

# Next-Generation Seizure Therapy

Balancing Efficacy and Cognition with  
Optimized Waveforms and Personalized Targeting



Zhi-De **Deng**, PhD

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Experimental Therapeutics & Pathophysiology Branch  
National Institute of Mental Health, NIH

# Faculty Conflict of Interest Disclosure

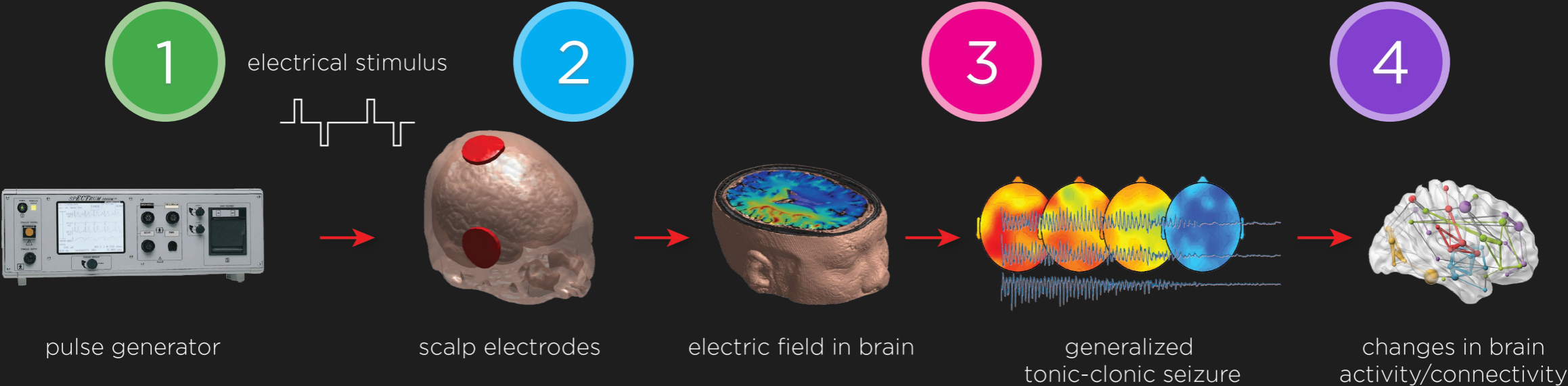
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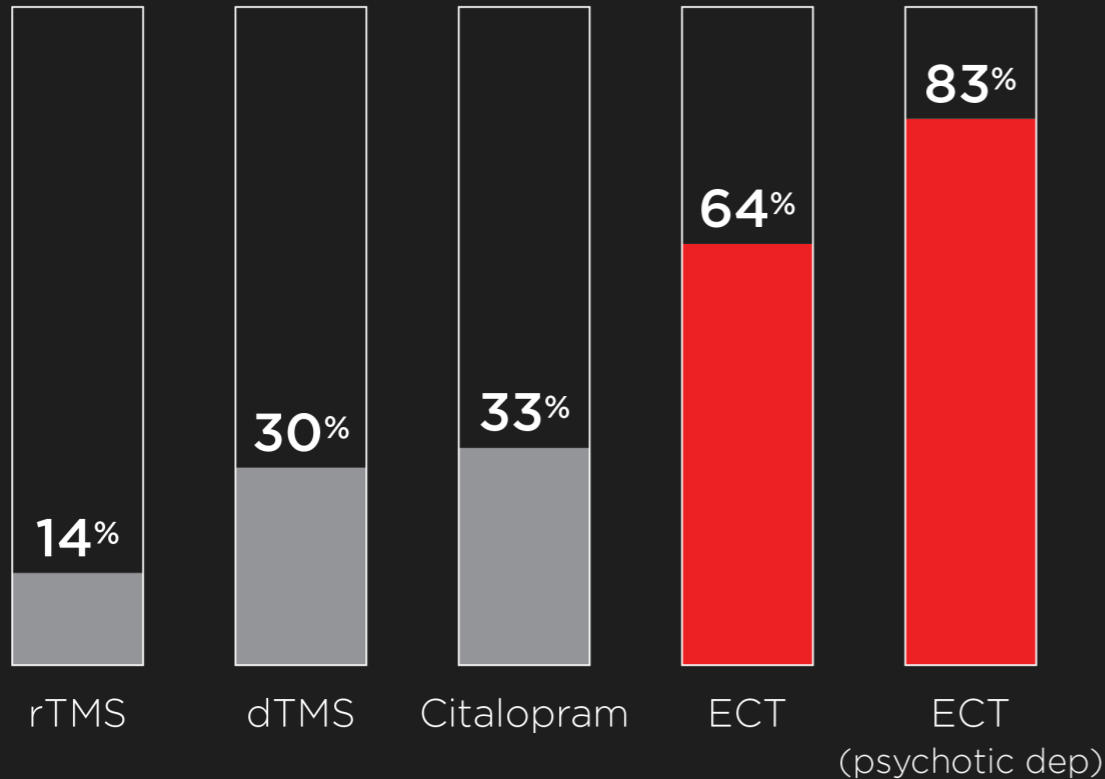
I have the following potential conflict(s) of interest to report:

Type of affiliation / financial interest	Name of commercial companies
Receipt of grants/research supports	National Institute of Mental Health (NIMH) Intramural Research Program
Receipt of honoraria or consultation fees	None
Participation in a company sponsored speaker's bureau	None
Stock shareholder	None
Spouse/partner	None
Other support (please specify)	Co-inventor on patents and patent applications owned by NIH, Columbia University, MIT, University of New Mexico, and NEVA Electromagnetics

# Electroconvulsive therapy

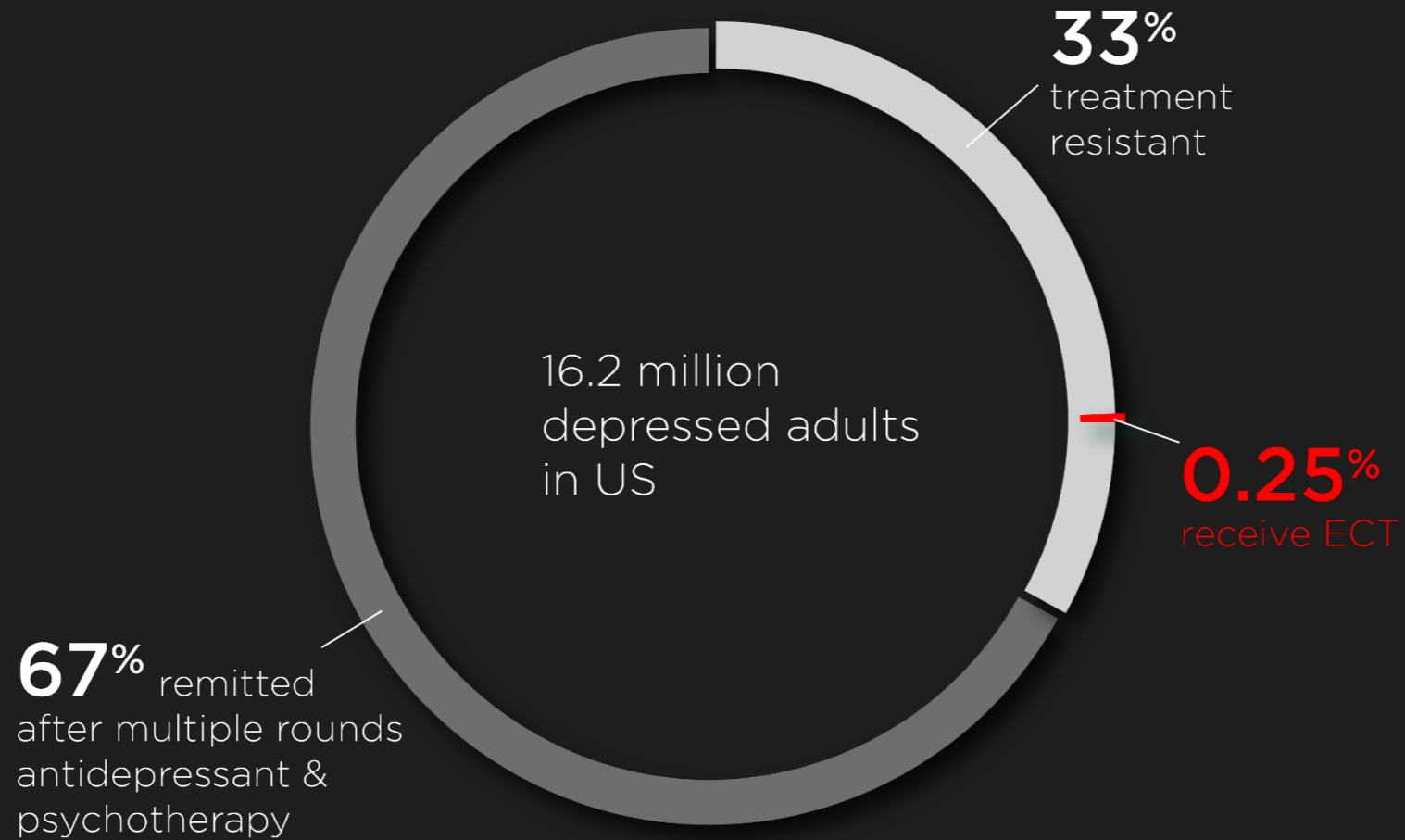


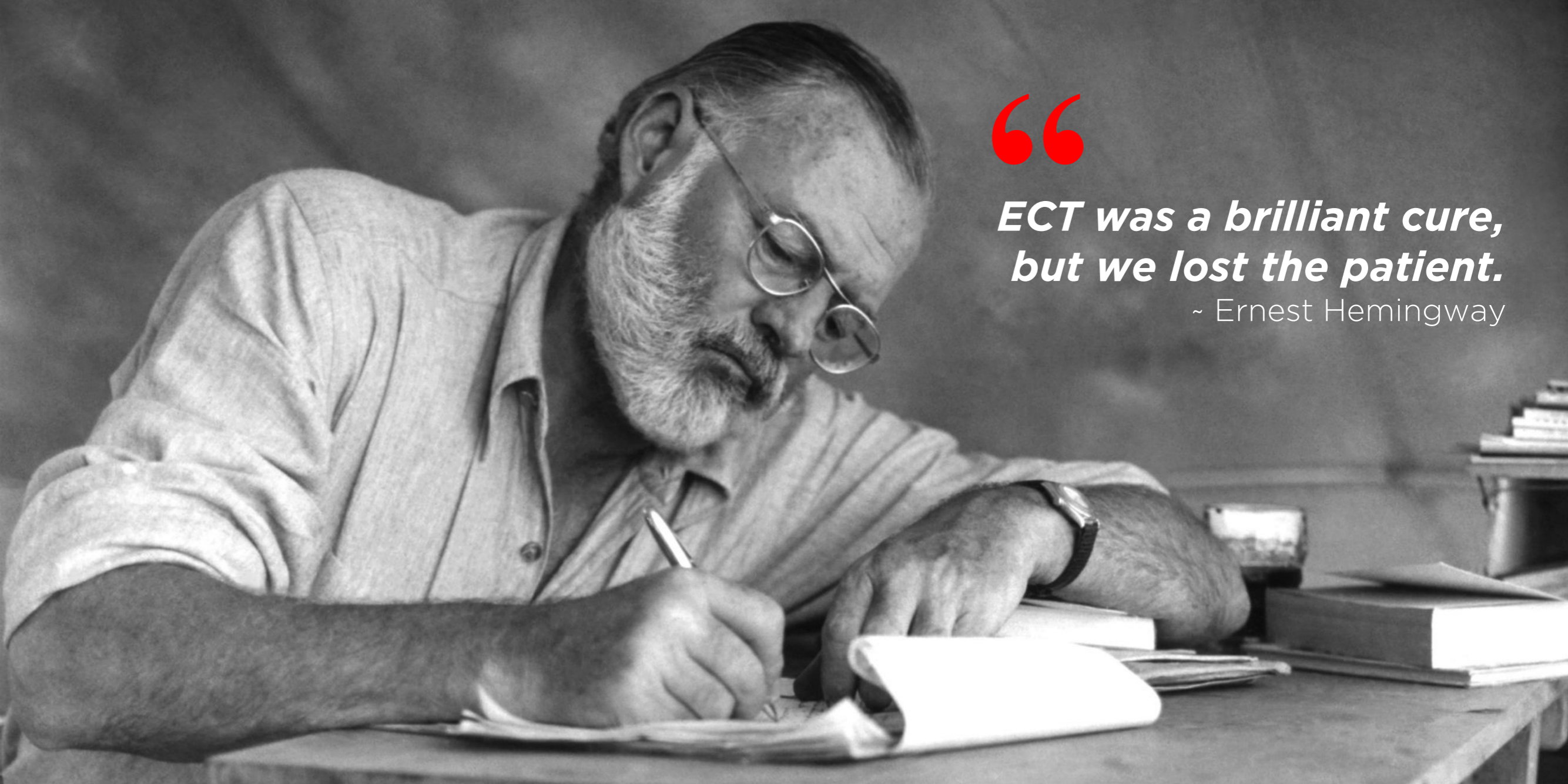
## Remission rate



ECT is...

the most effective treatment for severe major depressive disorder, catatonia, mania, suicidal ideation, or any condition where “there is a need for rapid, definitive response.” (FDA 2011)



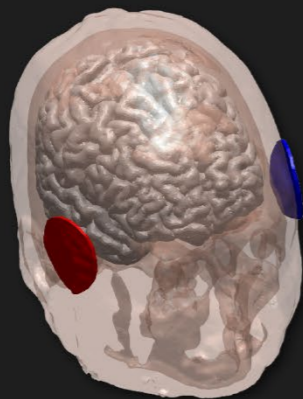


“

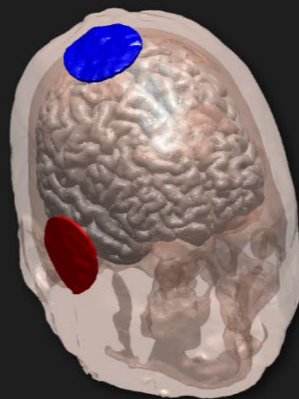
***ECT was a brilliant cure,  
but we lost the patient.***

~ Ernest Hemingway

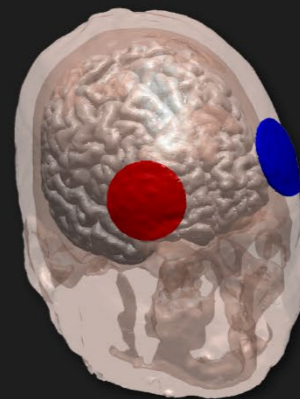
Bilateral



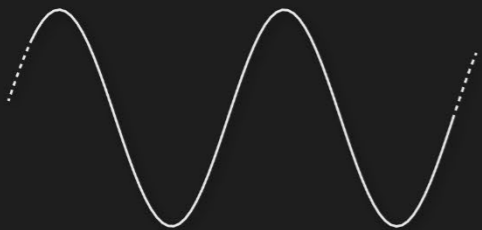
Right unilateral



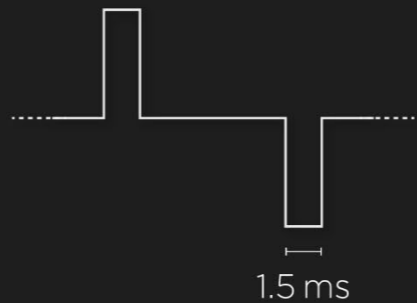
Bifrontal



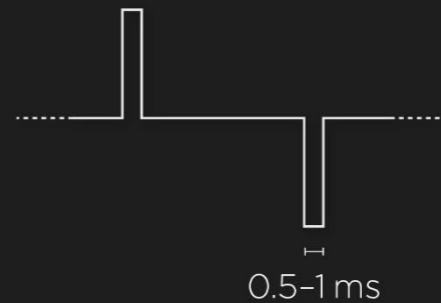
Sine wave



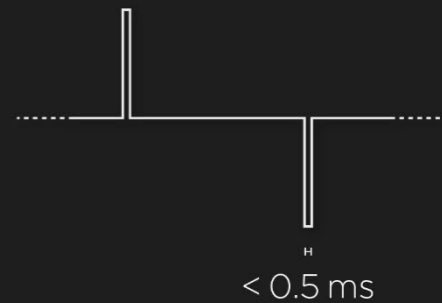
Standard pulse



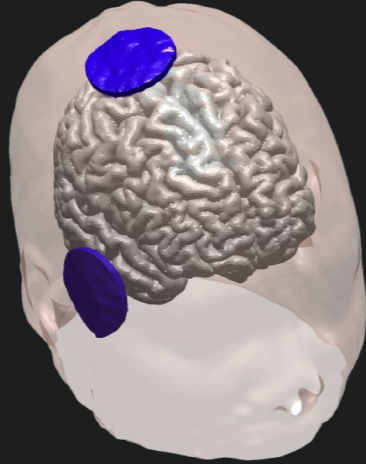
Brief pulse



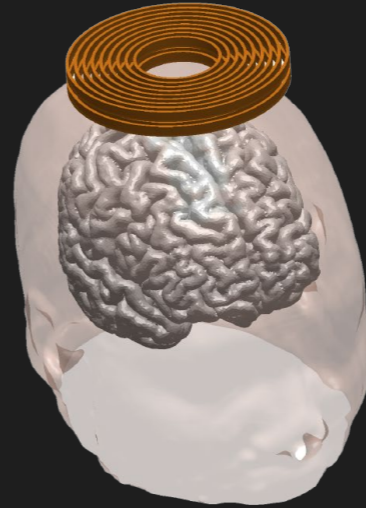
Ultrabrief pulse



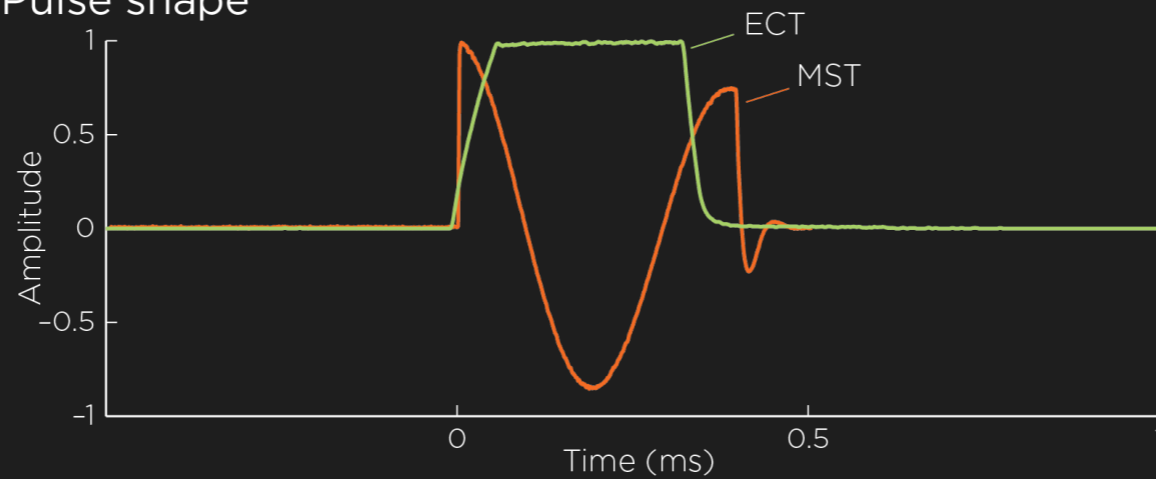
ECT



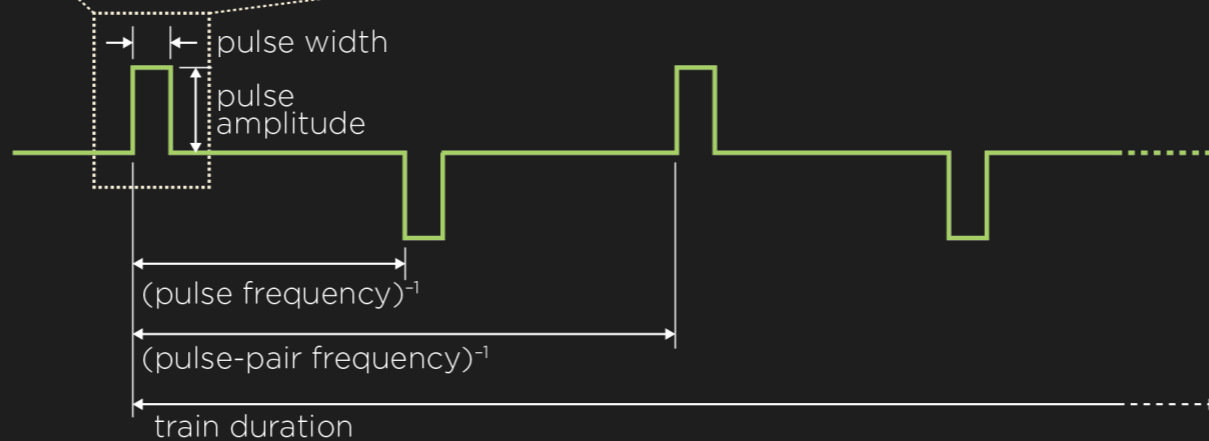
Magnetic seizure therapy  
(MST)



