

Electric Field Induced by Electroconvulsive Therapy

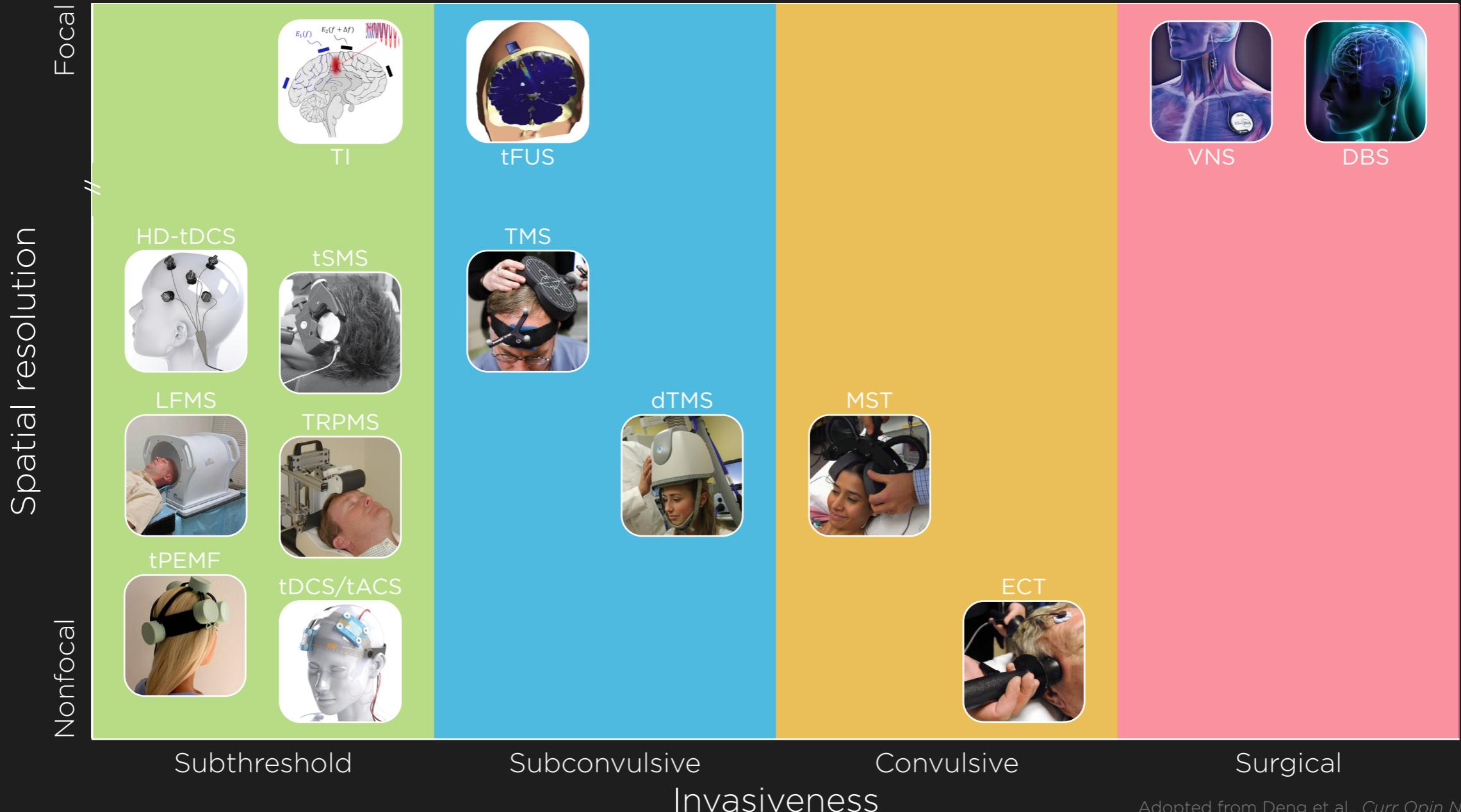
Rethinking ECT Dosing

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

Disclosure

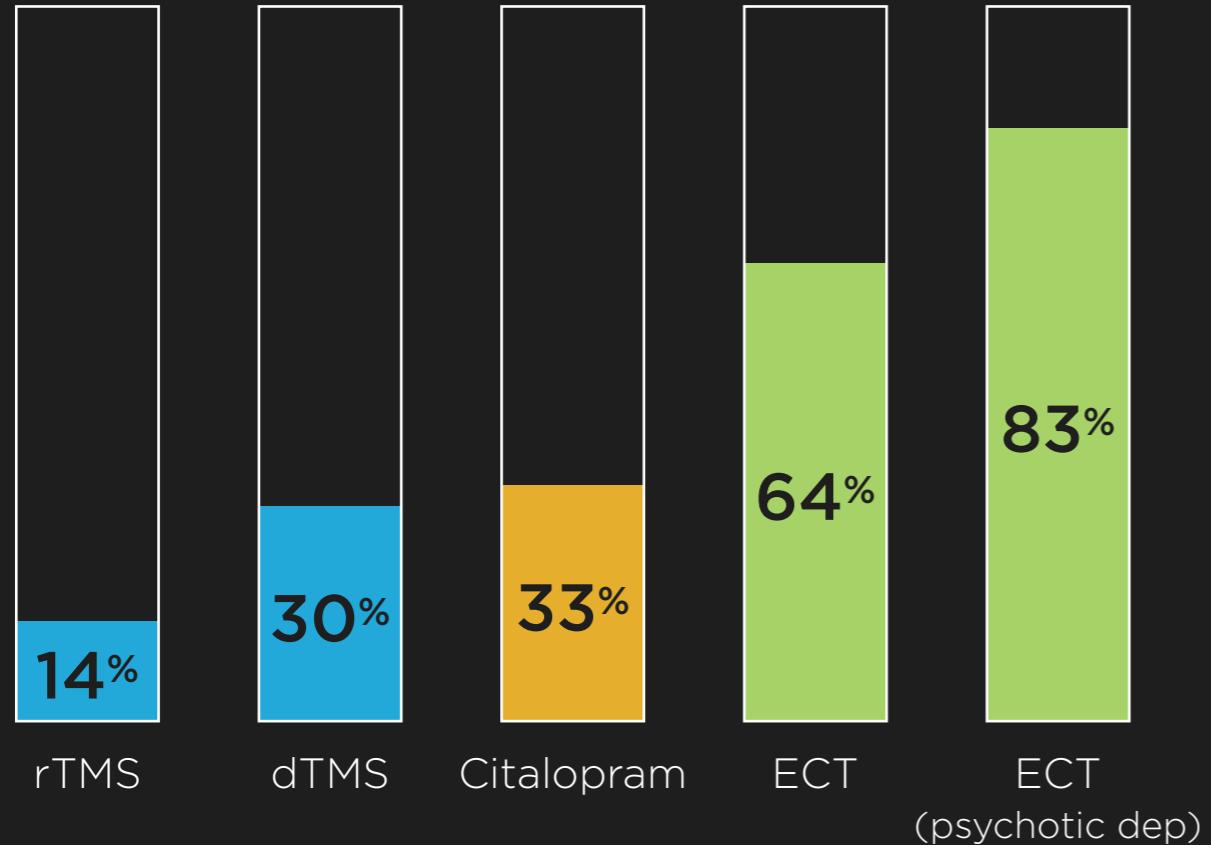
I declare that I do not have a financial interest, arrangement or affiliation with a commercial organization that may have a material interest in the subject matter of my presentation.

This work is supported in part by the NIMH Intramural Research Program and a NARSAD Young Investigator Award.



