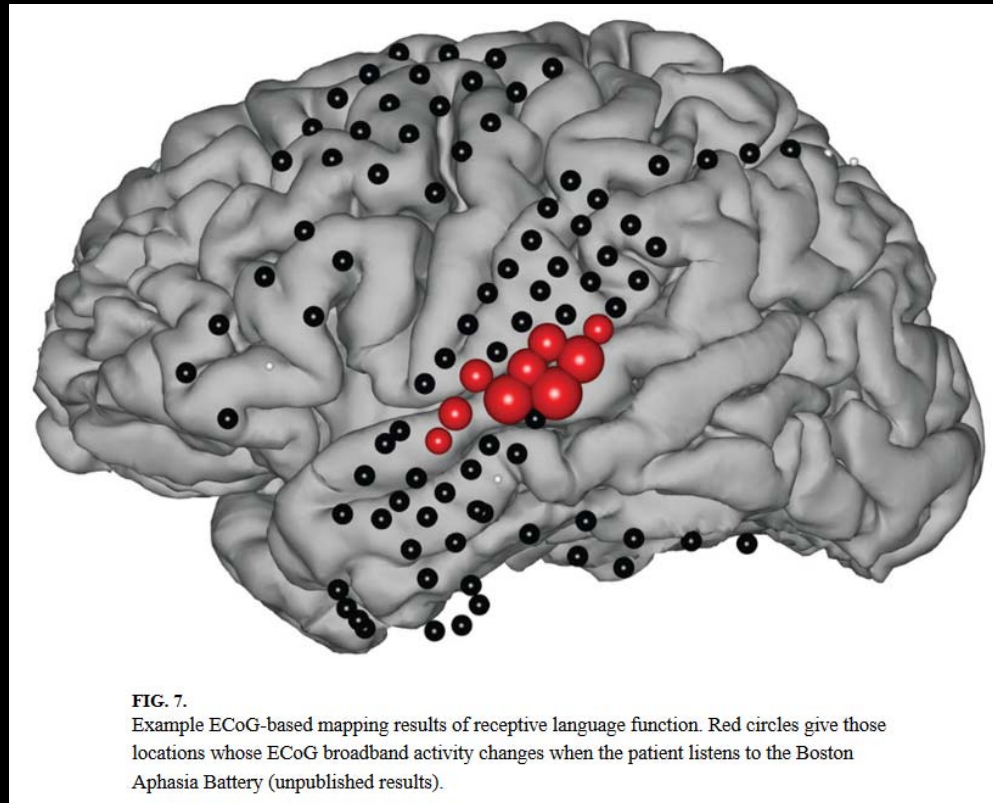


**(A) Before excluding a trial affected by a spike discharge.**



**(B) After excluding a trial affected by a spike discharge.**

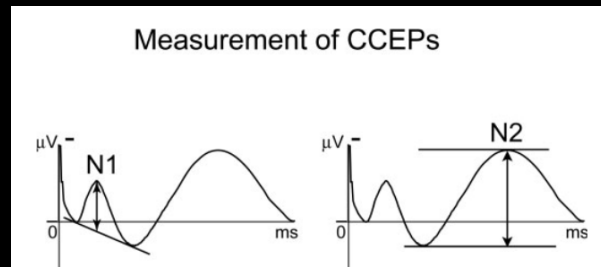
**Real-time** high-gamma-based mapping. Verbal stimulus listening induced high-gamma changes in the superior temporal gyrus.



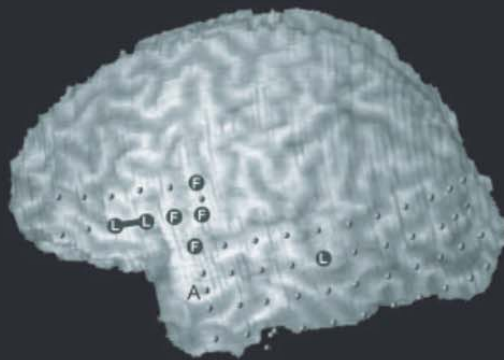
Ritaccio et al., J Clin Neurophysiol 2018