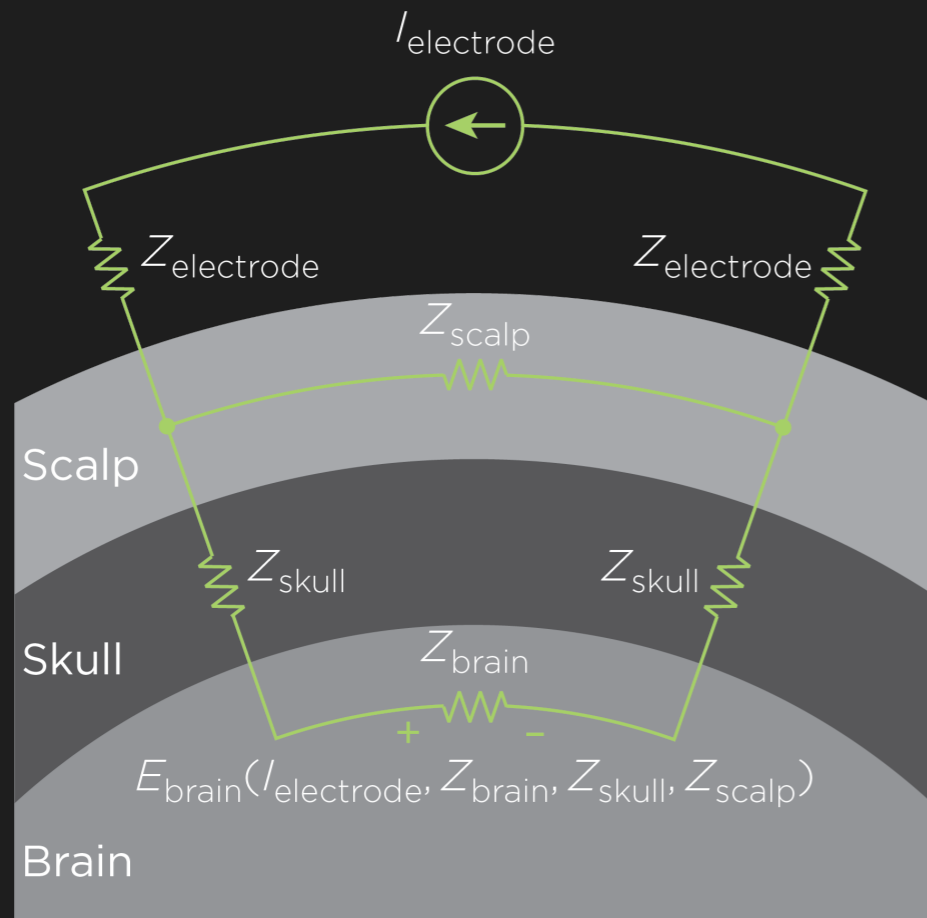
### A. Pulse shape



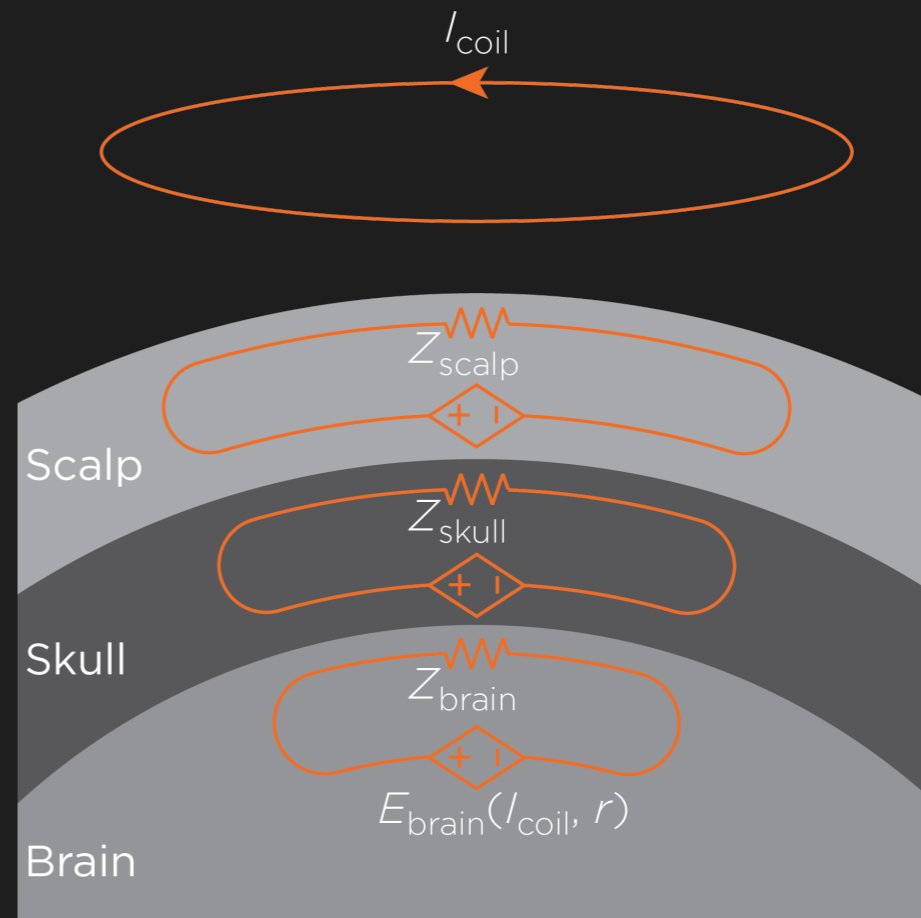
### B. Pulse train parameters

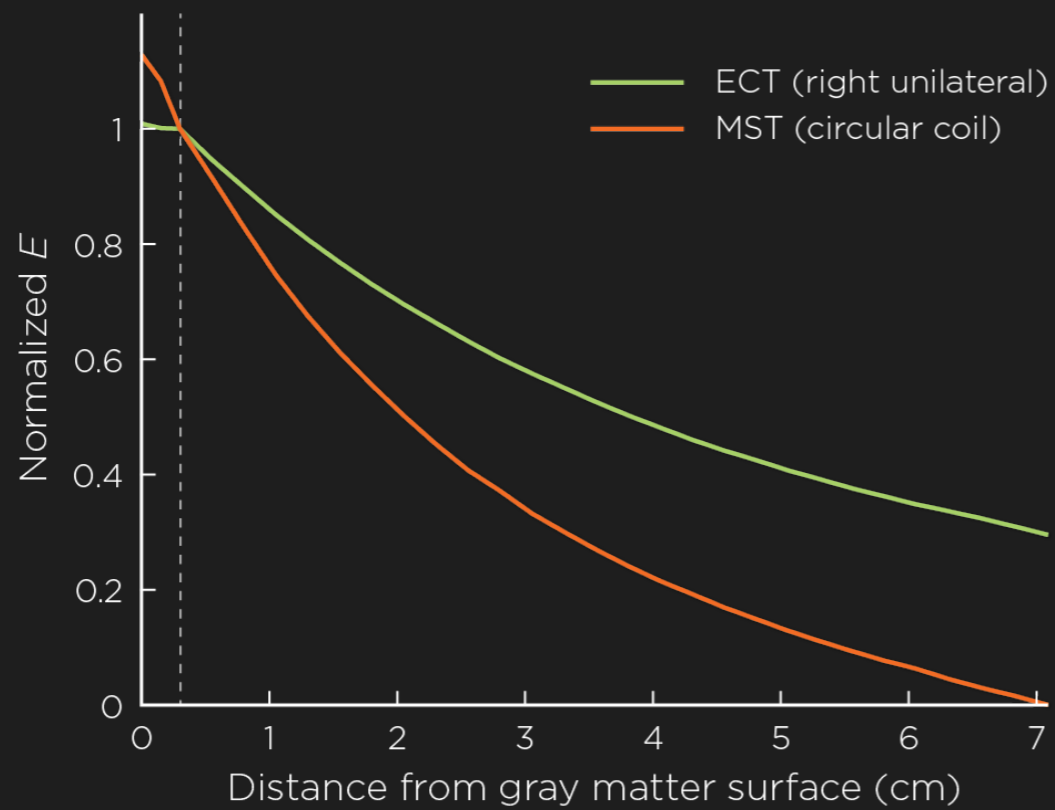


# ECT

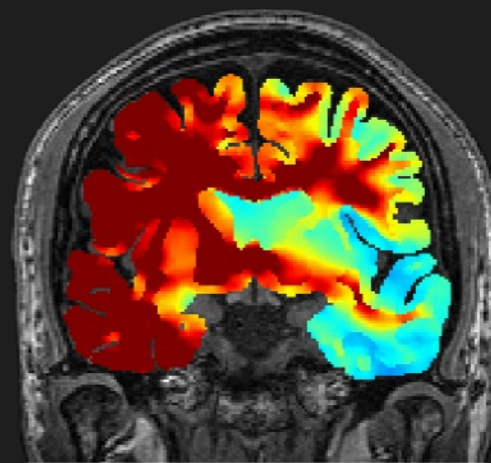


# MST

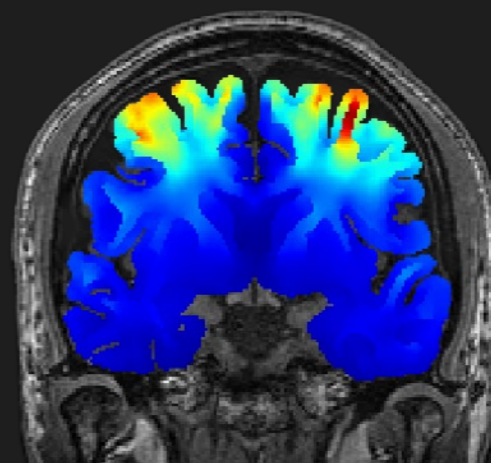




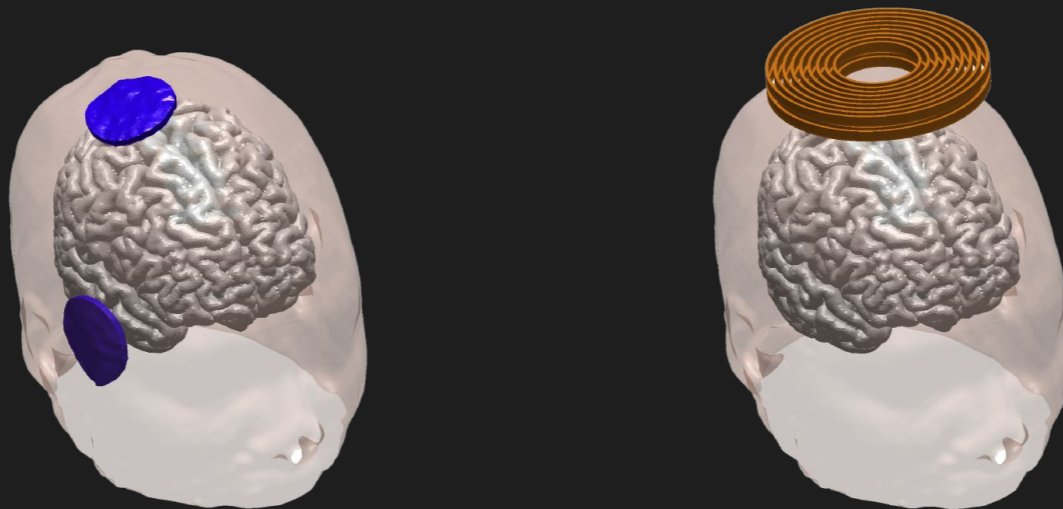
ECT



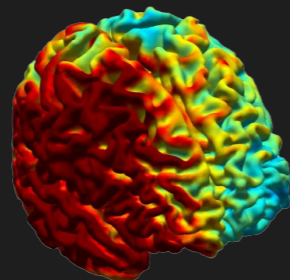
MST



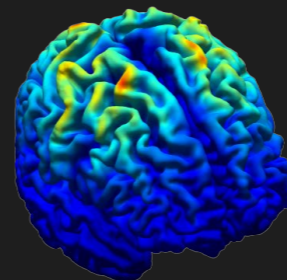
# Stimulated brain volume



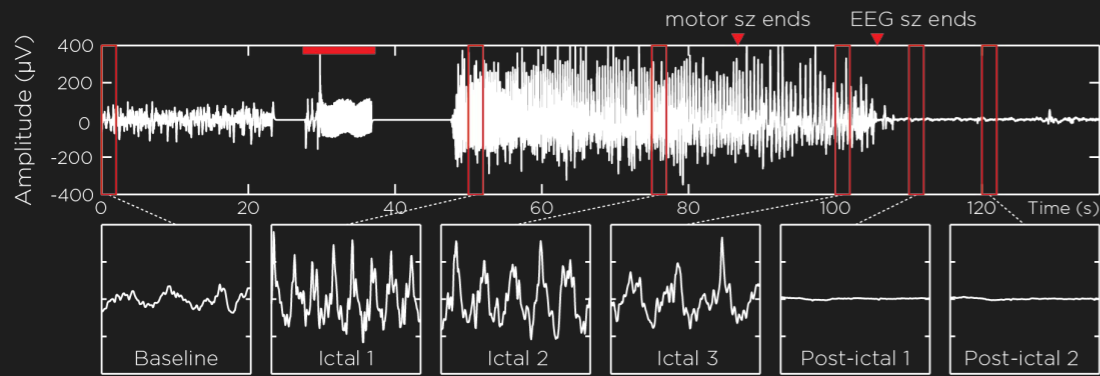
ECT  
> 90%



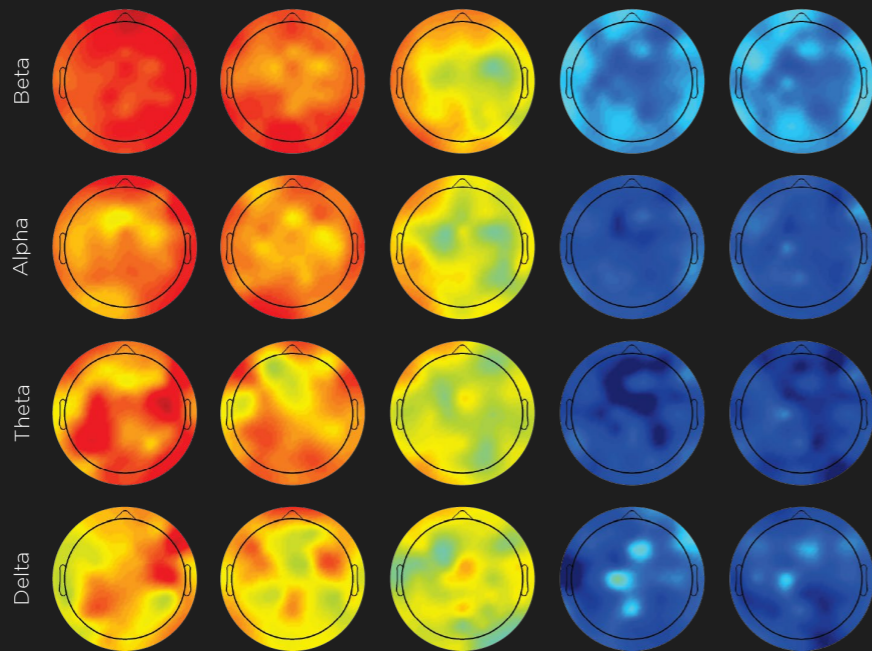
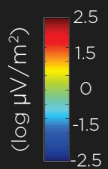
MST  
< 20%



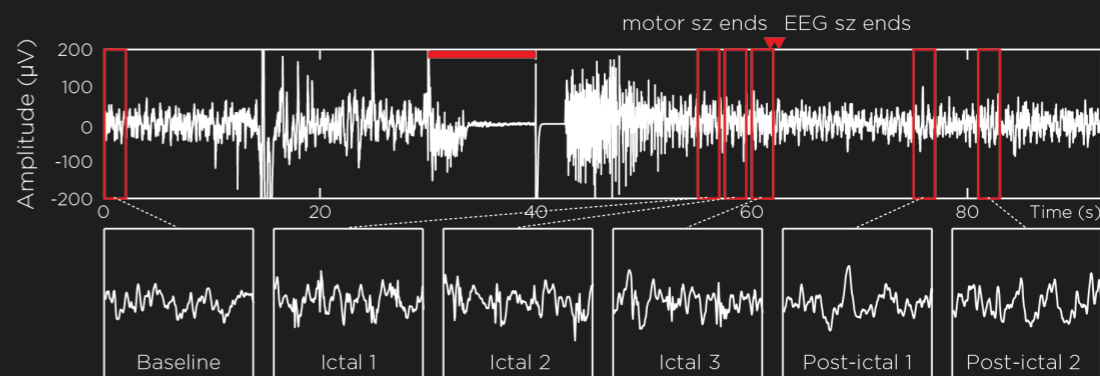
# ECT seizure



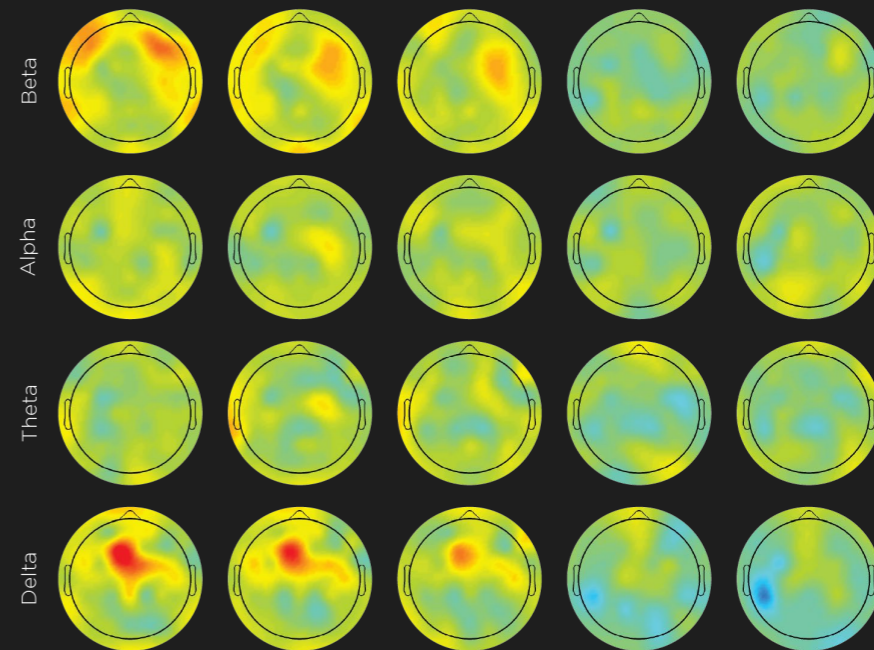
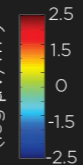
CSD power relative to baseline  
( $\log \mu\text{V}/\text{m}^2$ )