Adopted from Deng et al., *Curr Opin Neurobiol*, 2015

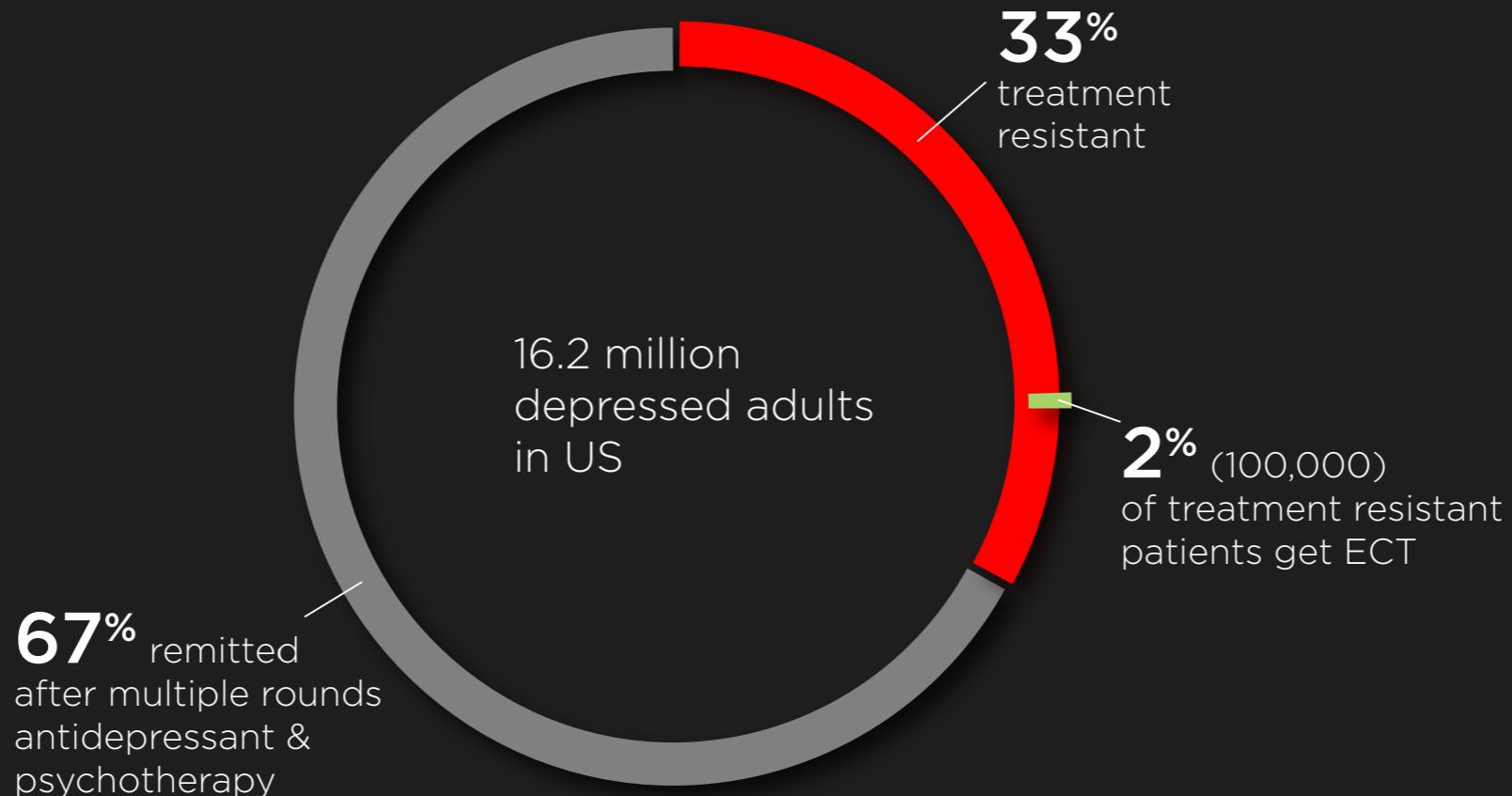
Remission rate



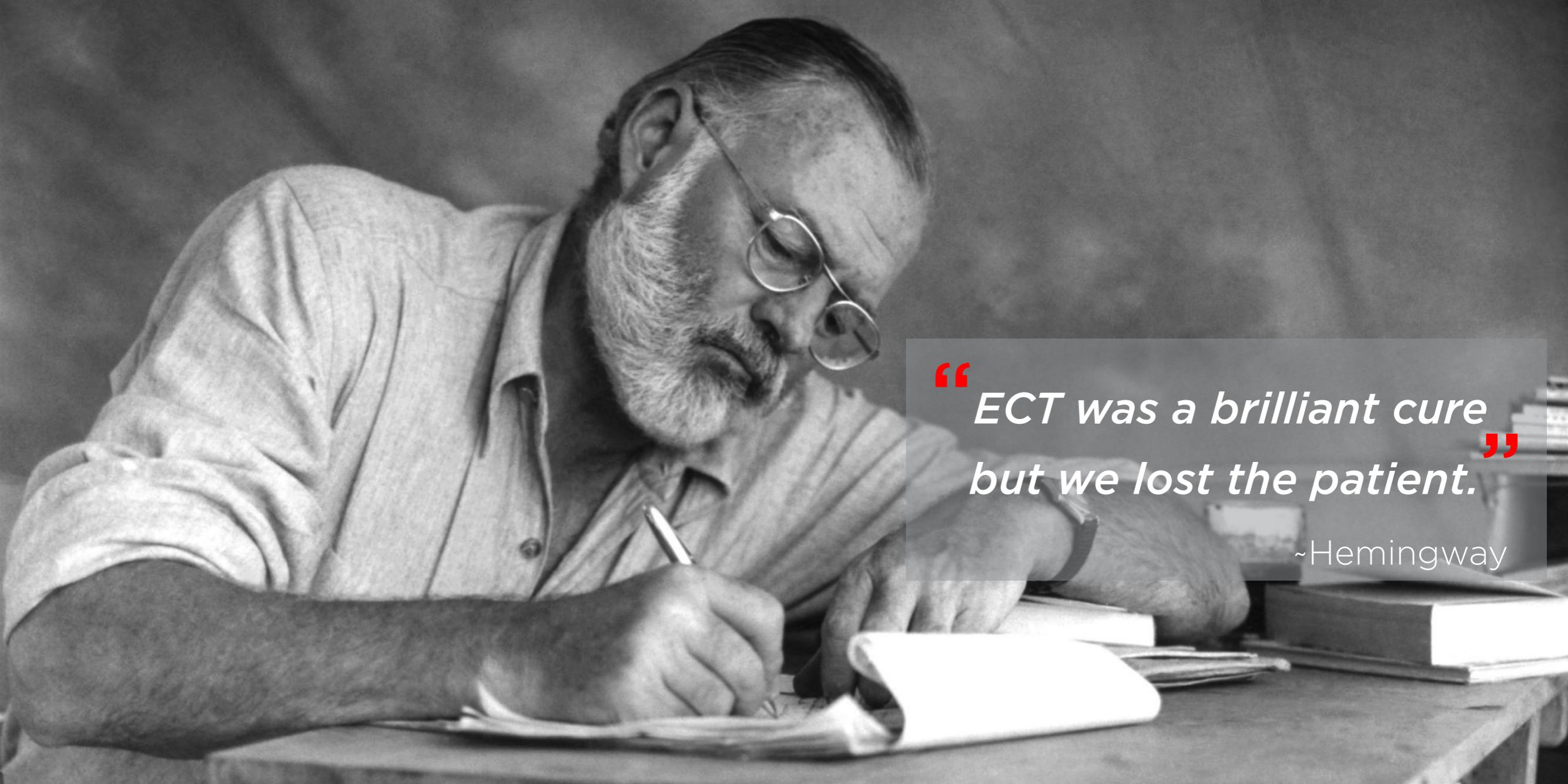
ECT is...