# Single-pulse stimulation-induced neural responses.

## Cortico-cortical evoked potential (CCEPs) (Matsumoto et al. Brain 2004)



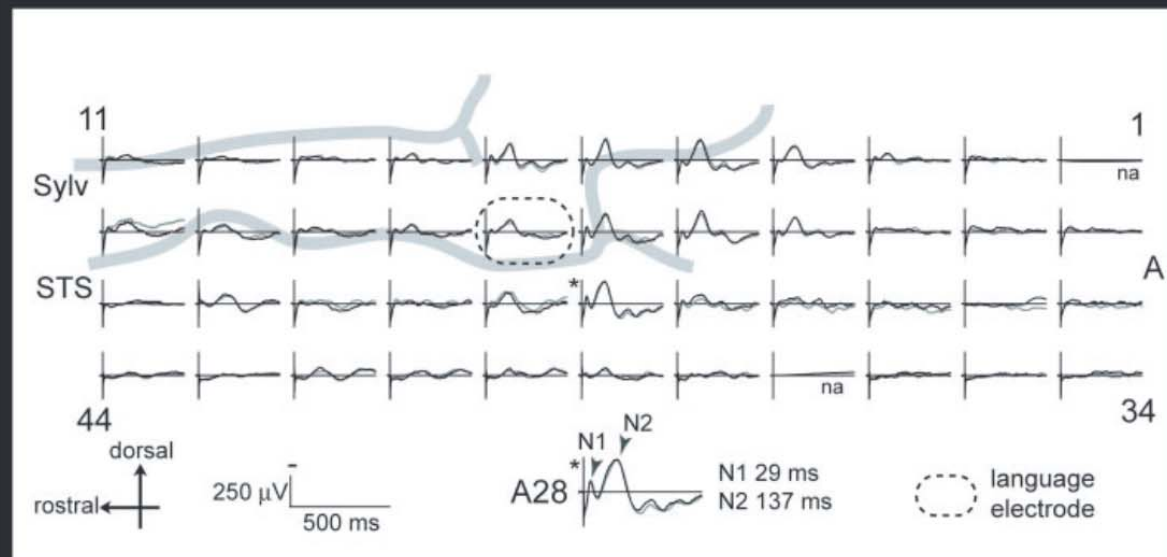
Patient 1



● Bipolar stimulation

L Language

F Face motor



Deep white matter    Shallow white matter    Gray matter    Outside the brain

**CCEPs**

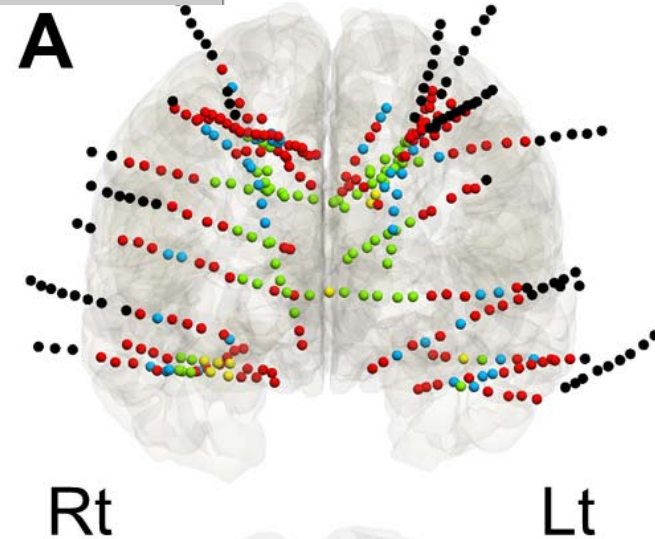
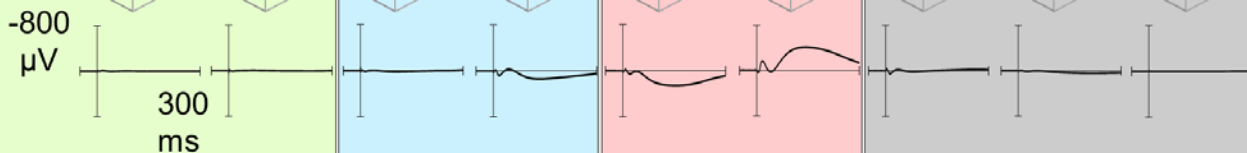
**B.**  
Bipolar



**C.**

I-1    I-2    I-3    I-4    I-5    I-6    I-7    I-8    I-9    I-10    I-11

**D.**  
Laplacian



Mitsuhashi et al.  
Clin Neurophysiol  
2020.



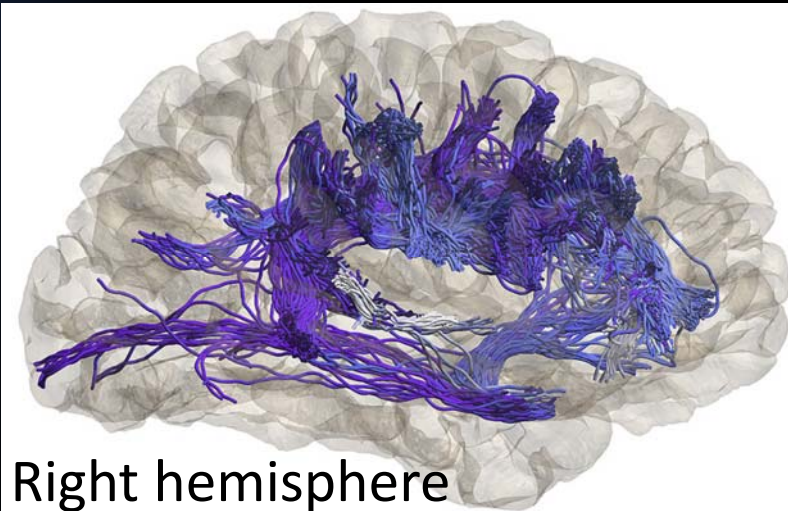
# 4D visualization of CCEP/CCSR-based effective connectivity

(e.g., Sugiura et al., NeuroImage 2020)

**CCSRs from  
lateral-occipital sites**

4D dynamic tractography animates neural propagations via white matter tracts.

Right STG Stimulation  
-40 ms



Right hemisphere



CCEP or CCSR



(Brian Silverstein et al. NeuroImage 2020)

CCEP/CCSR are useful measures to assess the effective connectivity from distant sites.

Advantage:

No need of patient cooperation.

Intraoperative measurement is possible.

Limitation:

Need to incorporate additional information (e.g., anatomy, stimulation results) for the optimal interpretation.

4D dynamic tractography: a potential to improve the understanding of network dynamics supporting cognitive function.

## Acknowledgement

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