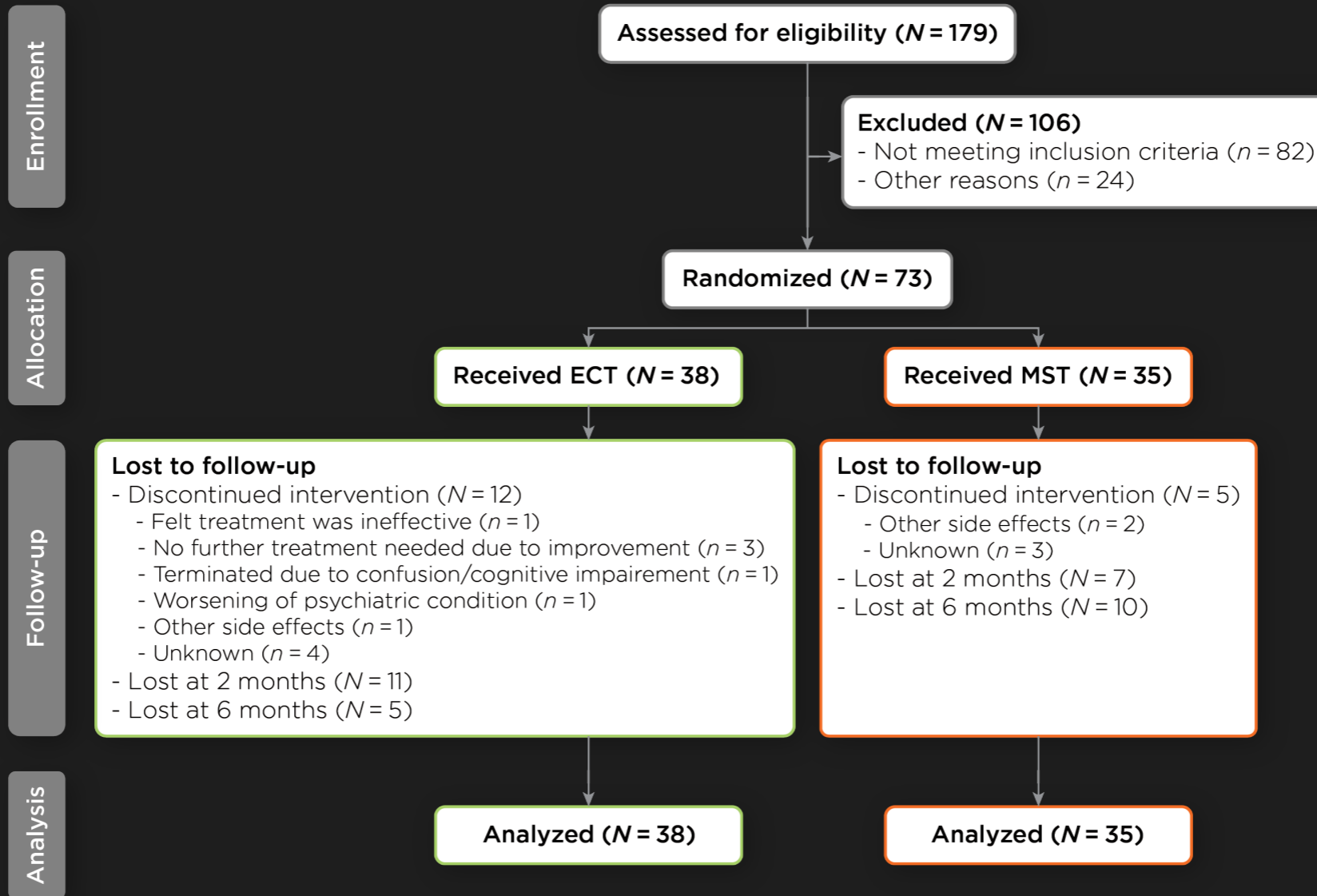


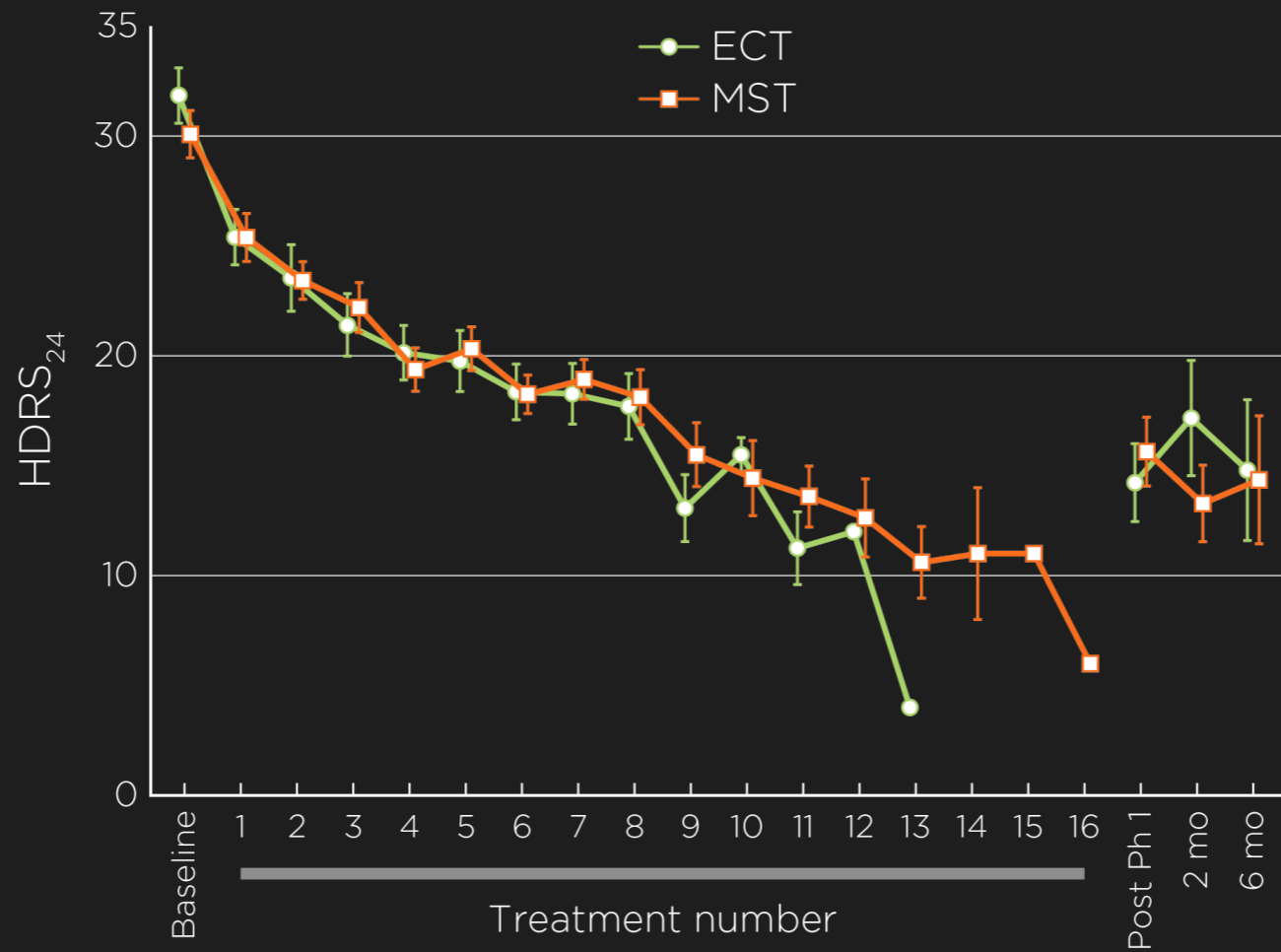
# MST seizure



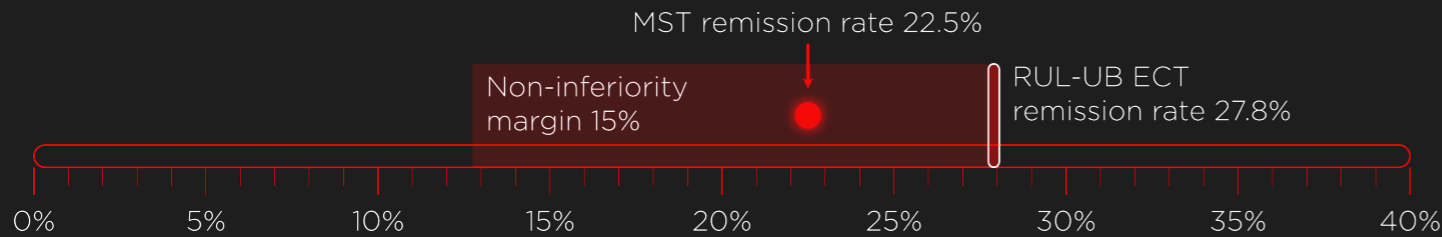
CSD power relative to baseline  
( $\log \mu\text{V}/\text{m}^2$ )





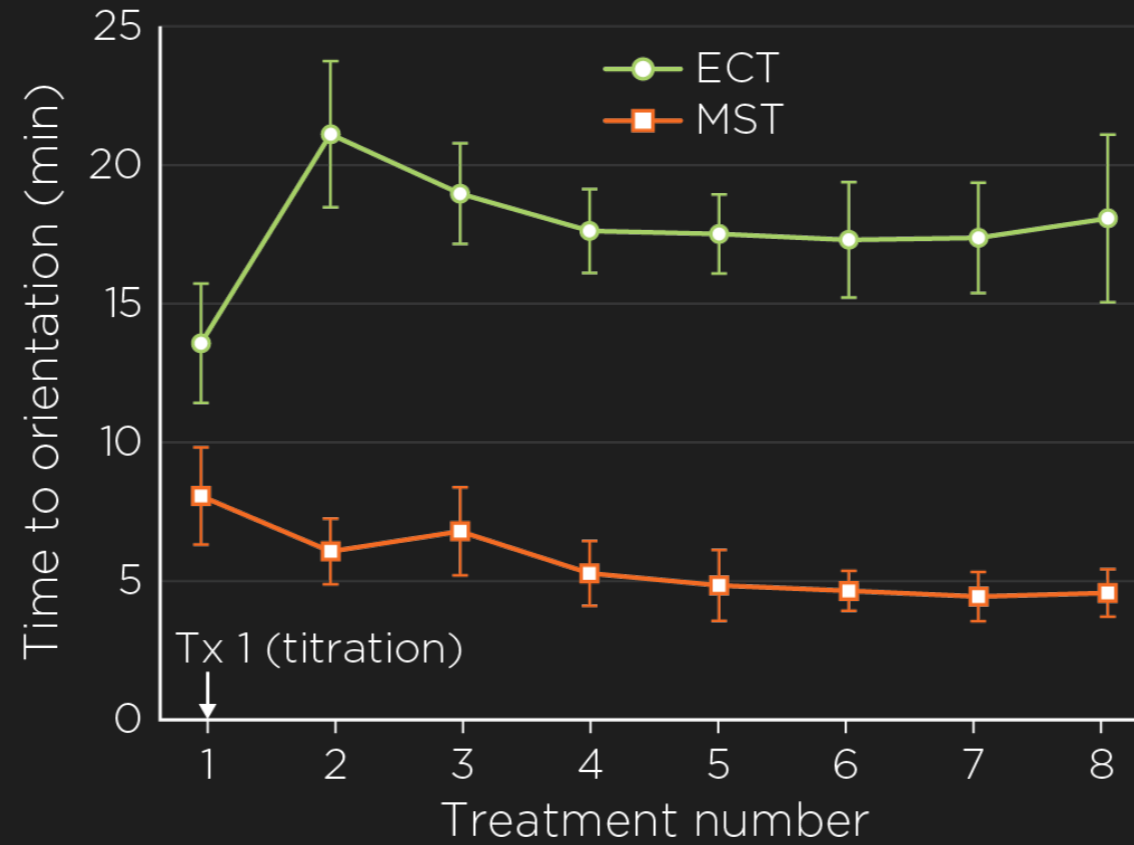


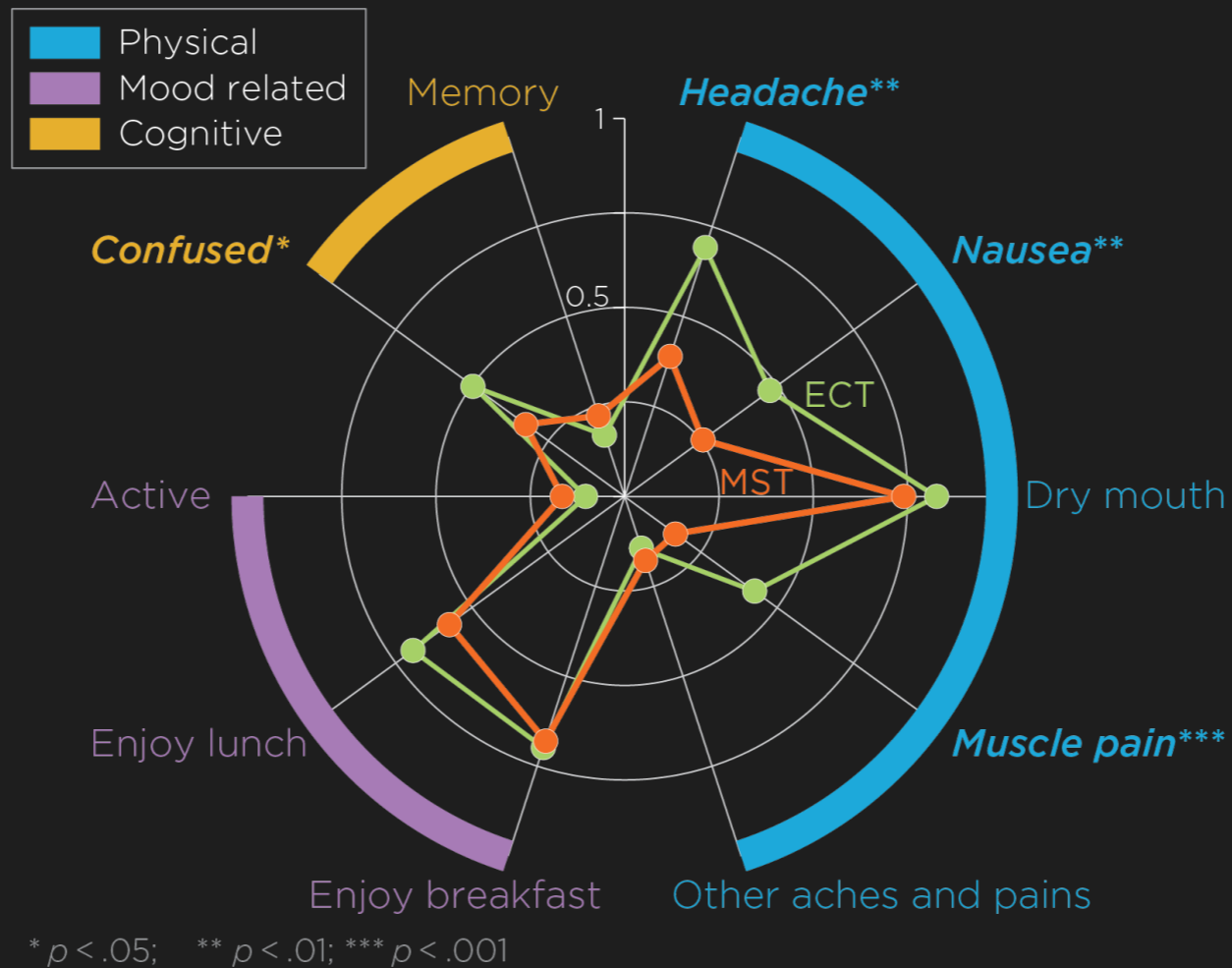
# CREST-MST trial 2026

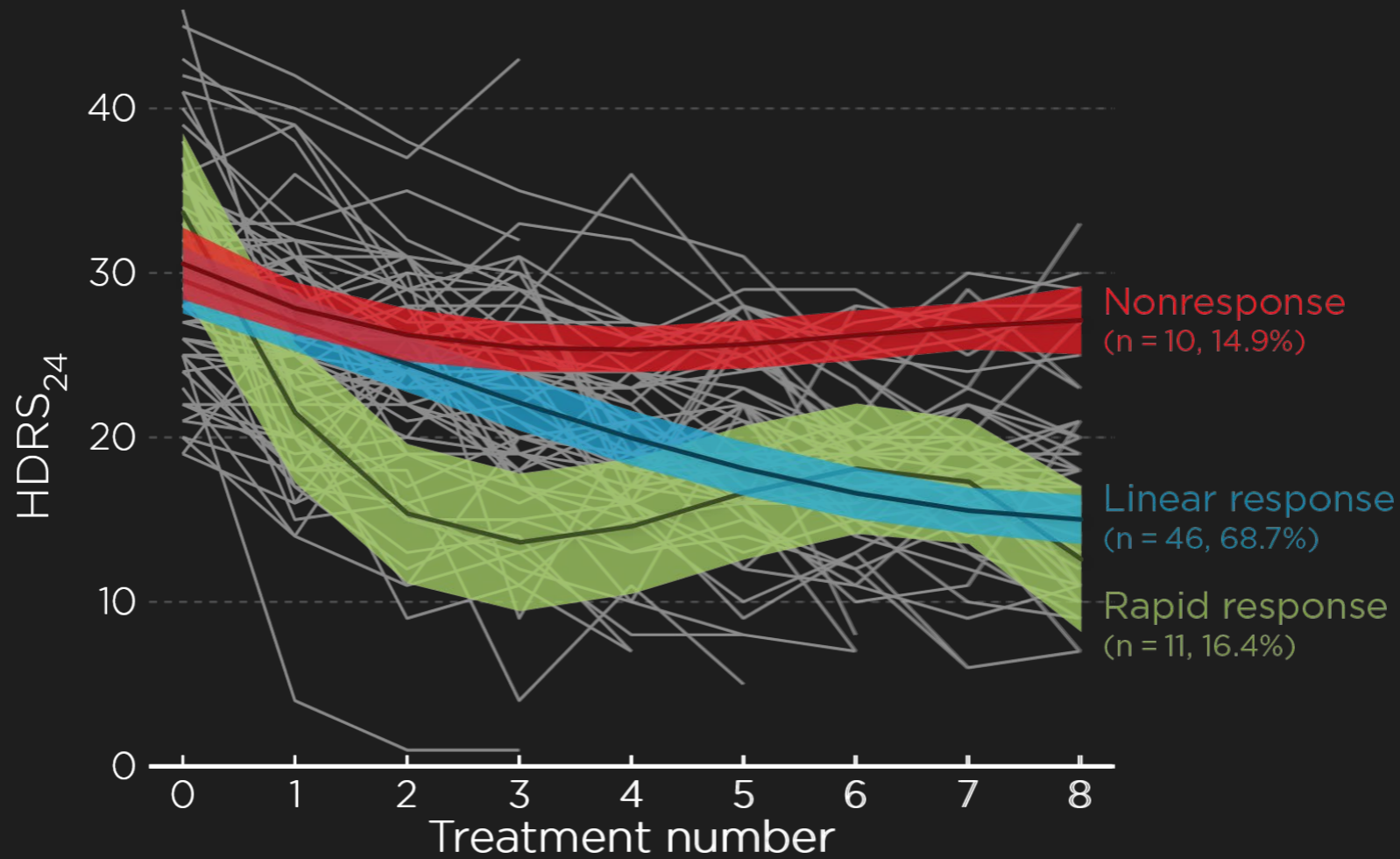


↳ MST falls within the pre-set margin  
= **non-inferiority efficacy**

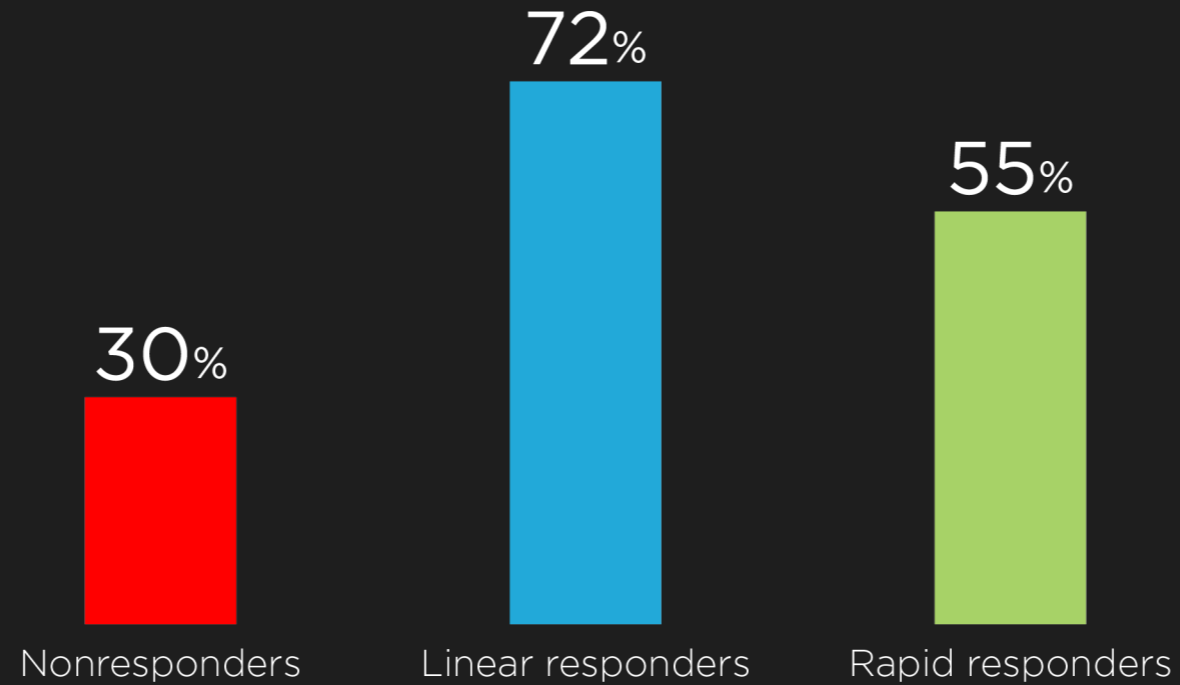
- ↳ 239 double-blinded patients:  
120 ECT vs 119 MST
- ↳ Identical 48% suicidality remission
- ↳ **Memory advantage for MST**  
severe worsening on the  
Autobiographical Memory Test  
17.3% ECT vs. 2.7% MST