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)



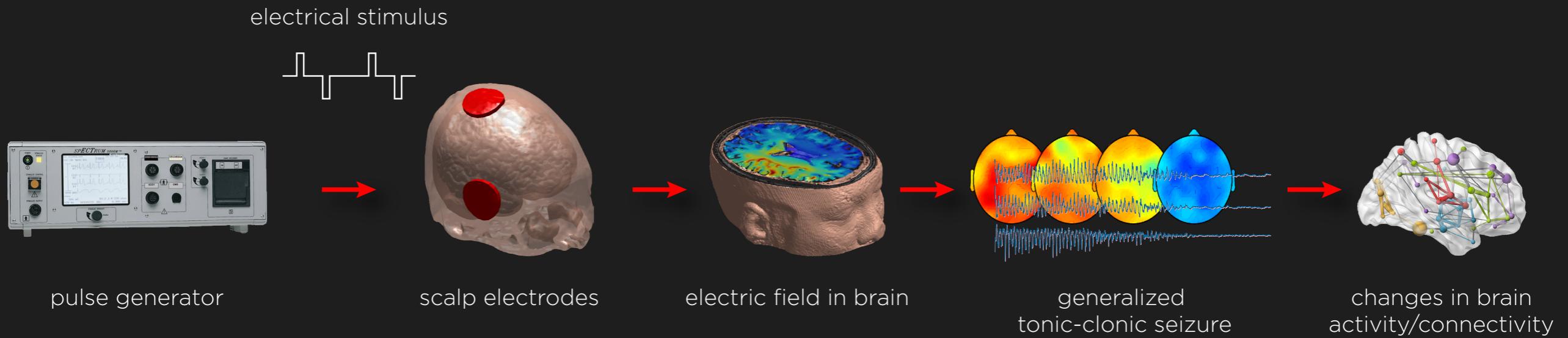
Data extrapolated from STAR*D report



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

~Hemingway

ECT in a nutshell



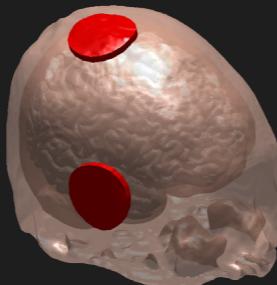
1

electrical stimulus



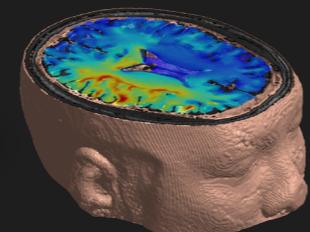
pulse generator

2



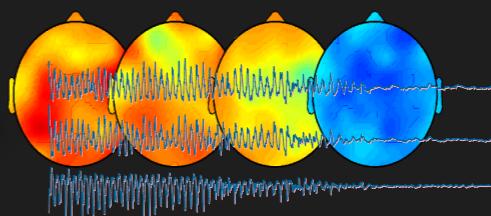
scalp electrodes

3

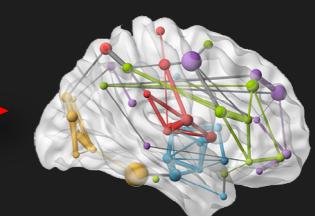


electric field in brain

4



generalized
tonic-clonic seizure



changes in brain
activity/connectivity

Current amplitude control

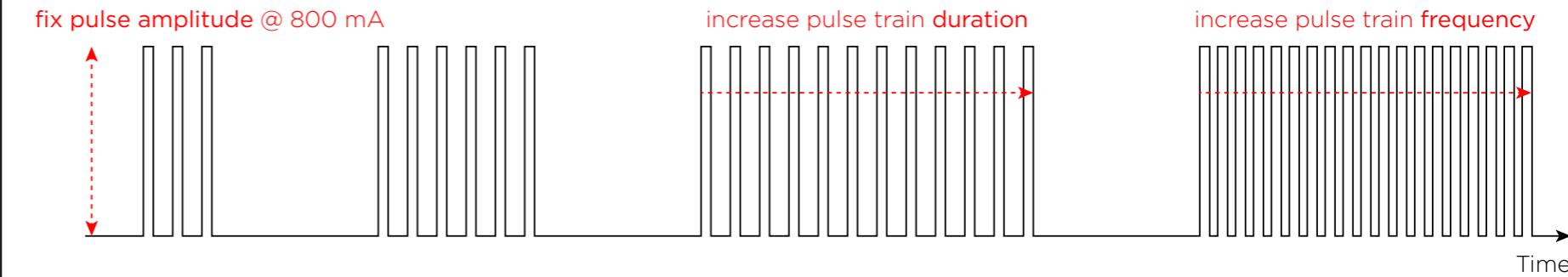
What current amplitude control?



Conventional ECT titration

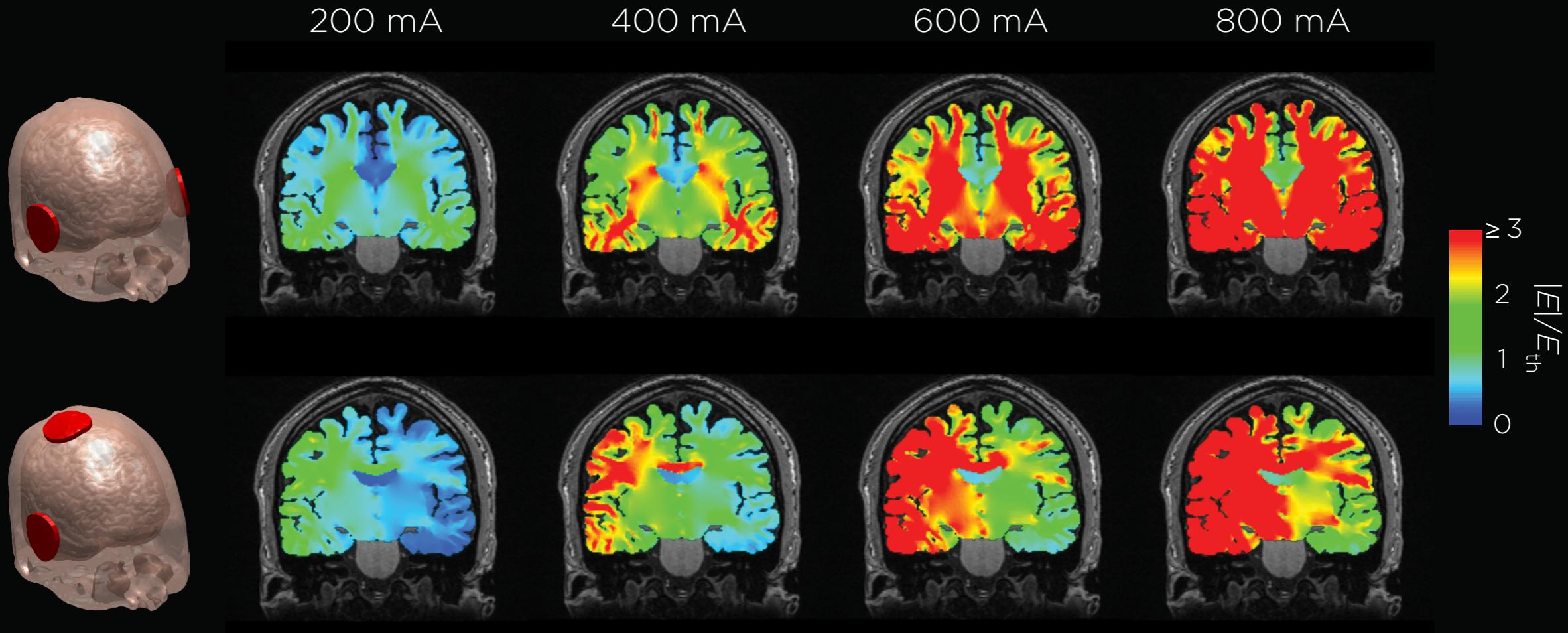
Increase train frequency
and/or duration...

...with pulse amplitude
fixed at 800mA

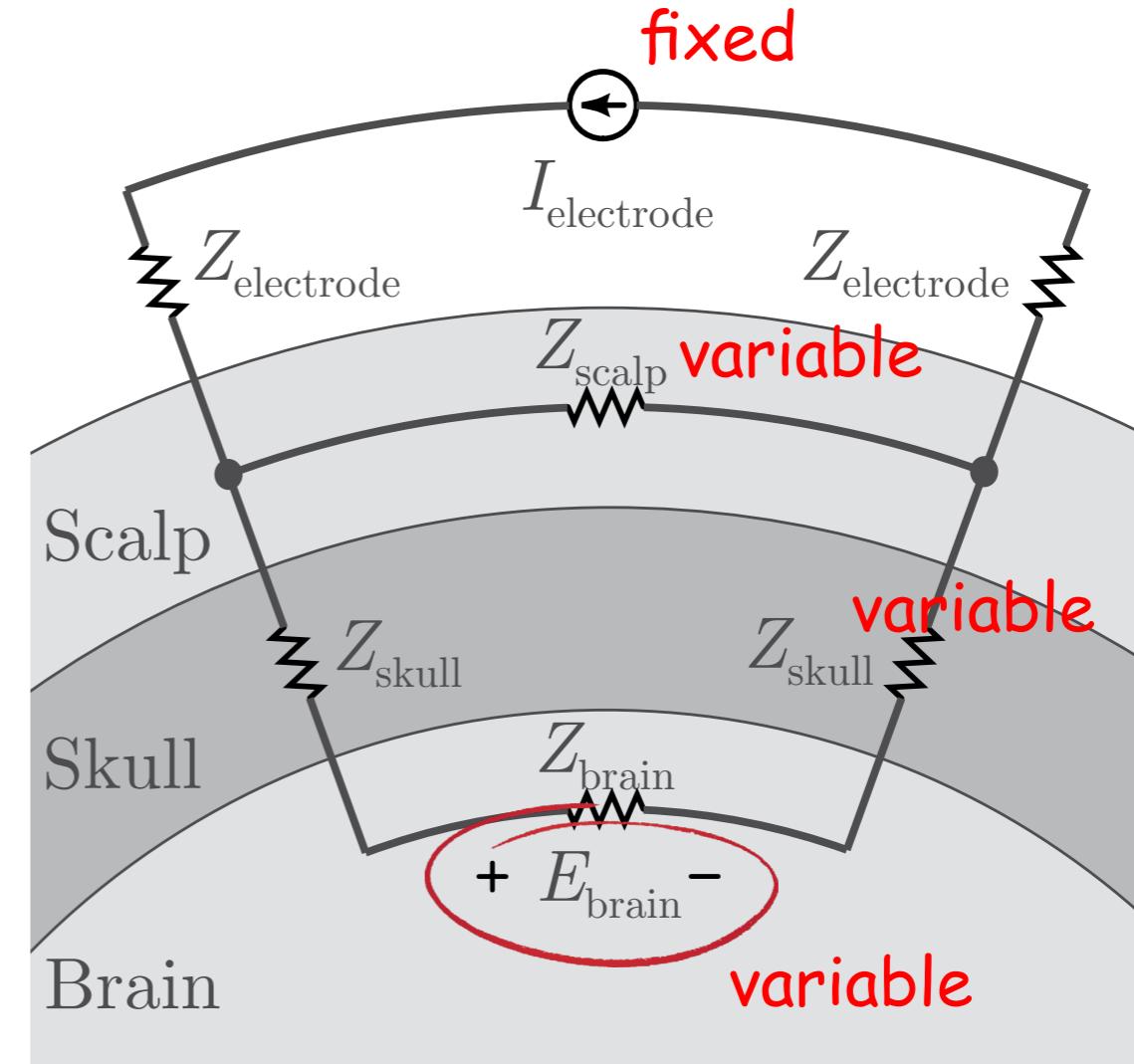


1

High current amplitude contributes to side effects



Fixed current amplitude contributes to variability



Convulsive Therapy
10(2):93-123 © 1994 Raven Press, Ltd., New York

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.*

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.

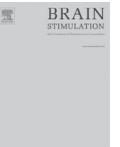
“

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**. ”

“The effects of tDCS are **highly variable**
... with around 50% of individuals having poor or
absent responses.”


Contents lists available at [ScienceDirect](#)

Brain Stimulation

journal homepage: www.brainstimjnl.com


Variability in Response to Transcranial Direct Current Stimulation of the Motor Cortex

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Keywords:
 Transcranial direct current stimulation (TDCS)
 I-waves
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 Motor cortex
 Facilitation

ABSTRACT

Background: Responses to a number of different plasticity-inducing brain stimulation protocols are highly variable. However there is little data available on the variability of response to transcranial direct current stimulation (TDCS).

Objective: We tested the effects of TDCS over the motor cortex on corticospinal excitability. We also examined whether an individual's response could be predicted from measurements of onset latency of motor evoked potential (MEP) following stimulation with different orientations of monophasic transcranial magnetic stimulation (TMS).

Methods: Fifty-three healthy subjects participated in a crossover-design. Baseline latency measurements with different coil orientations and MEPs were recorded from the first dorsal interosseous muscle prior to the application of 10 min of 2 mA TDCS (0.057 mA/cm²). Thirty MEPs were measured every 5 min for up to half an hour after the intervention to assess after-effects on corticospinal excitability.

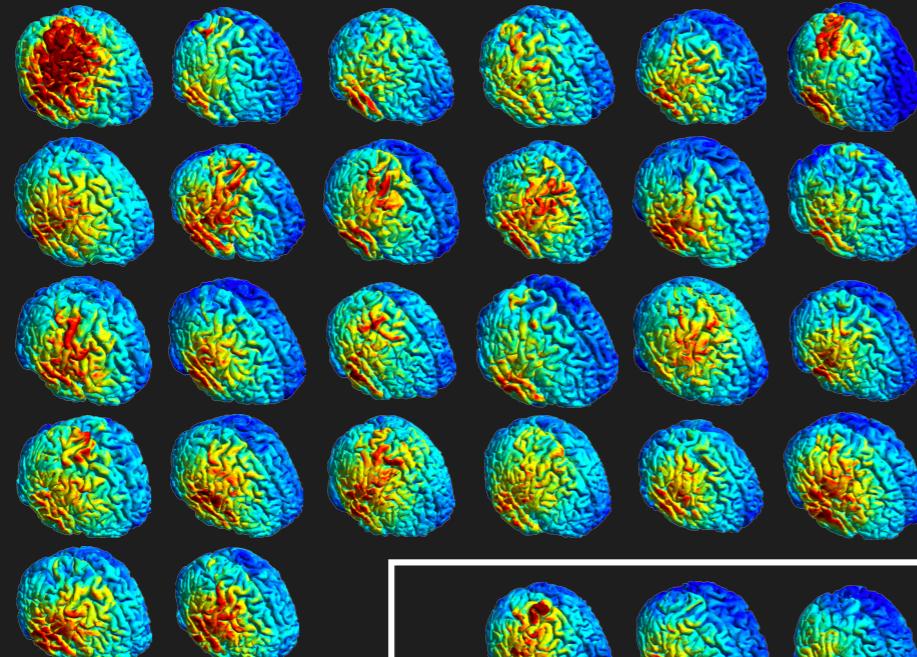
Results: Anodal TDCS at 2 mA facilitated MEPs whereas there was no significant effect of 2 mA cathodal TDCS. A two-step cluster analysis suggested that approximately 50% individuals had only a minor, or no response to TDCS whereas the remainder had a facilitatory effect to both forms of stimulation. There was a significant correlation between the latency difference of MEPs (anterior–posterior stimulation minus latero-medial stimulation) and the response to anodal, but not cathodal TDCS.