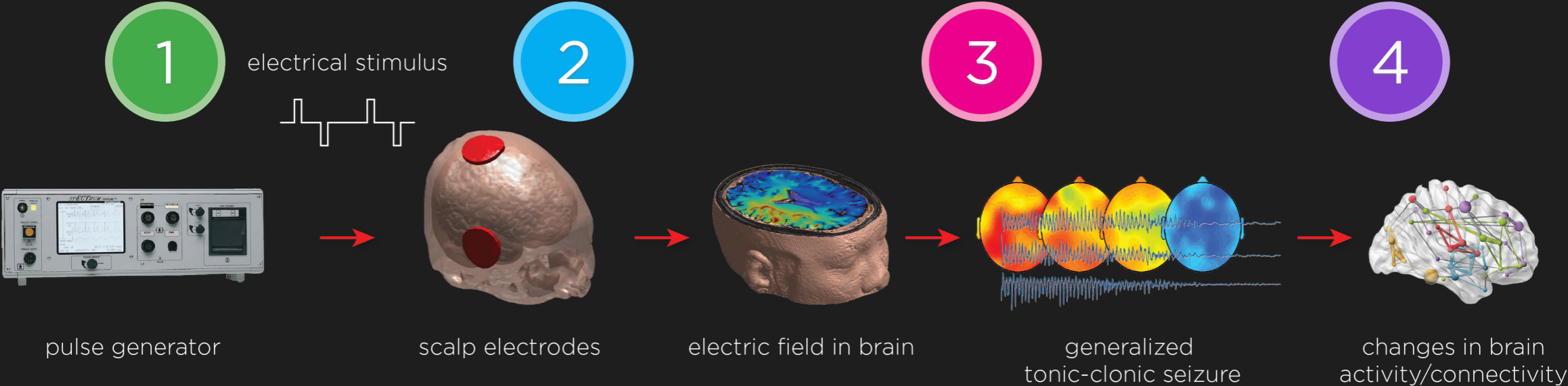




Family history of psychosis, affective disorder



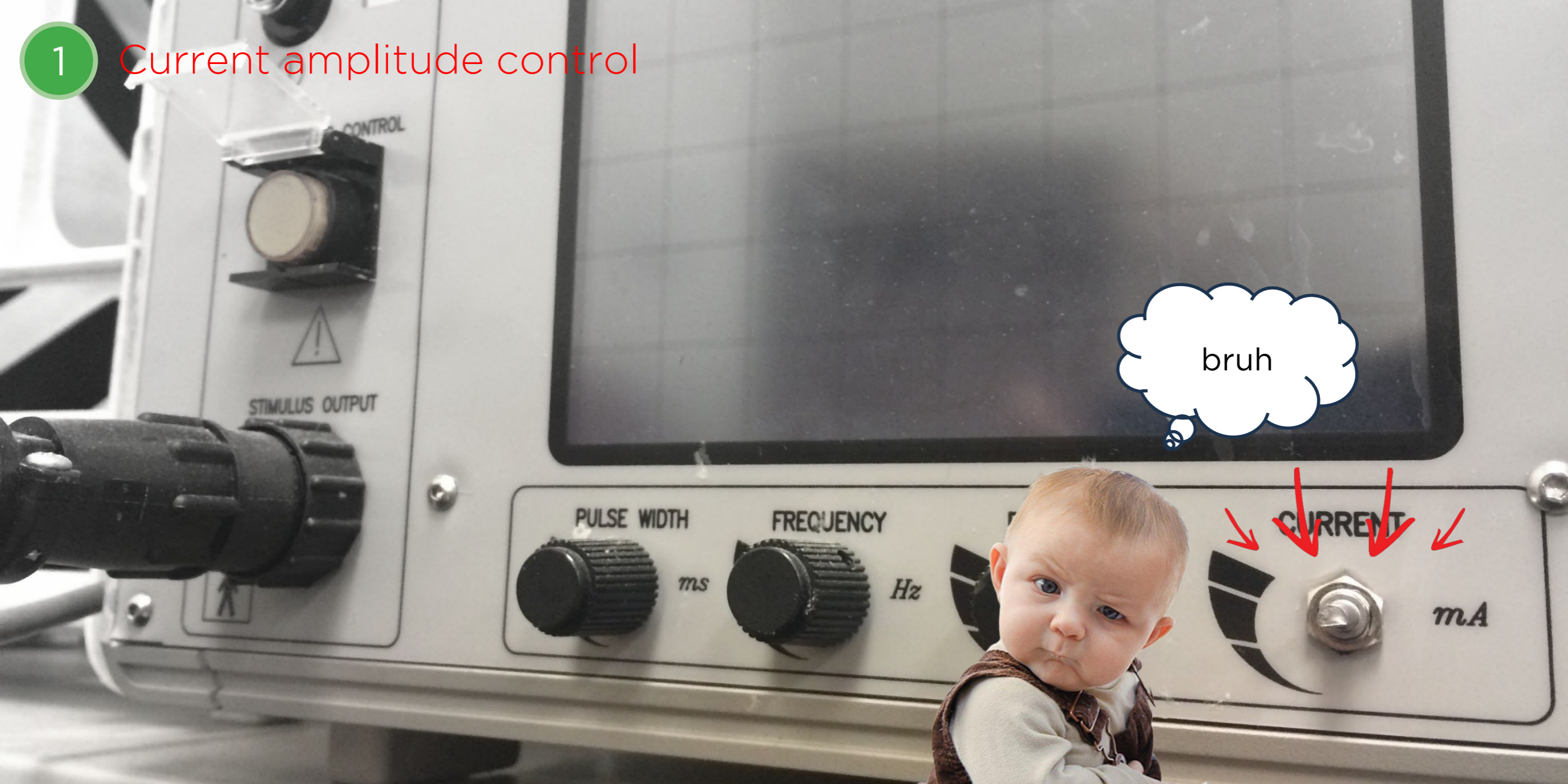
# Reengineering ECT



1

# Current amplitude control

bruh



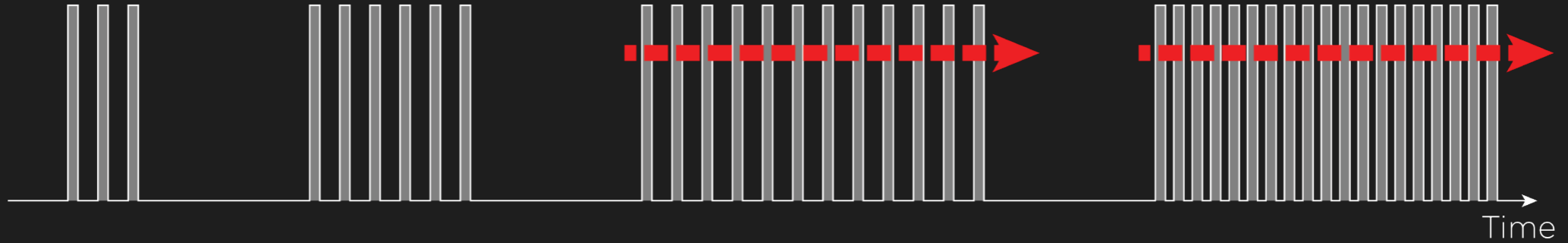
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# Conventional ECT titration

fix pulse amplitude @ 800 mA

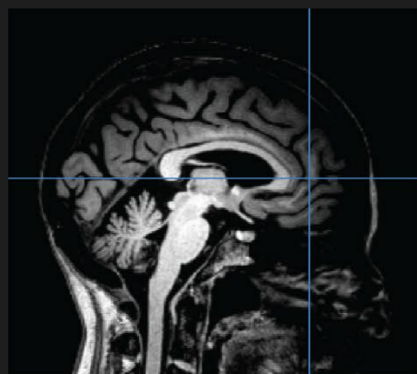
increase pulse train duration

increase pulse train frequency

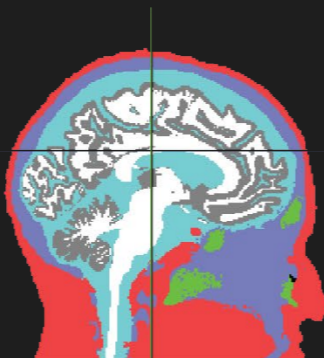


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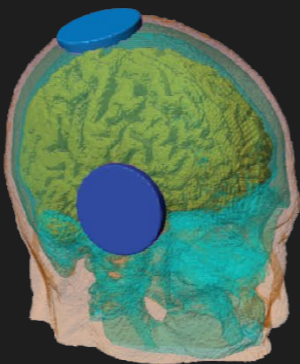
# Computational electric field modeling



individual MRI

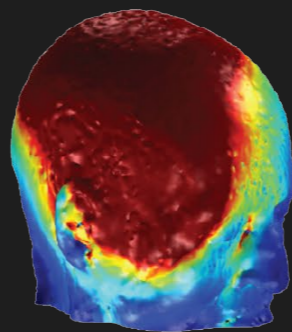


tissue segmentation

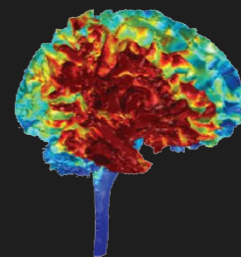


electrode geometry  
& placement

$$\nabla \cdot \sigma \nabla \phi = 0$$
$$\mathbf{E} = -\nabla \phi$$



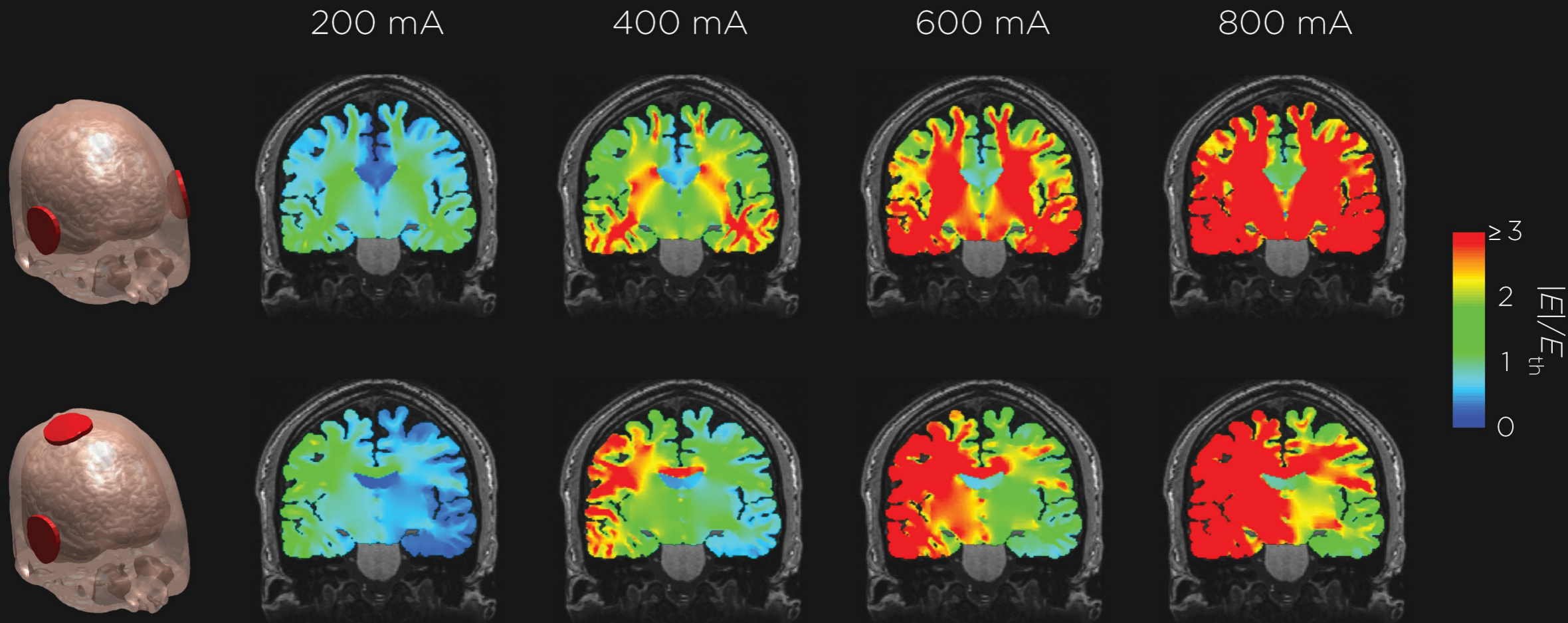
finite element solver



electric field analysis

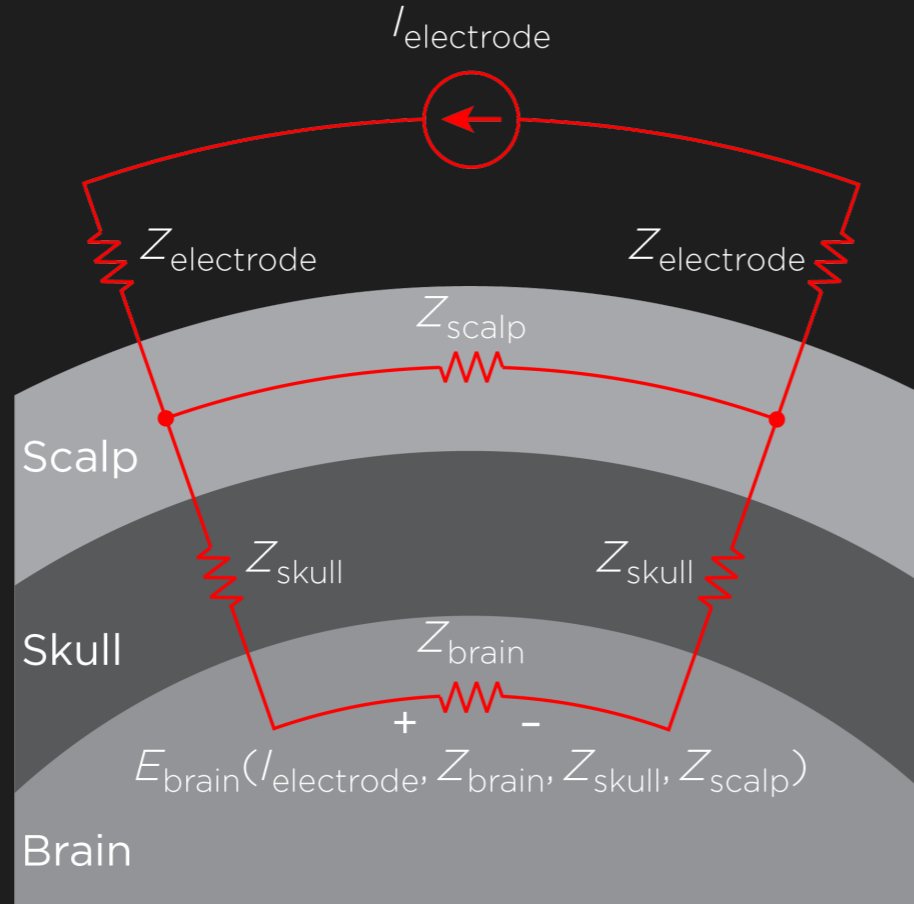
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**High** current amplitude contributes to **side effects**



1

**Fixed** current amplitude contributes to **variability**



Fixed electrode current



Variable tissue impedance



Variable intracranial  
electric field

## Physical Properties and Quantification of the ECT Stimulus: I. Basic Principles

\*†Harold A. Sackeim, Ph.D., ‡James Long, B.A., \*Bruce Luber, Ph.D.,  
\*†James R. Moeller, Ph.D., §†Isak Prohovnik, Ph.D., \*†D. P. Devanand, M.D.,  
and \*†Mitchell S. Nobler, M.D.

*\*Departments of Biological Psychiatry and §Brain Imaging, New York State Psychiatric  
Institute, New York; †Department of Psychiatry, College of Physicians and Surgeons, Columbia  
University, New York; and the ‡James Long Company, Bedford Hills, New York, U.S.A.*

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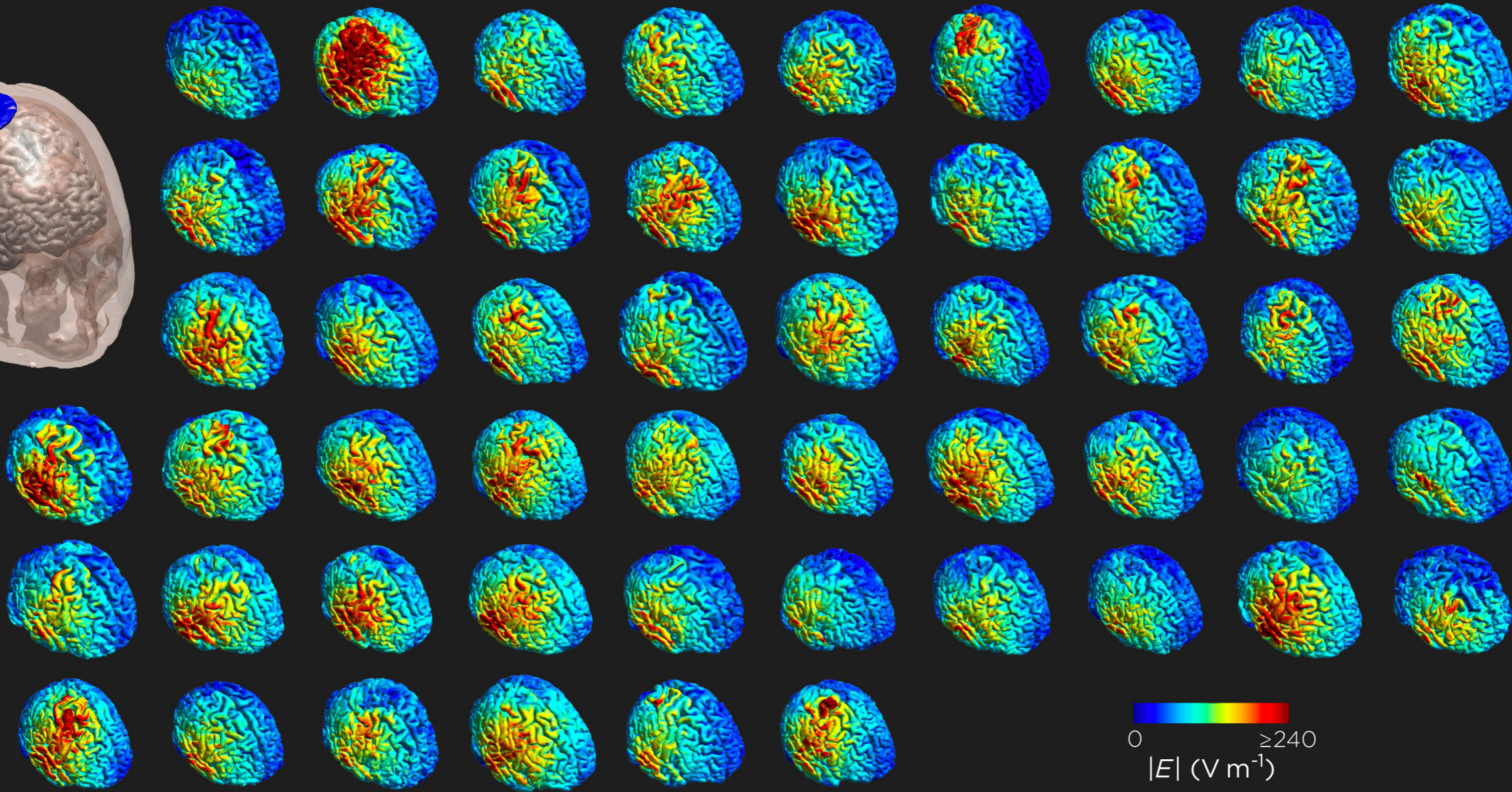
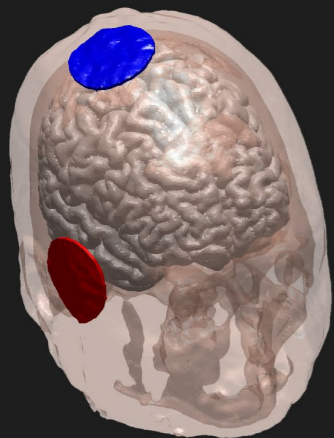
**Summary:** The physical properties of the electroconvulsive therapy (ECT) stimulus markedly affect both efficacy and side effects. We review basic principles in characterizing these physical properties and in quantifying the ECT stimulus. The topics discussed include the application of Ohm's law, alternative composite units of ECT dosage (energy and charge), the use of constant-current, constant-voltage, and constant-energy principles in ECT devices, the nature of current shunting in ECT and the determinants of impedance, the relations between impedance and seizure threshold, the seizure-eliciting efficiency of alternative stimulus waveforms and of stimulus parameter configurations, and the role of reactive components (capacitance and inductance) in the ECT circuit. New findings are also presented regarding several of these issues.