Conclusions: The large variability in response to these TDCS protocols is in line with similar studies using other forms of non-invasive brain stimulation. The effects highlight the need to develop more robust protocols, and understand the individual factors that determine responsiveness.

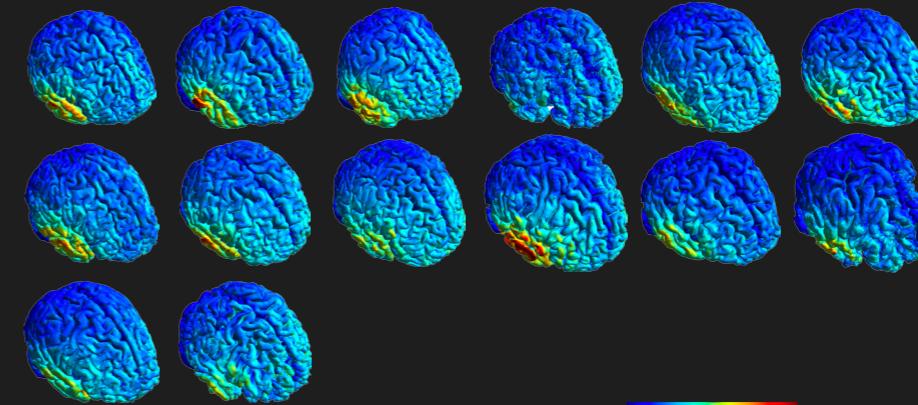
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1

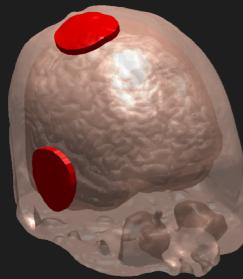
RUL ECT only



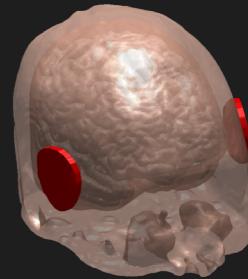
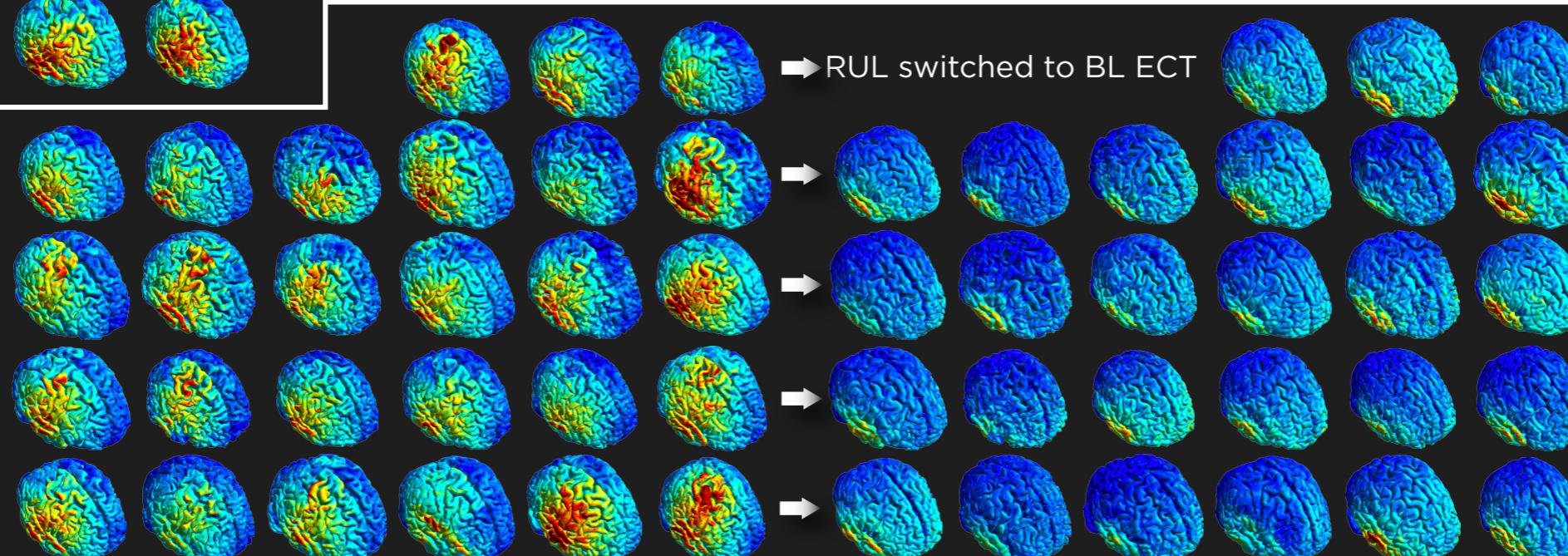
BL ECT only



0 $|E|$ ($V m^{-1}$) ≥ 240



→ RUL switched to BL ECT



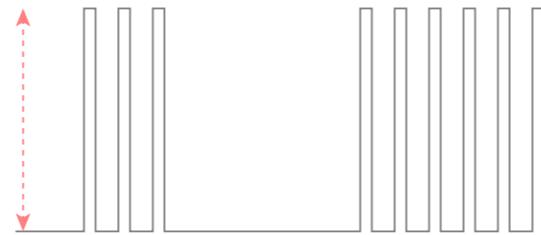
Titrate by current amplitude

Prevents overexposure of brain to suprathreshold stimulation

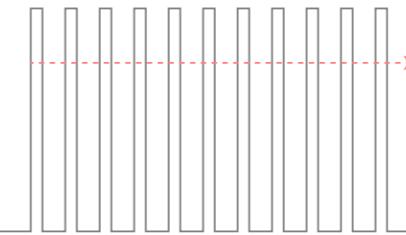
Compensates for variability in interindividual anatomy and excitability

Conventional ECT titration

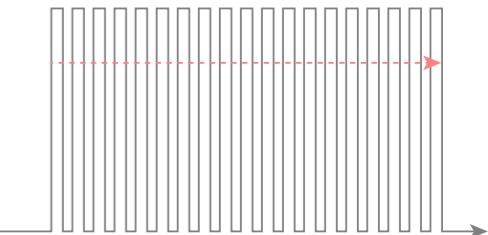
fix pulse amplitude @ 800 mA



increase pulse train duration

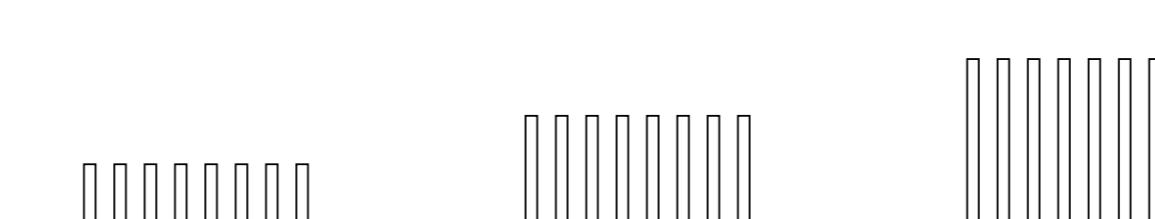


increase pulse train frequency



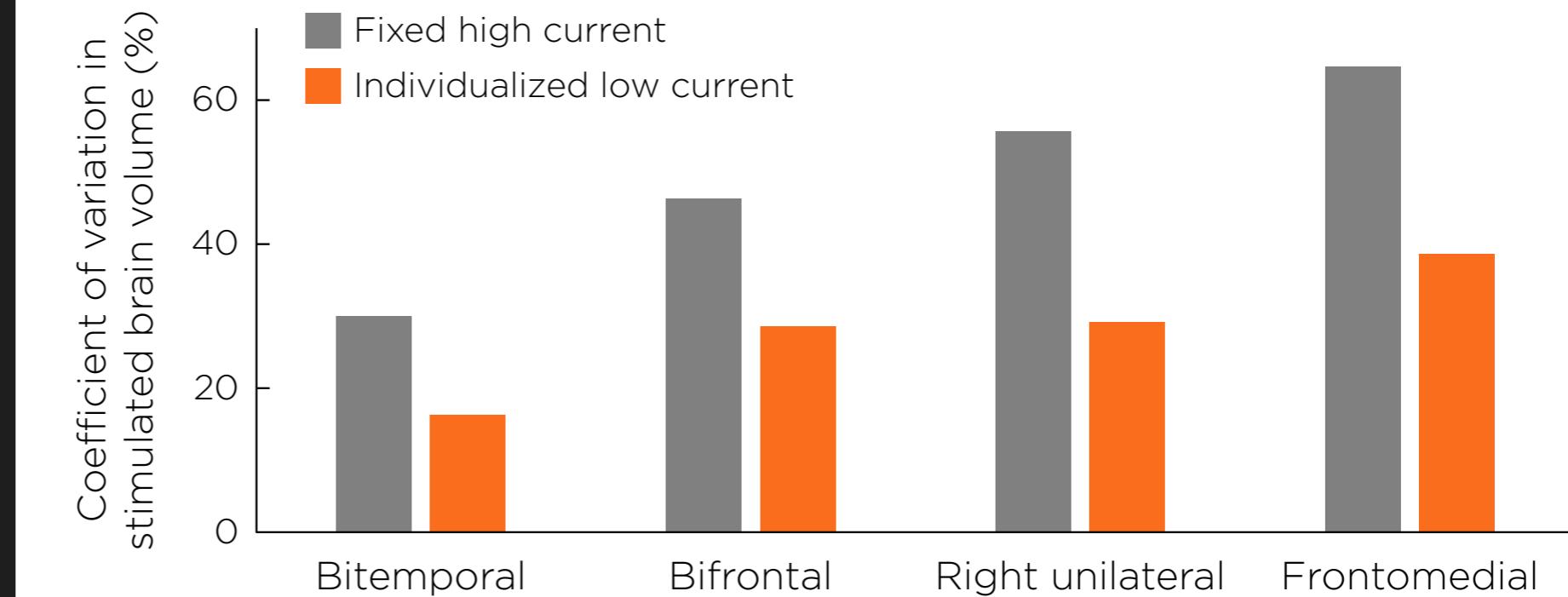
Time

Amplitude titration



Time

Individualized current
amplitude titration:
proof of concept



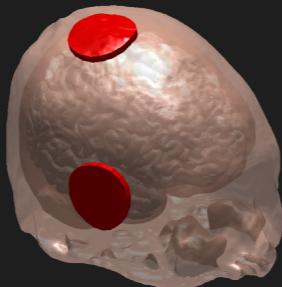
1