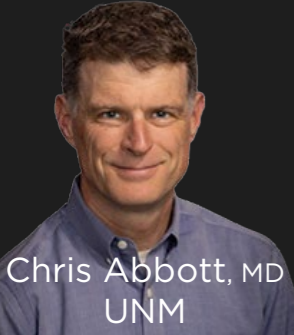
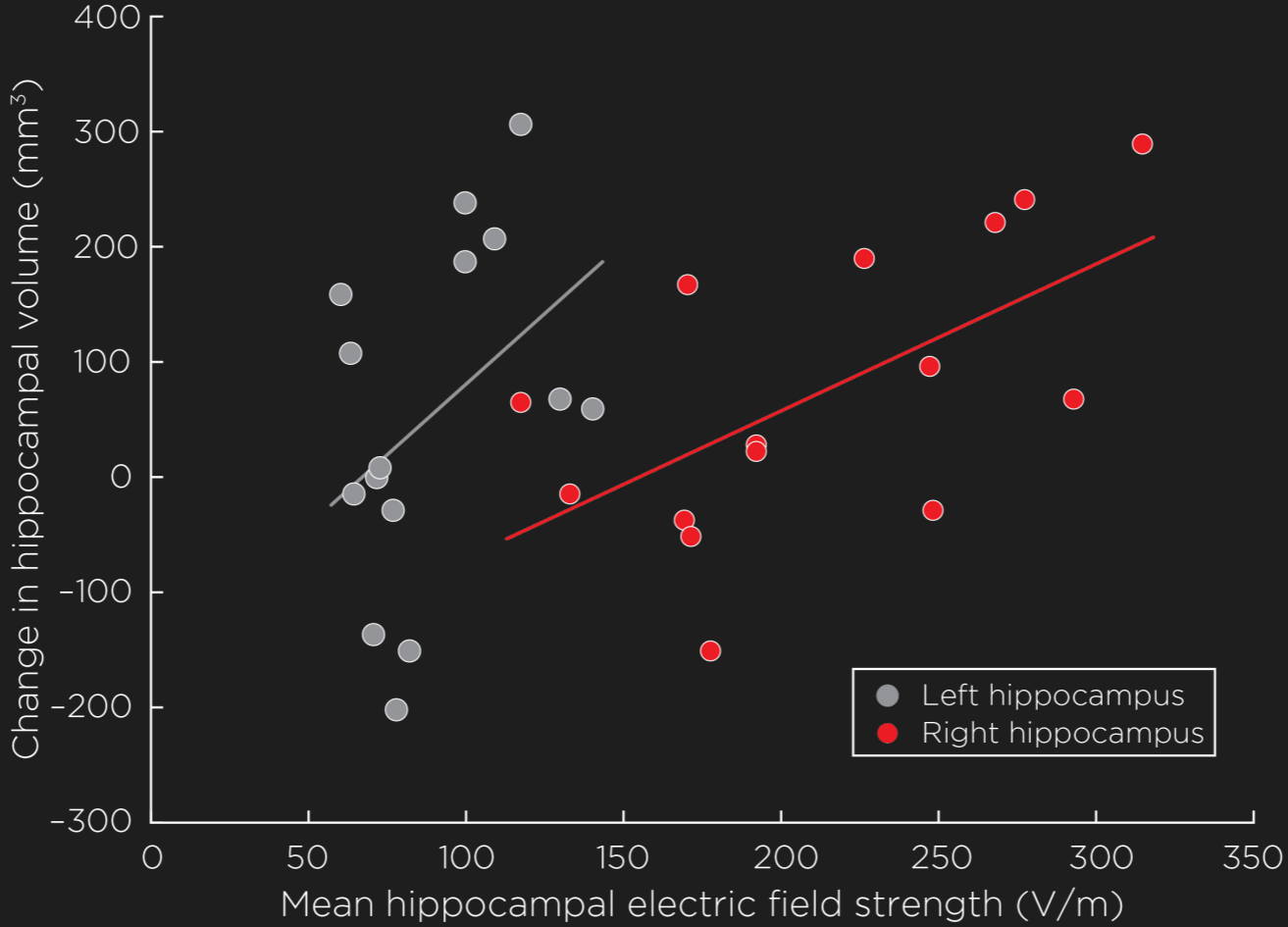
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“

For constant-current stimulation, we suggest that, in general clinical practice, the range of the threshold for seizure elicitation may be as wide as **40-fold**.

1



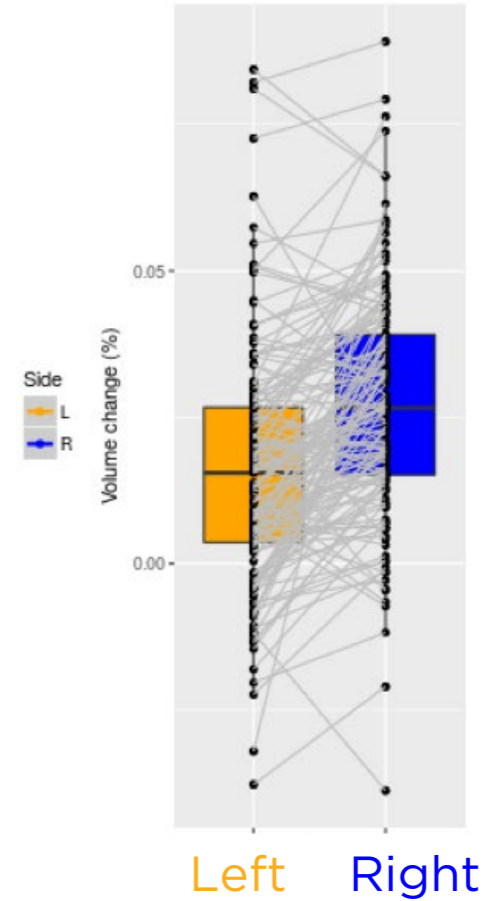
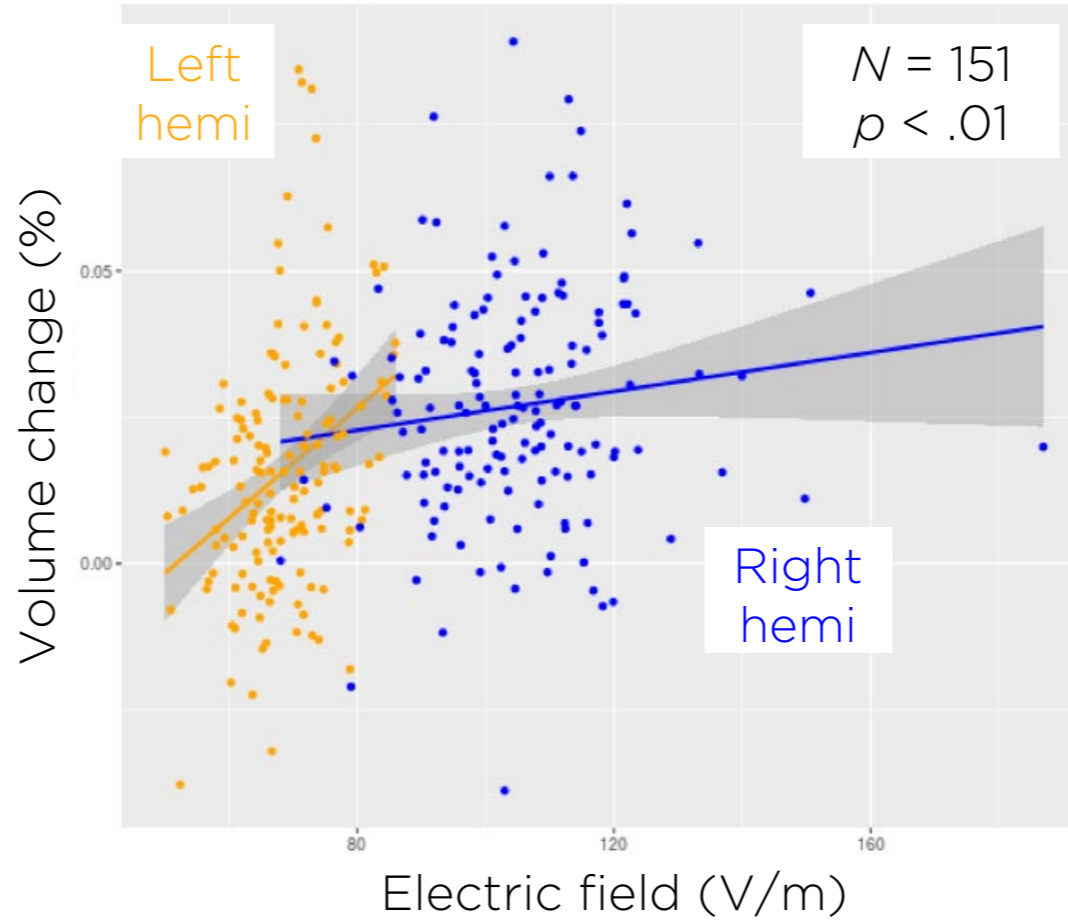


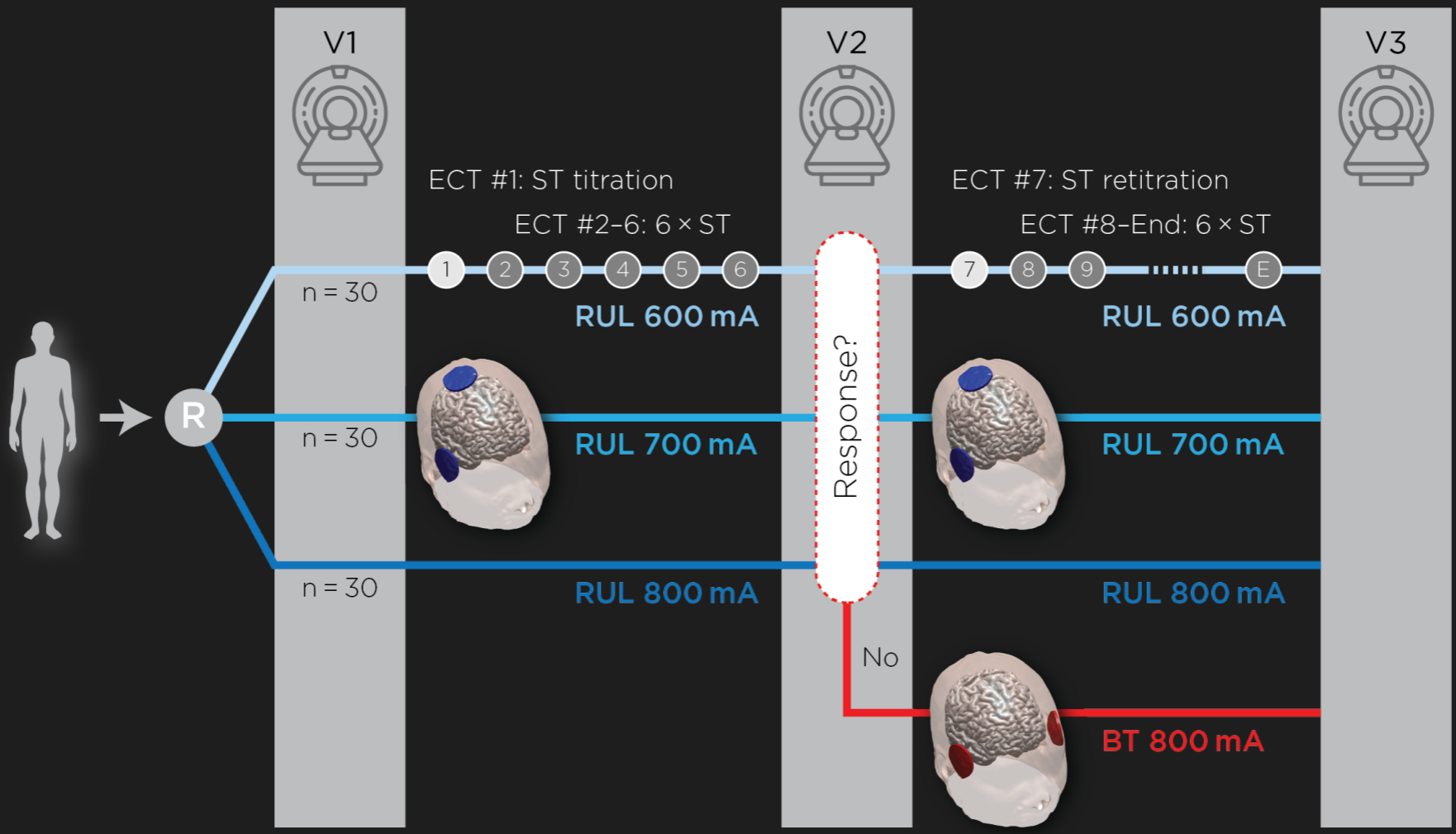
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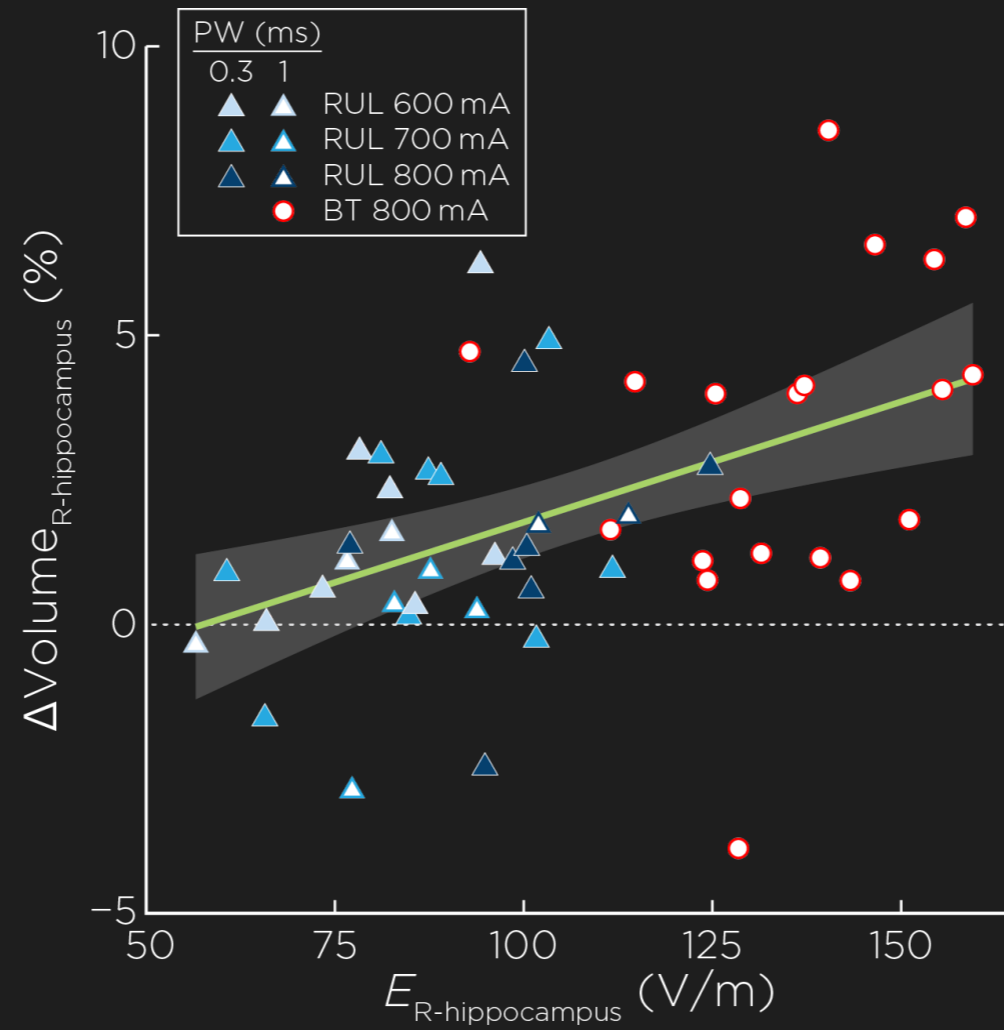
# Global ECT-MRI Research Collaboration (GEMRIC)