electrical stimulus



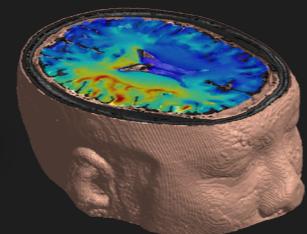
pulse generator

2



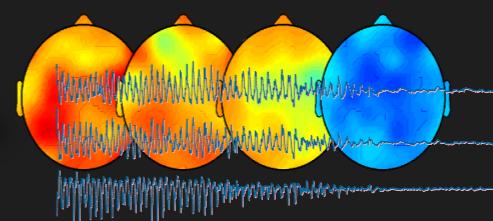
scalp electrodes

3



electric field in brain

4



generalized
tonic-clonic seizure



changes in brain
activity/connectivity

2

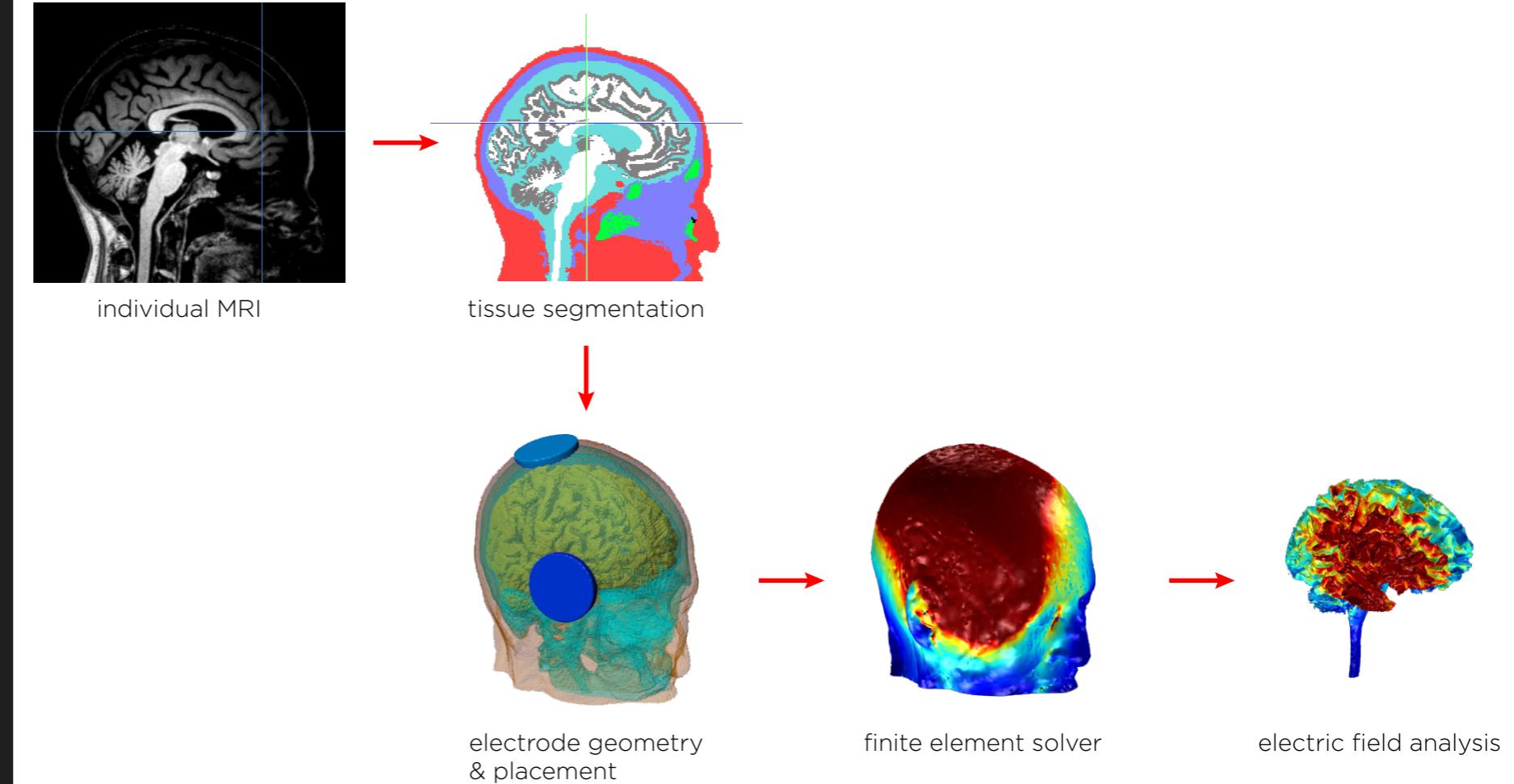
Cerletti 1930s

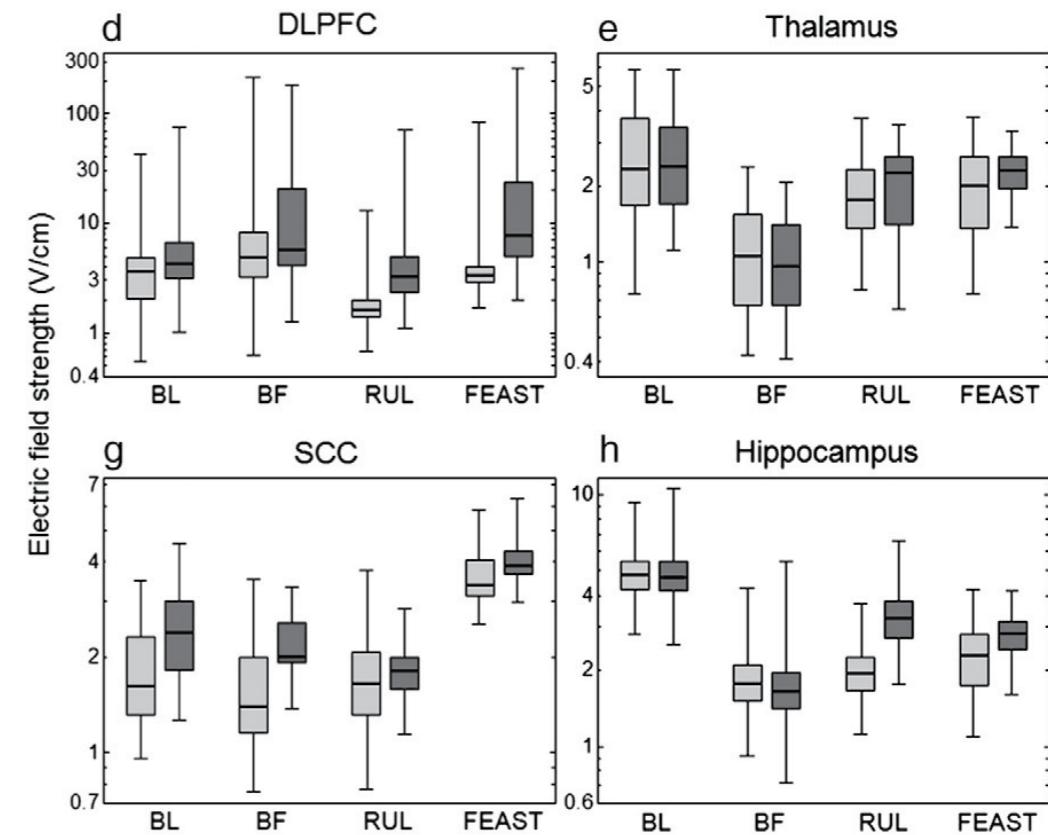
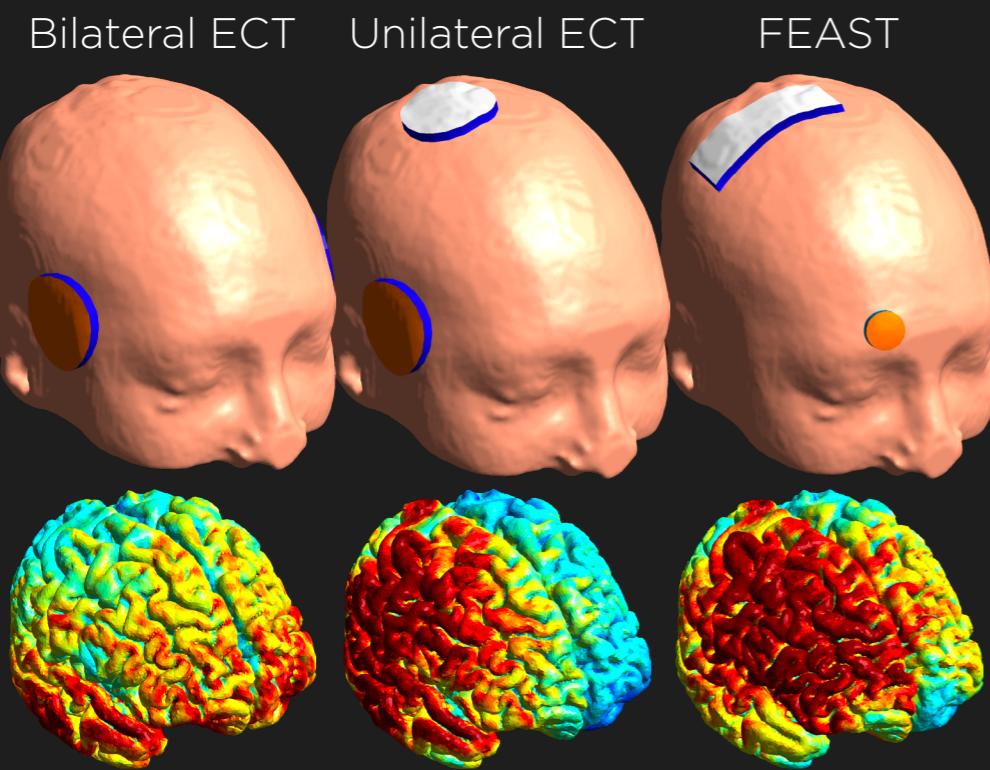