Leif Oltedal, MD/PhD  
Univ of Bergen

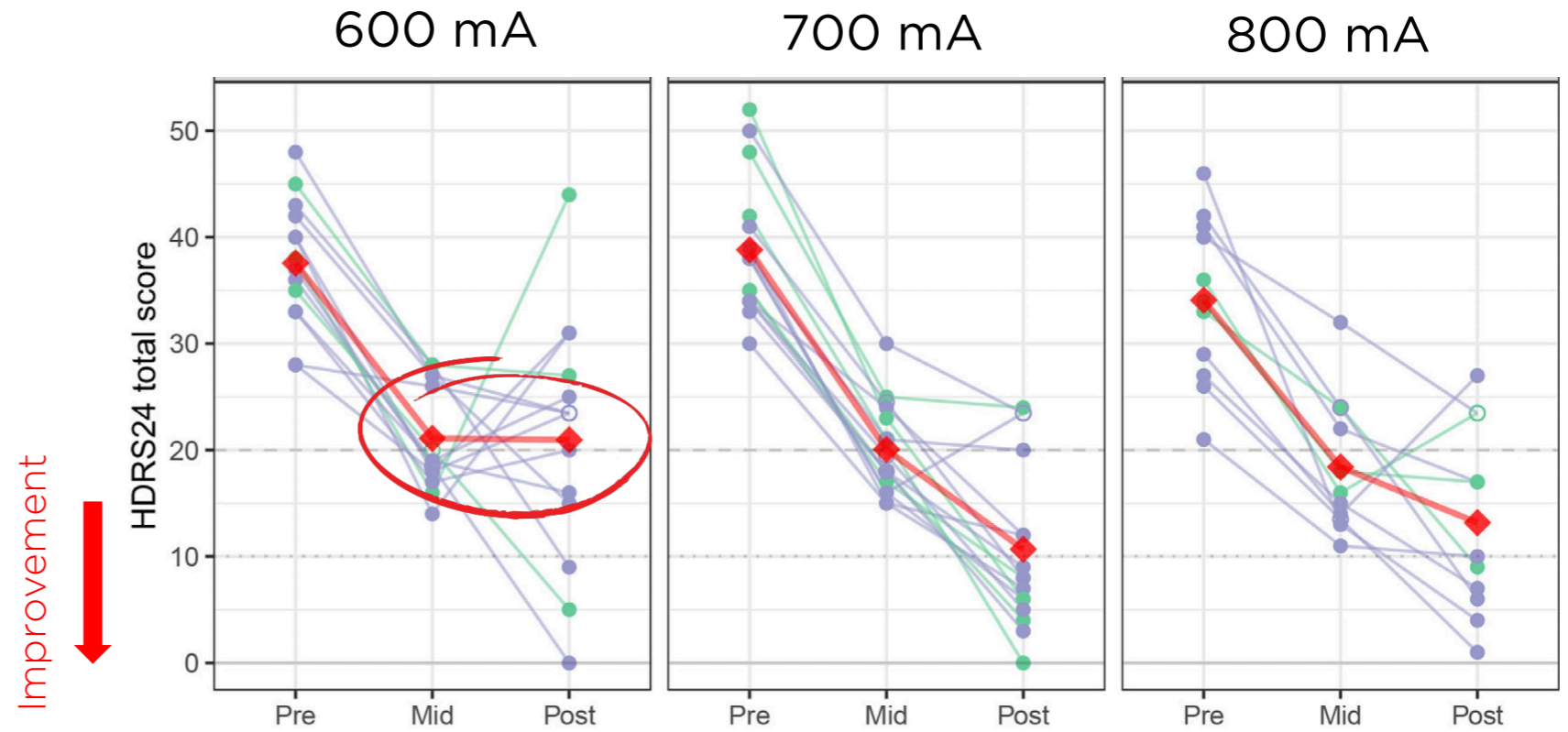
Miklos Argyelan, MD  
Hillside Hospital





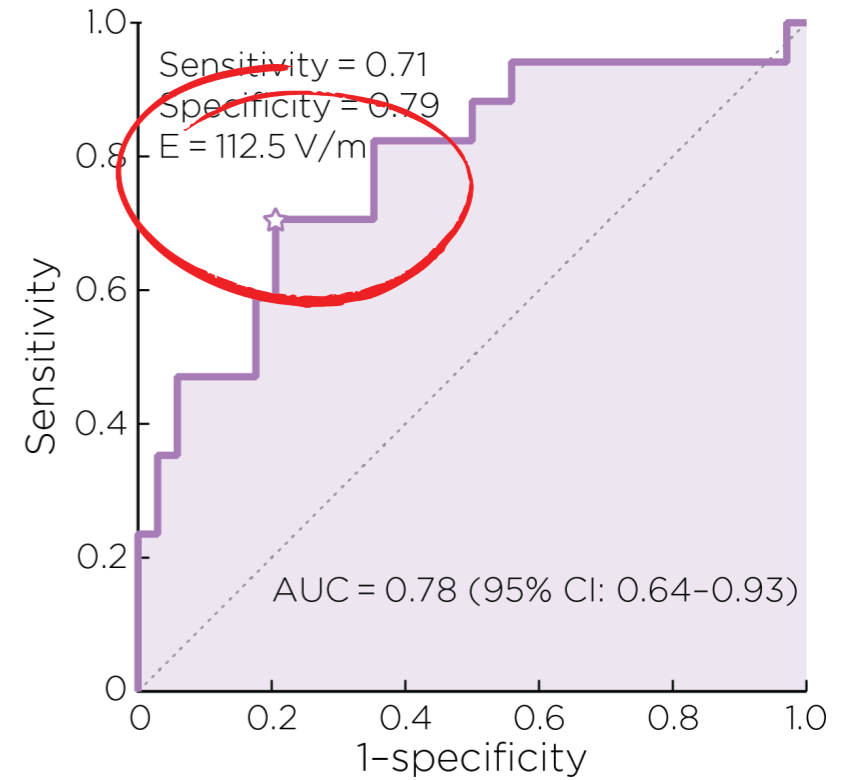
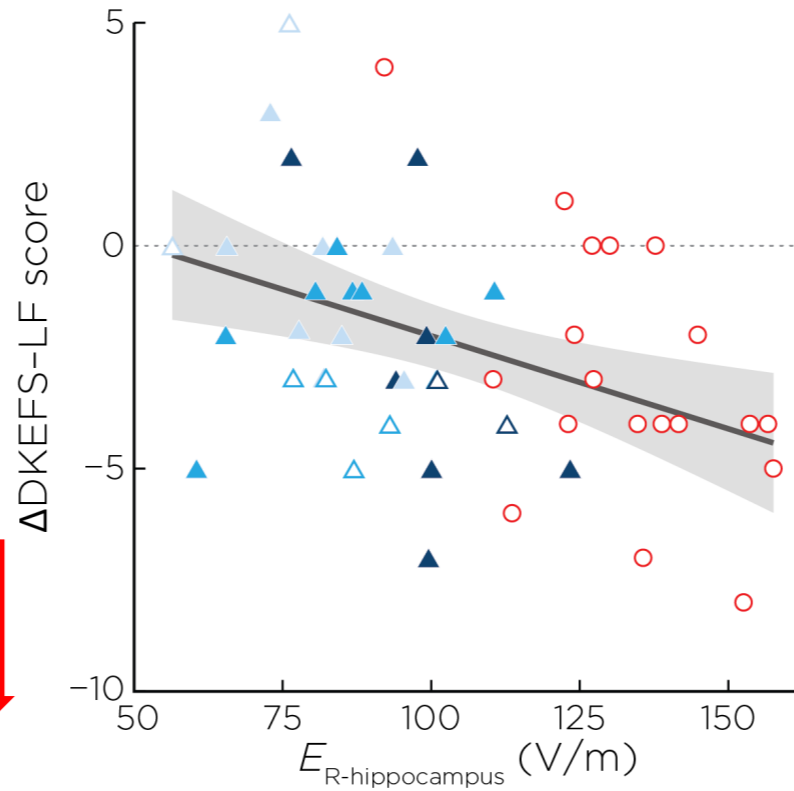


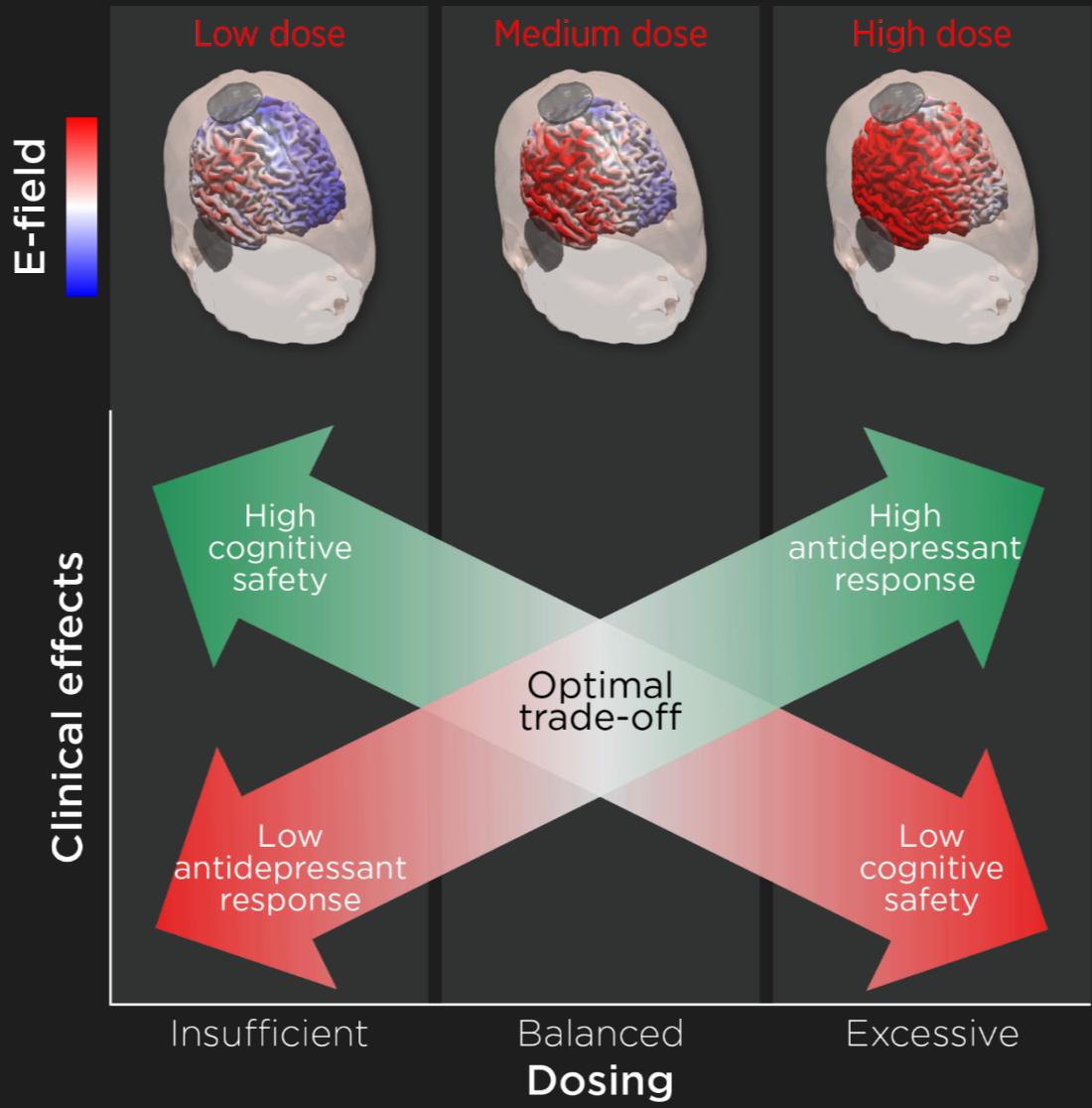
Lower amplitude  
comprises efficacy



Higher amplitude associated with cognitive impairment

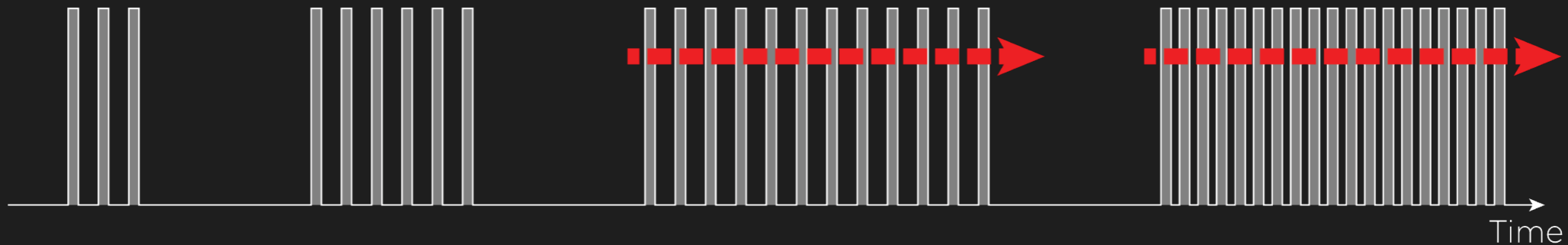
Cognitive impairment



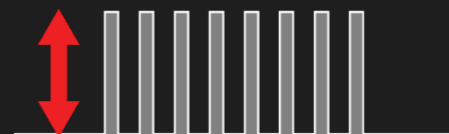
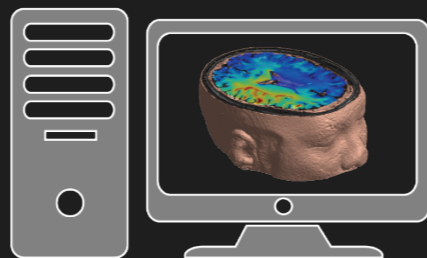
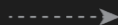


### Conventional ECT titration

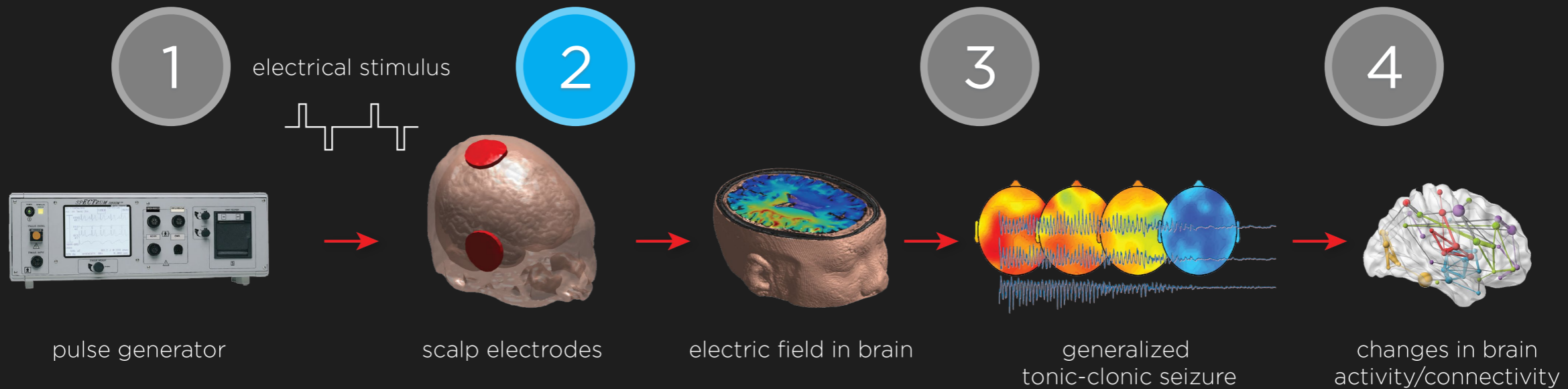
fix pulse amplitude @ 800 mA



### E-field informed ECT

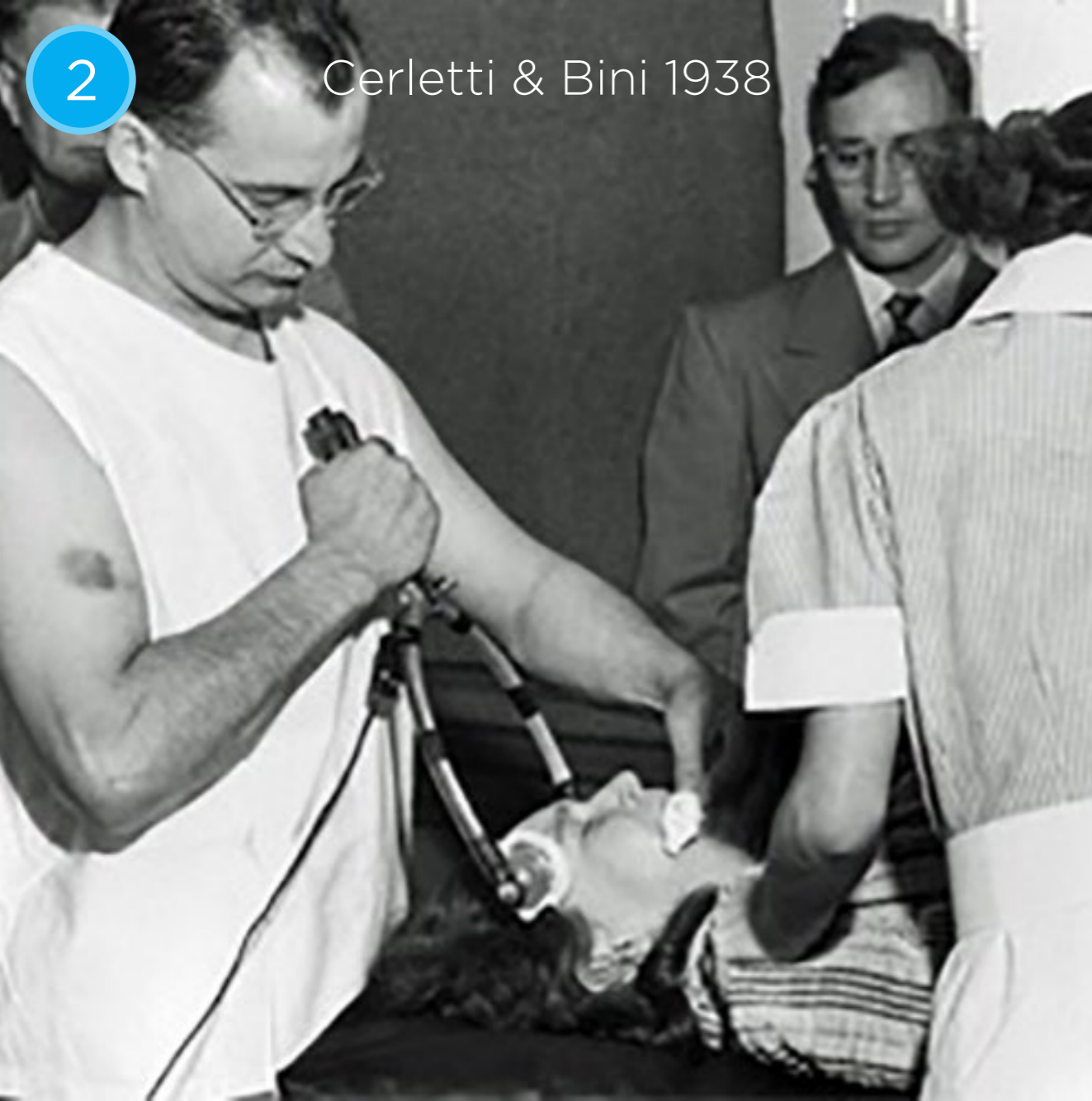


individualized current amplitude below the cognitive safety threshold



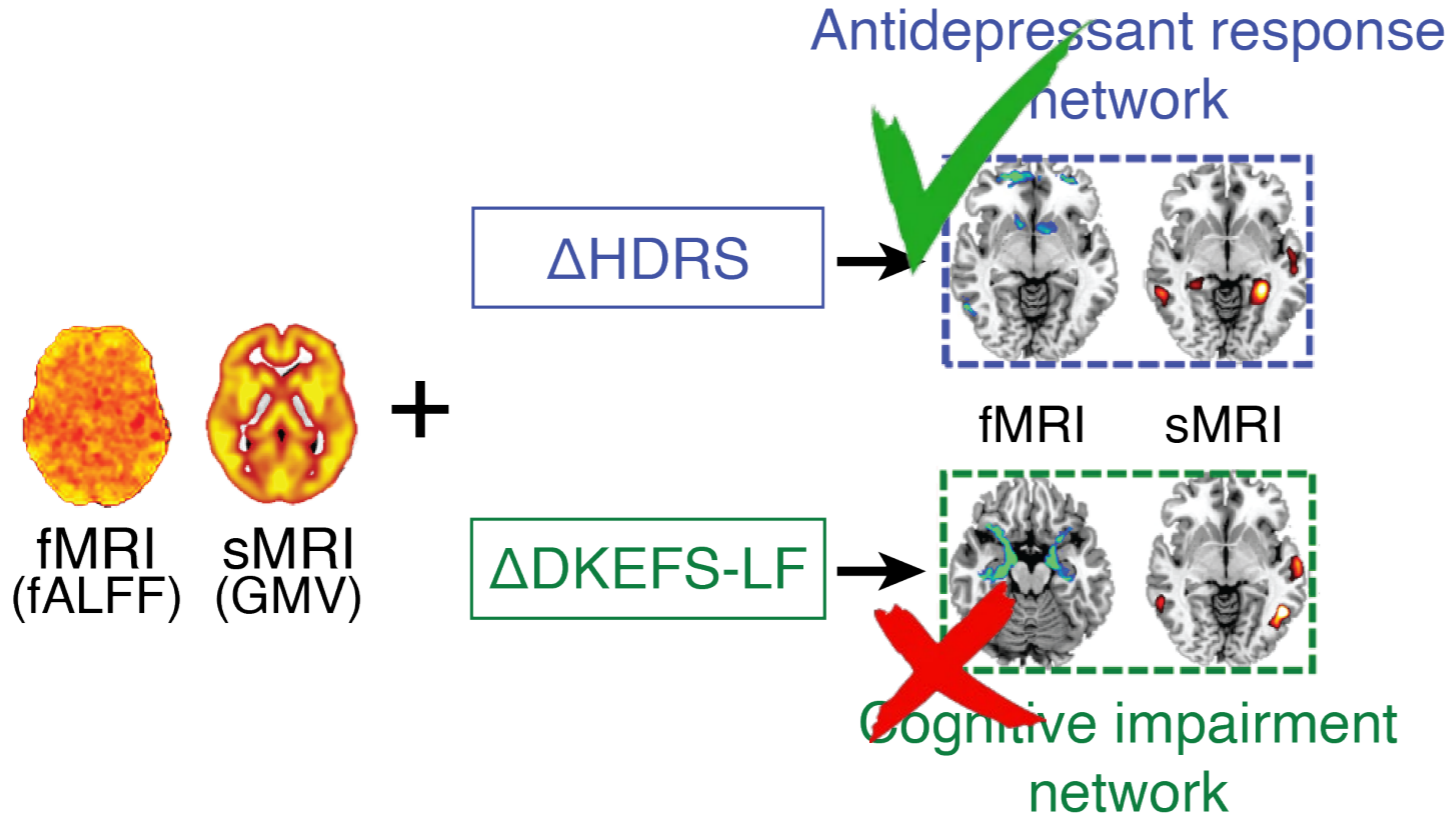
2

Cerletti & Bini 1938



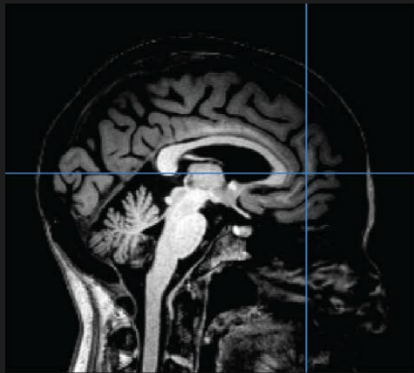
Modern day bilateral ECT



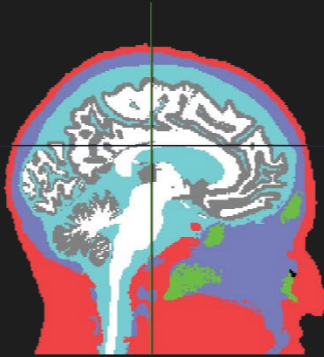


2

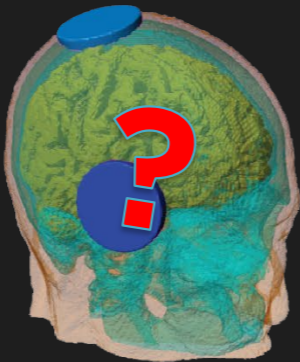
Run this backwards...



individual MRI

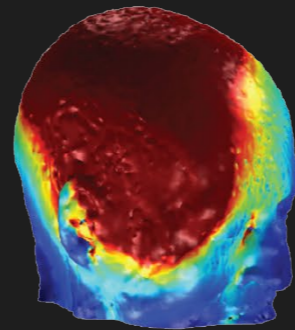


tissue segmentation

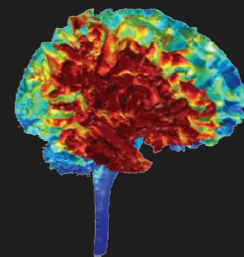


electrode geometry  
& placement

$$\nabla \cdot \sigma \nabla \phi = 0$$
$$\mathbf{E} = -\nabla \phi$$

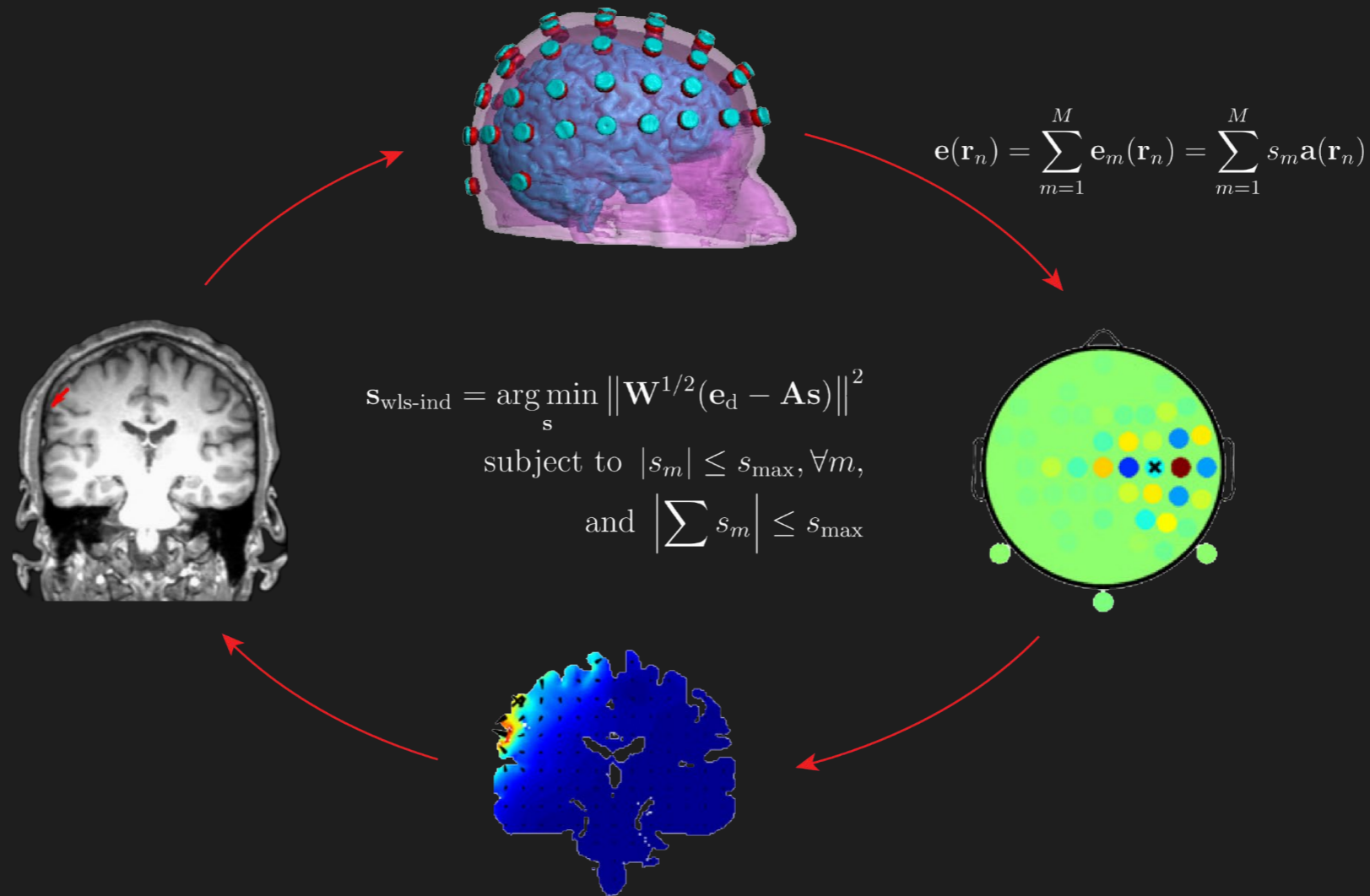


finite element solver



electric field analysis

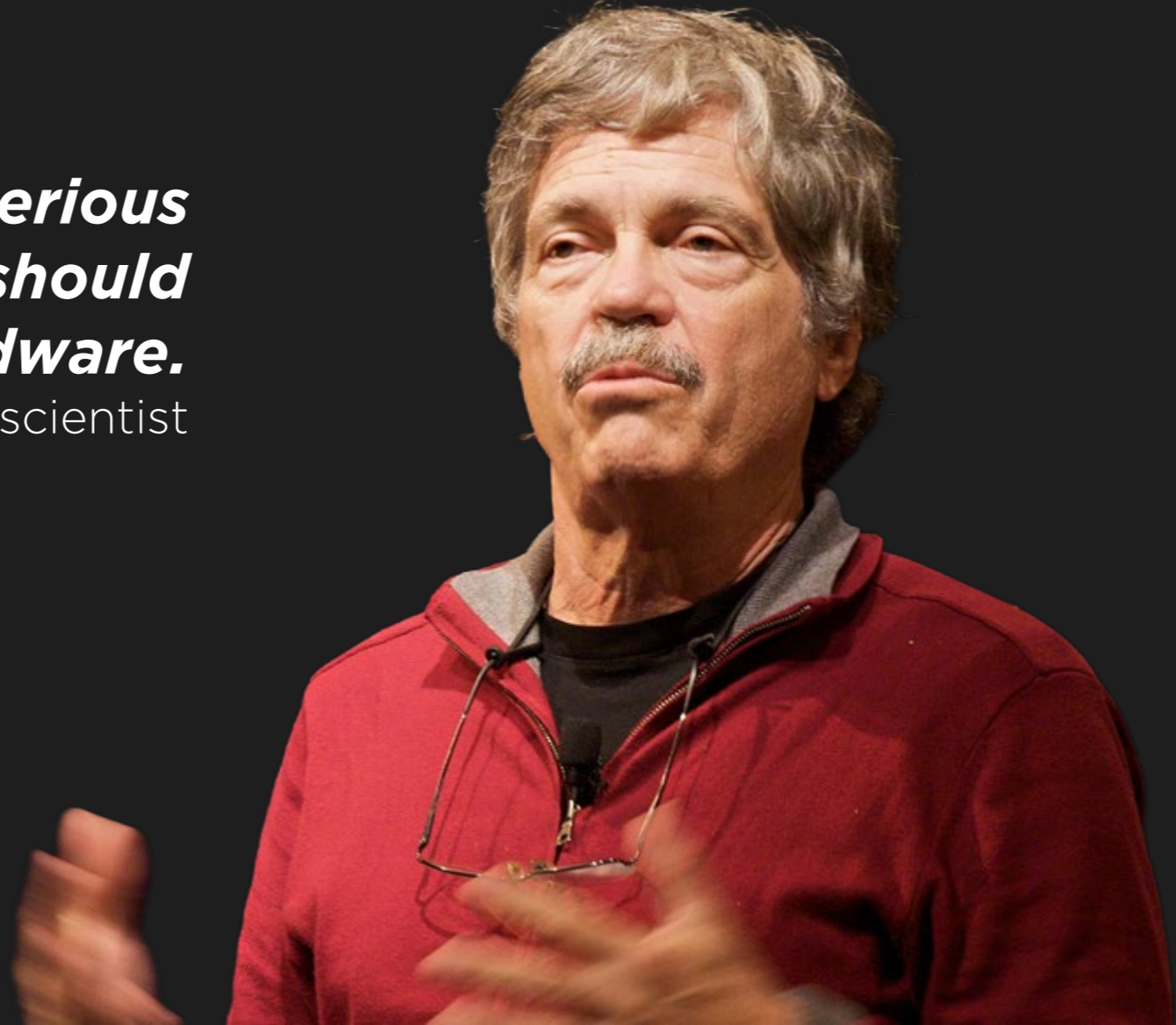
## 2 Multielectrode optimization



“

***People who are really serious  
about software should  
make their own hardware.***

~ Alan Kay, American computer scientist

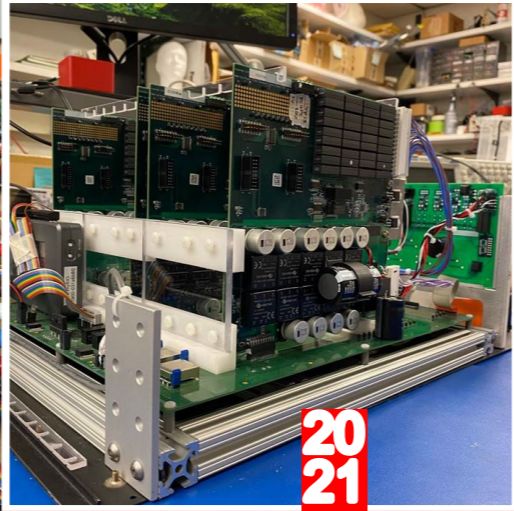


PROTOTYPING



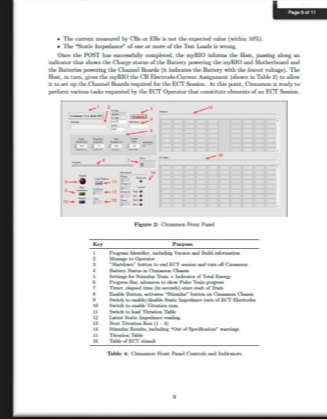
20  
20

ASSEMBLY



20  
21

USER INTERFACE  
PROGRAMMING/  
DOCUMENTATION



INVENTION  
DISCLOSURE,  
IP FILING

20  
23

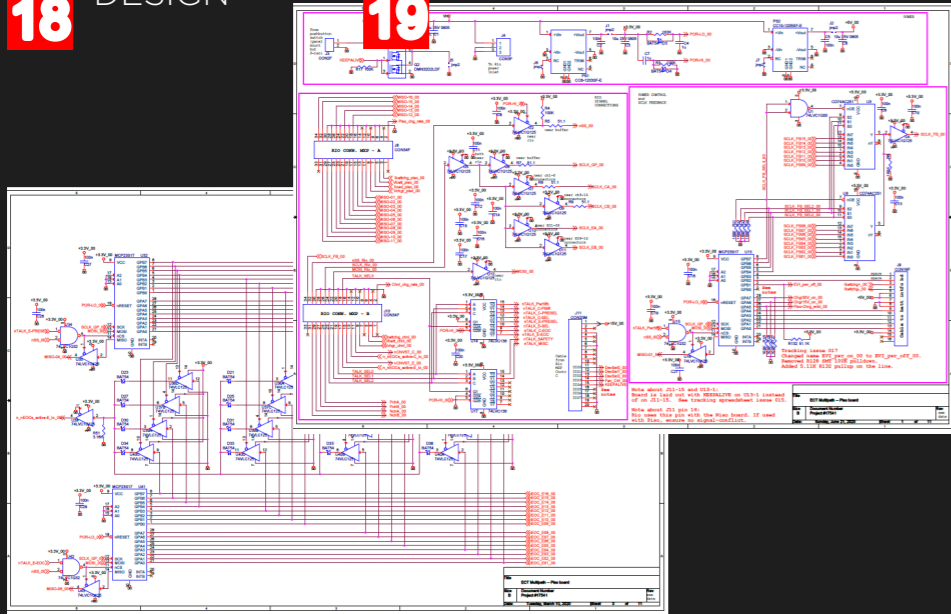
PRECLINICAL  
TESTING

20  
24

20  
18

DESIGN

20  
19

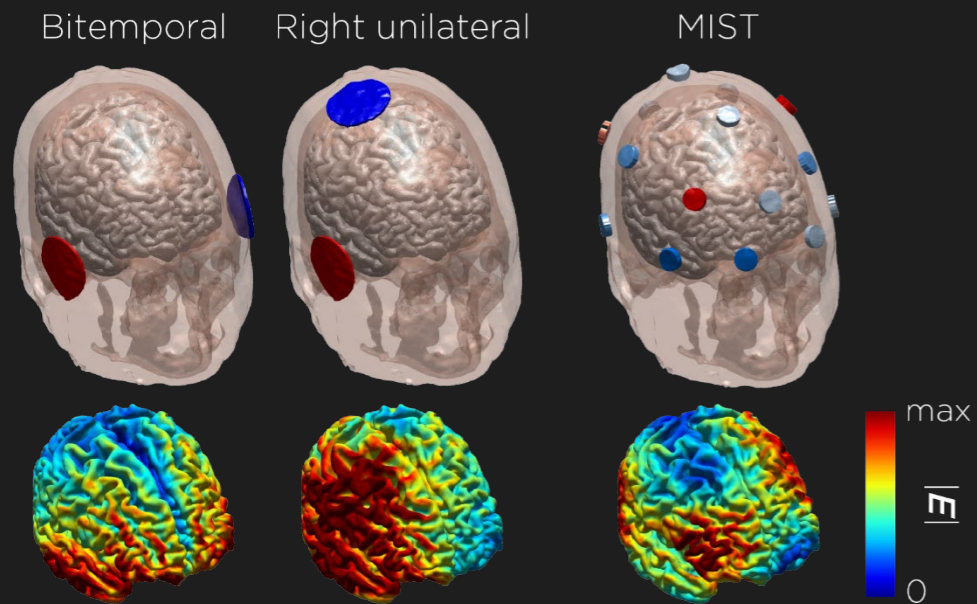


20  
22

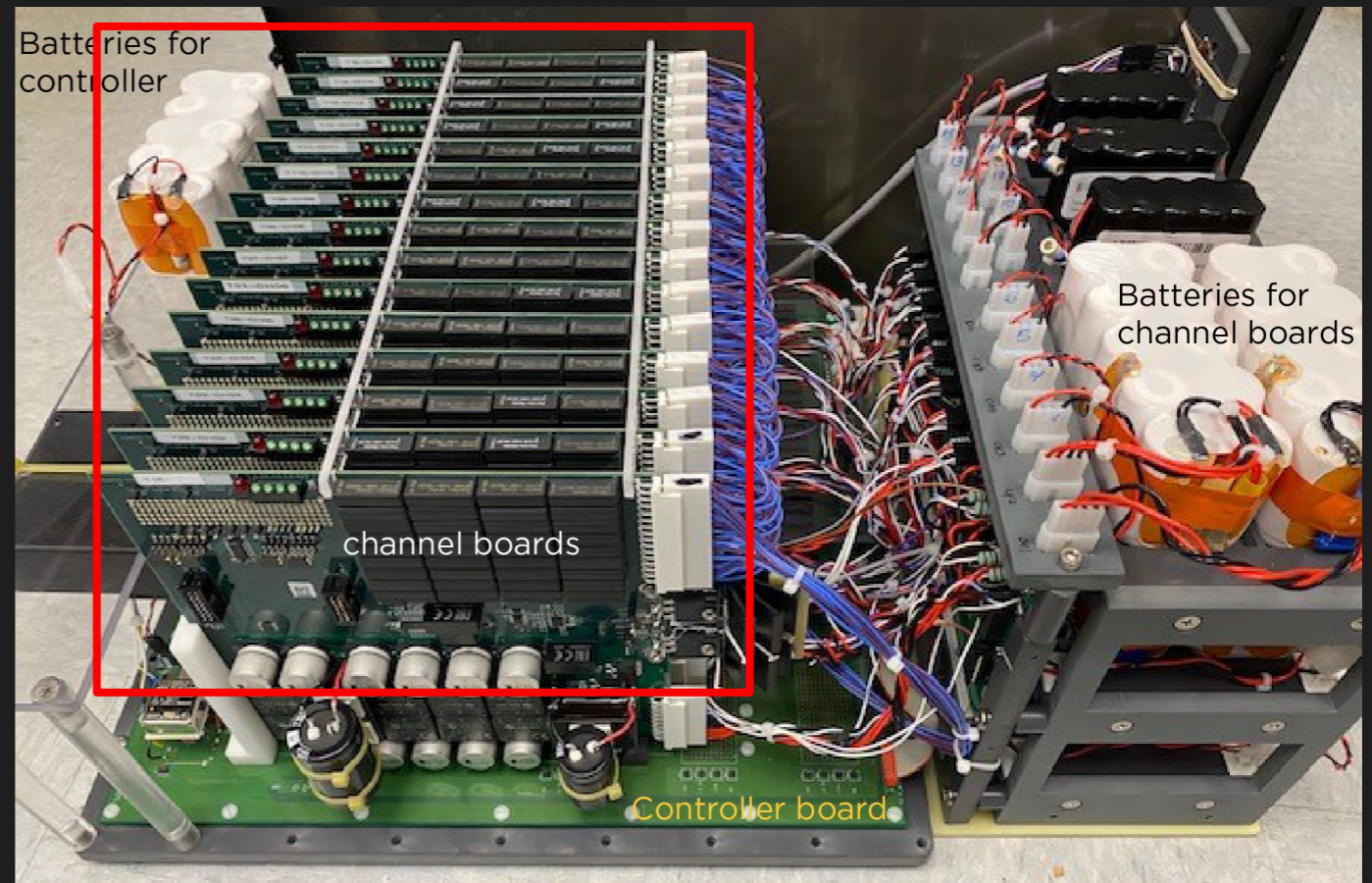
BOXING/  
TESTING



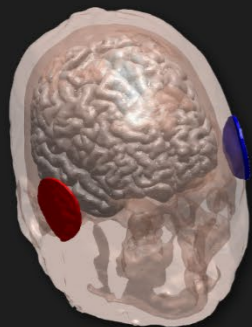
# Multichannel Individualized Stimulation Therapy (MIST)



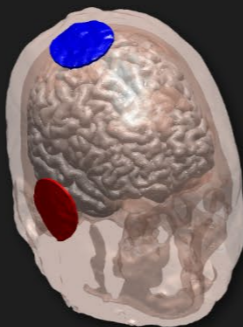
15 independently programmable  
current sources



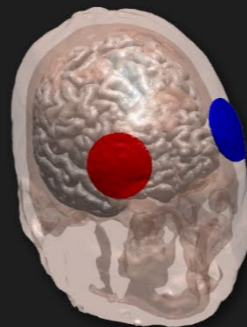
Bilateral



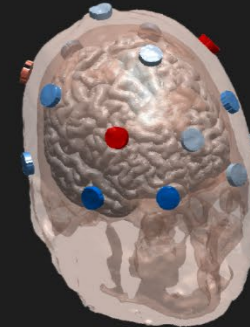
Right unilateral



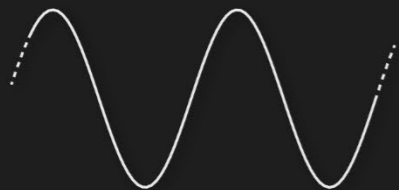
Bifrontal



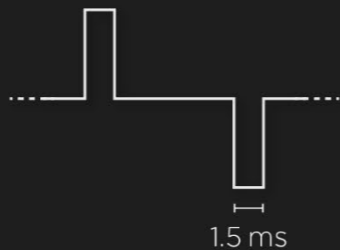
MIST



Sine wave



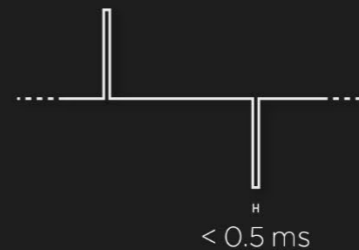
Standard pulse



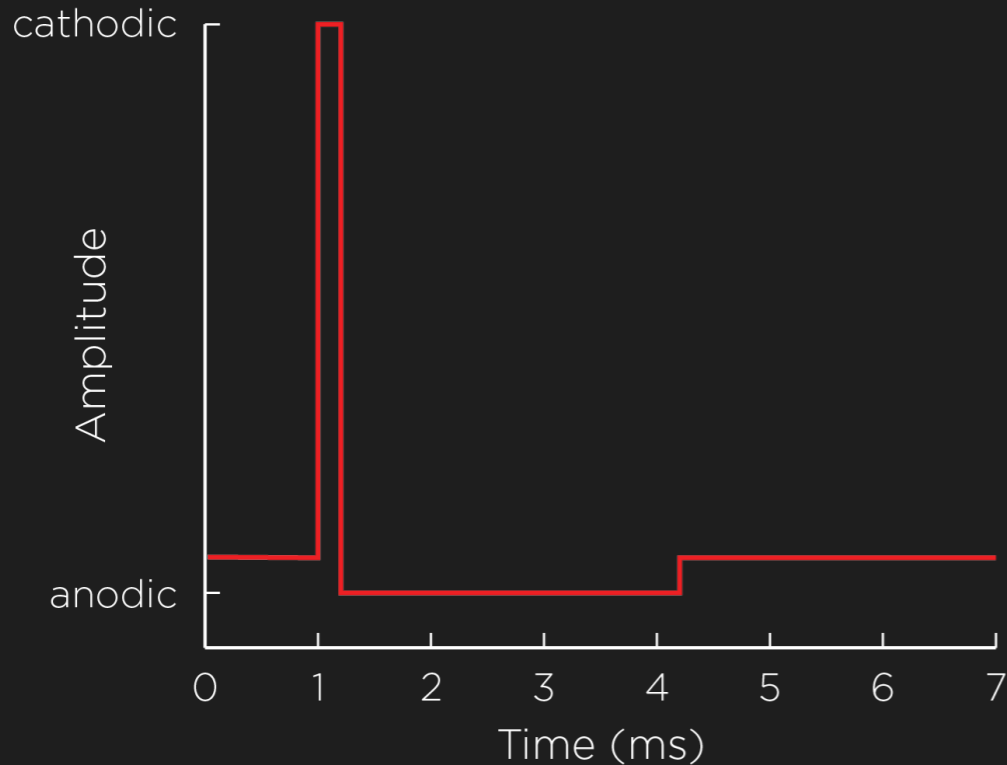
Brief pulse



Ultrabrief pulse



# More efficient and neural element-selective waveforms



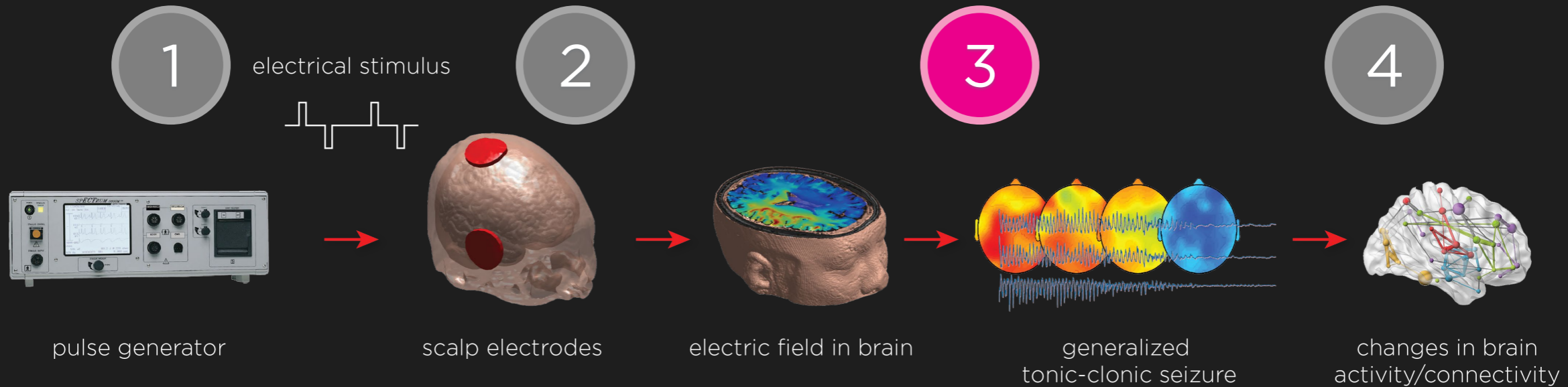
Modification of the pulse shapes resulted in an **improvement of up to 50%** for both the activation of resting neurons and the entrainment of bursting neurons.

(Hoffman et al., 2011)

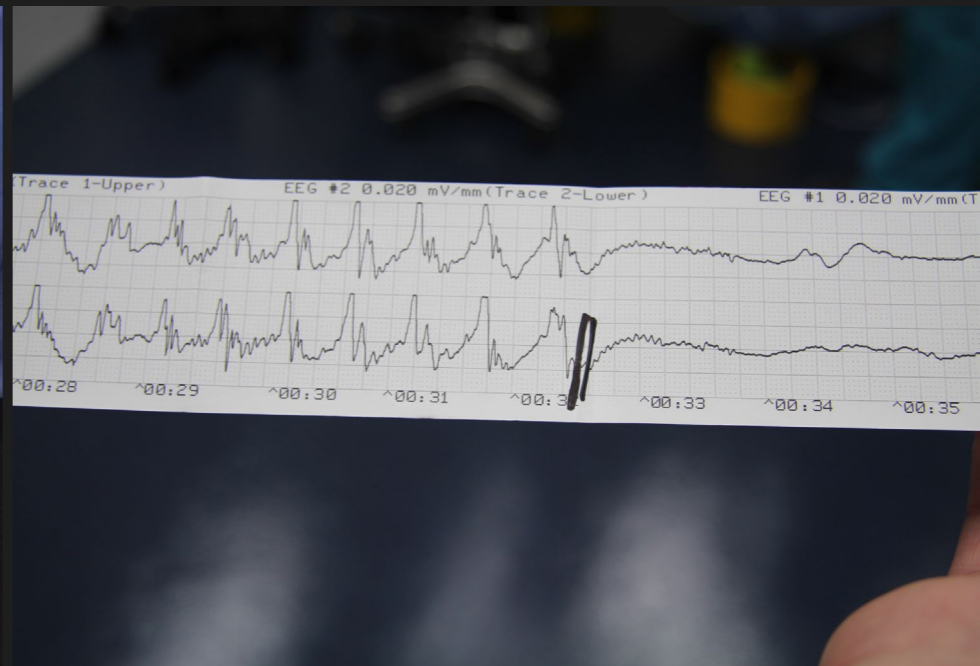


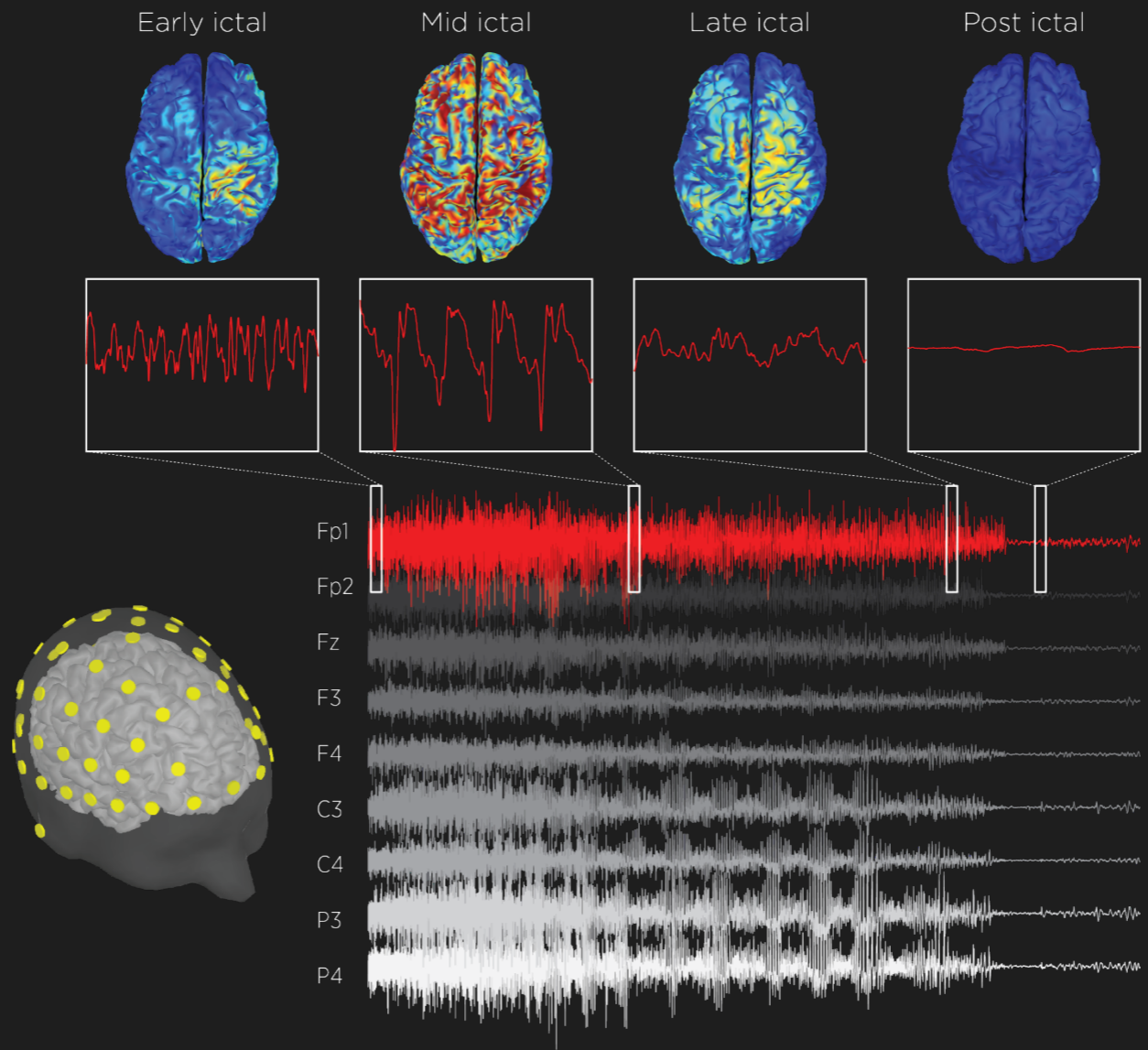
- Deng, Kim, Dold, Pritchard, Schor, Lisanby, “Systems and methods for **adjustable current** individualized stimulation therapy,” International Patent Application, PCT/US2025/27755, filed May 5, 2025.
- Deng, Pritchard, Kim, Dold, Schor, Lisanby, “Systems and methods for **multichannel** individualized stimulation therapy,” International Patent Application, WO 2024/215761 A1, filed Apr. 10, 2024. Entered national stage in both US and Europe in Oct. 2025.

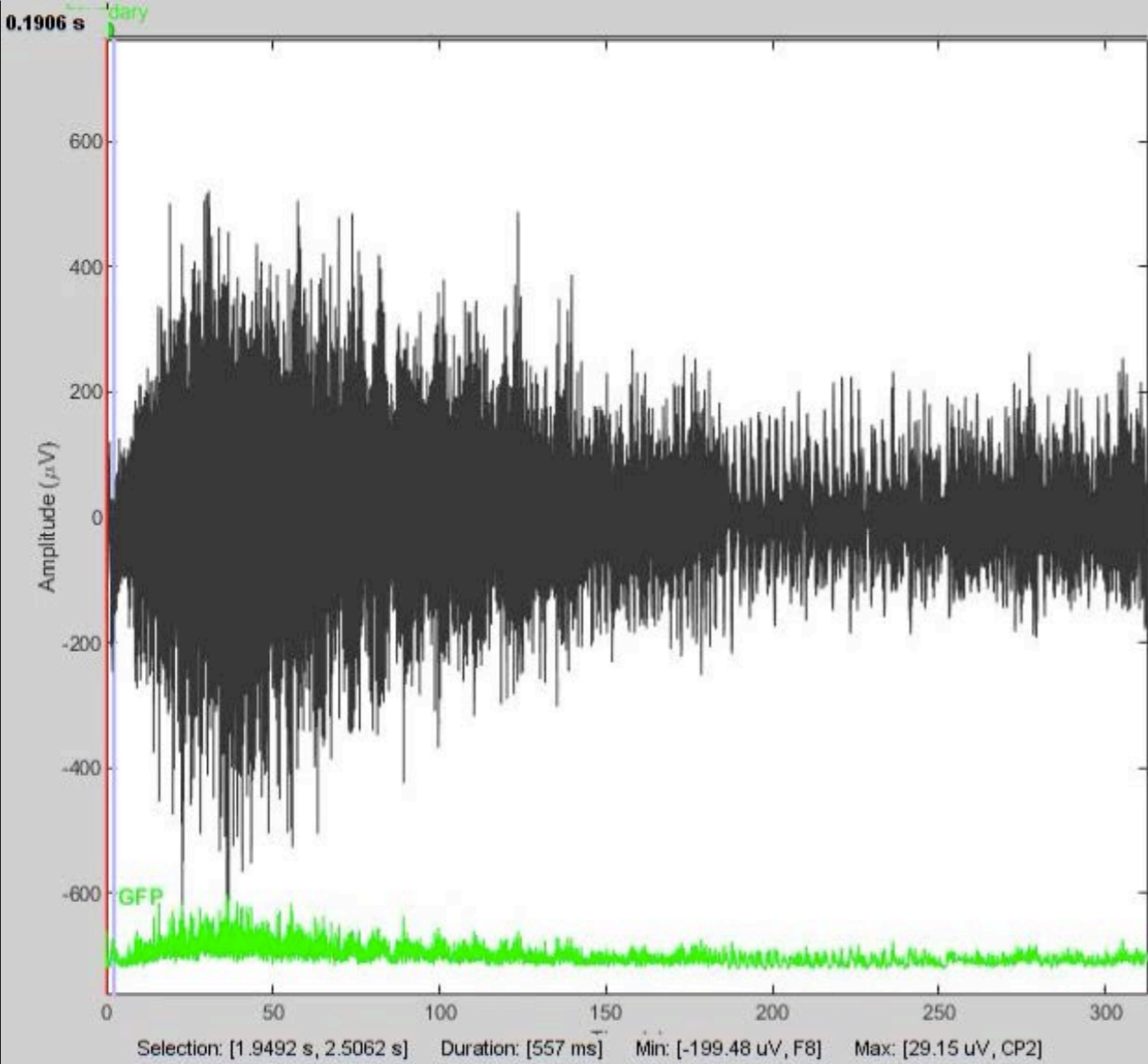




### 3 Clinical standard in seizure monitoring

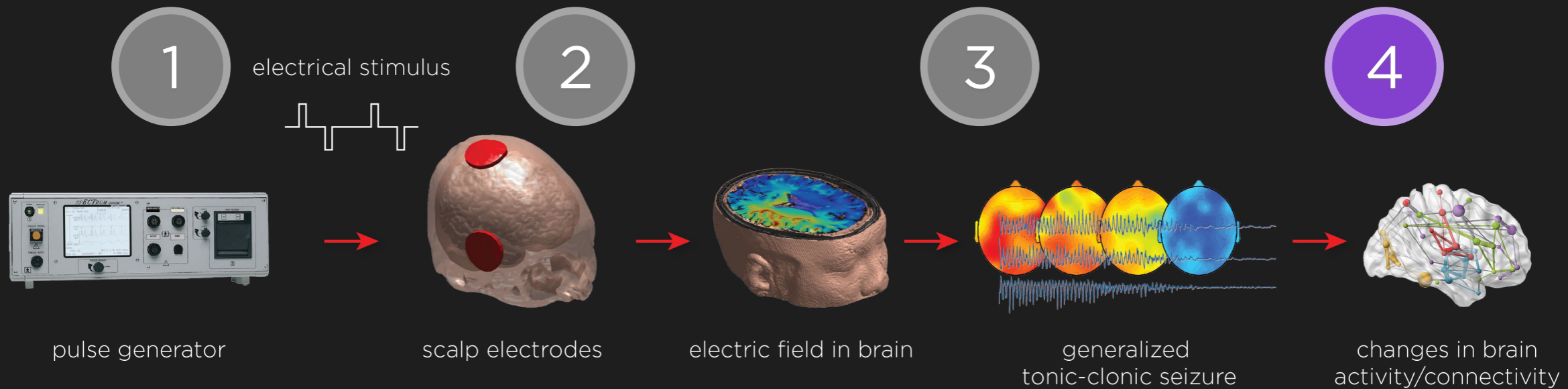






191ms



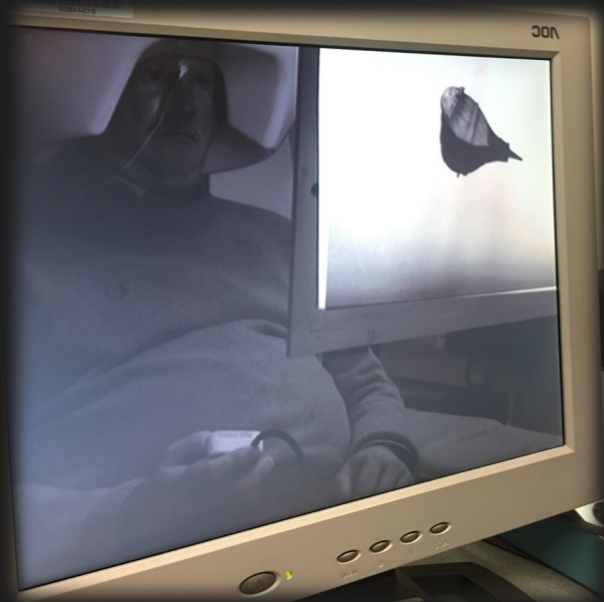


4

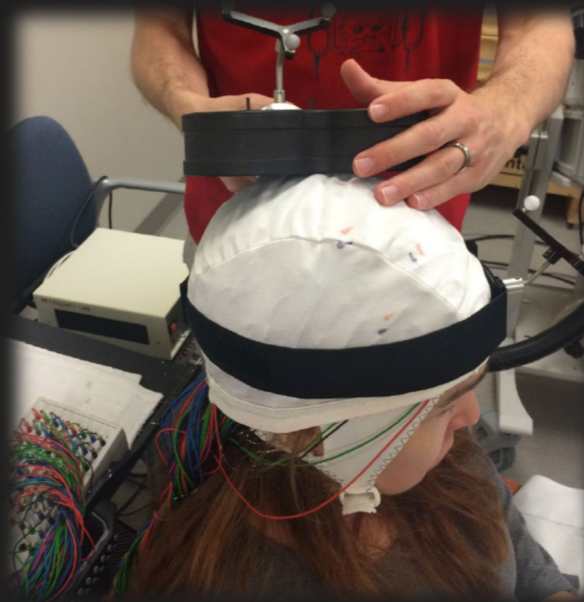
fNIRS imaging to measure postictal cortical spreading depression (collab w/Z. Rosenthal UPenn)



MEG to measure memory, decision making, and hippocampal function



TMS-EEG to measure cortical excitability changes

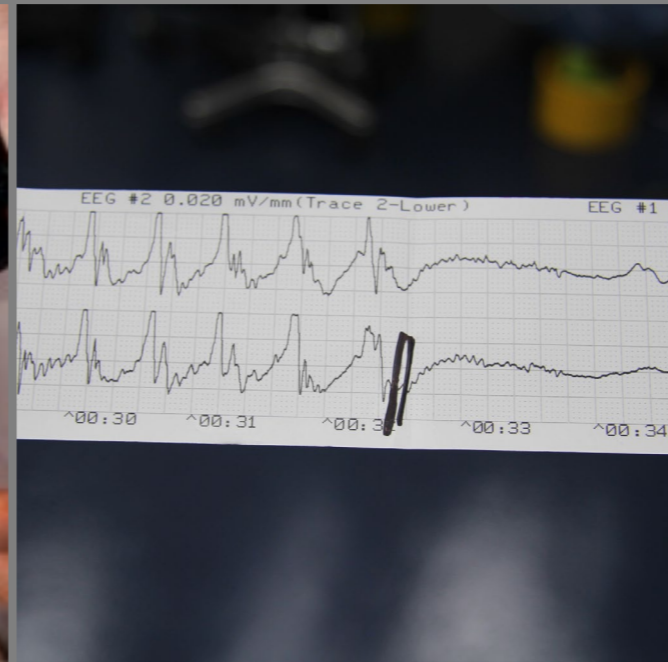
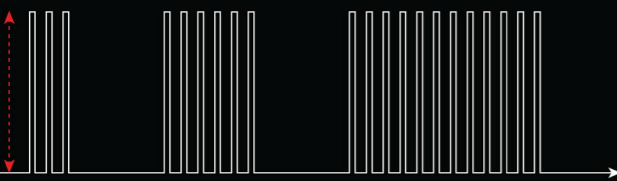
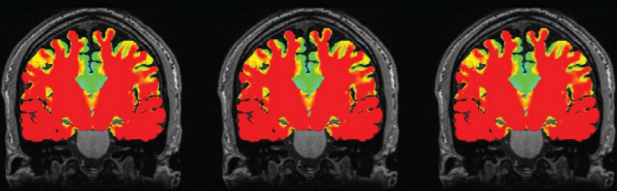


Facial expression analysis to study emotion



# Conventional ECT

800 mA      800 mA      800 mA



# Next gen ECT

200 mA      400 mA      600 mA