Modern day bilateral ECT



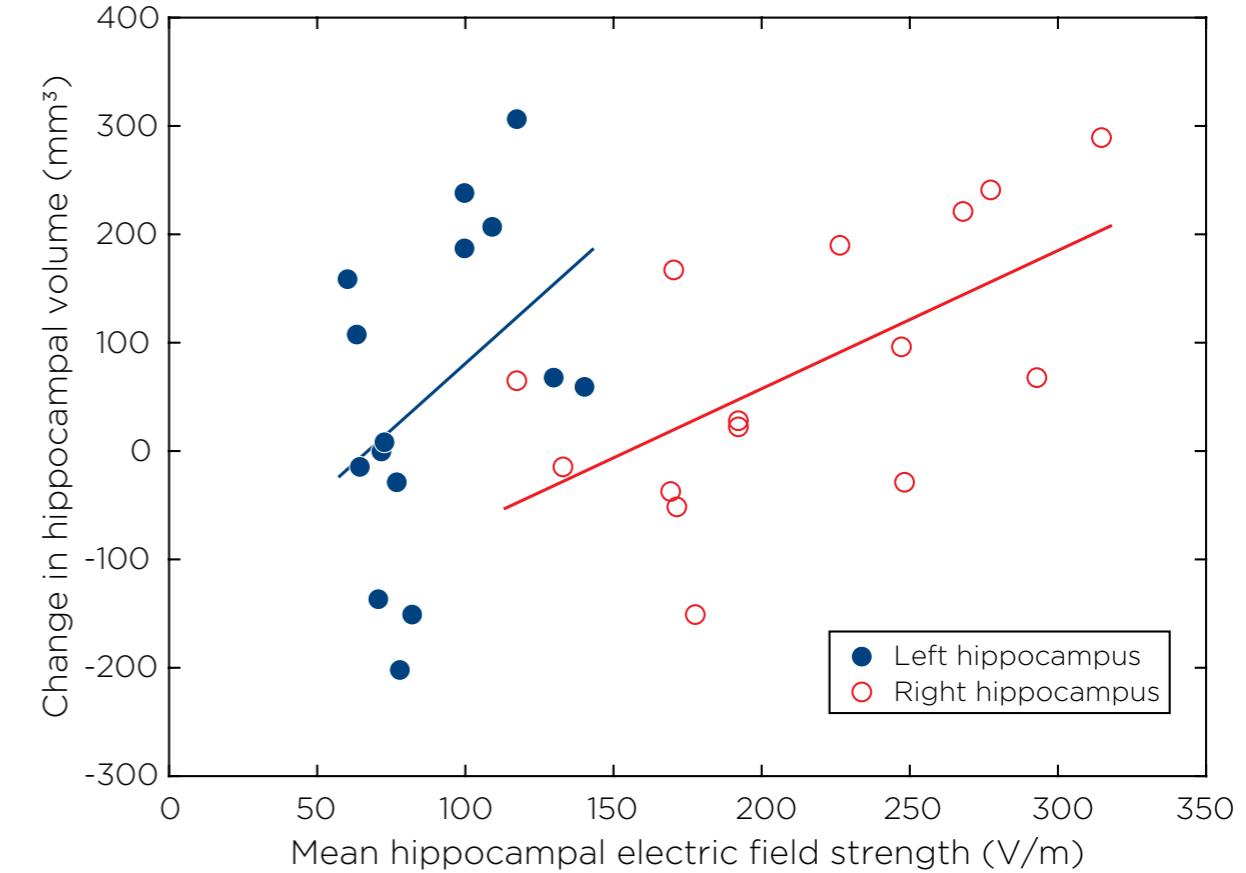
Computational electric field modeling

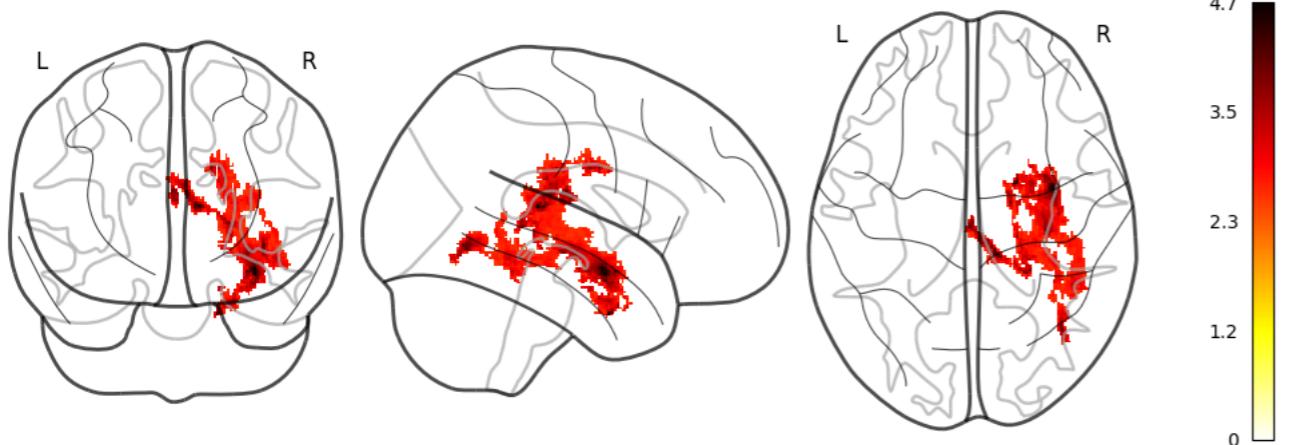




In actual ECT patients now...

Right unilateral ECT electric field strength at right hippocampus correlates with volumetric changes post ECT





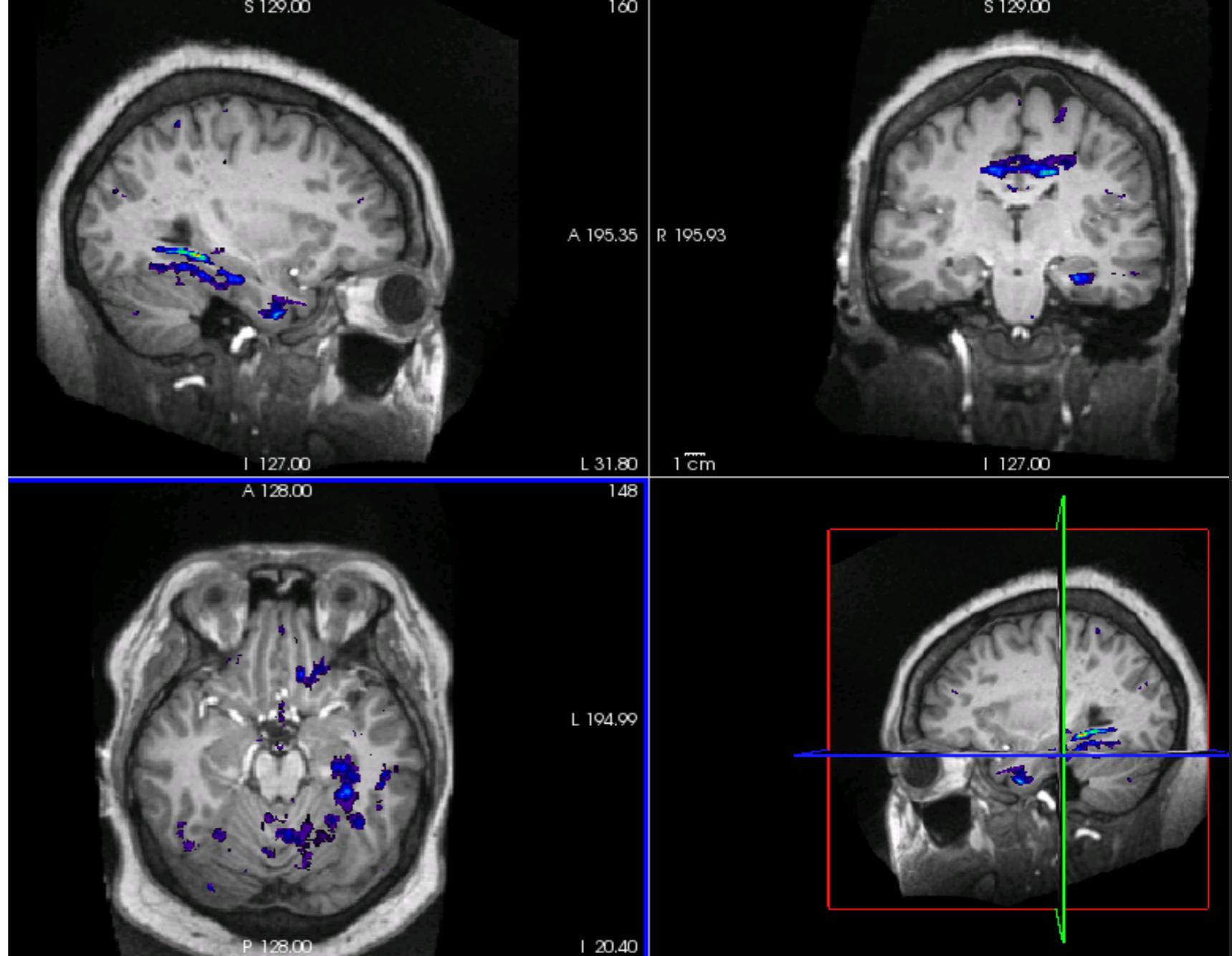
67 bilateral ECT patients
@ Rijinstate Hospital in Arnhem, Netherlands

Correlated electric field with post-treatment
MADRS score, controlling for age, sex, base-
line MADRS, and number of ECT sessions

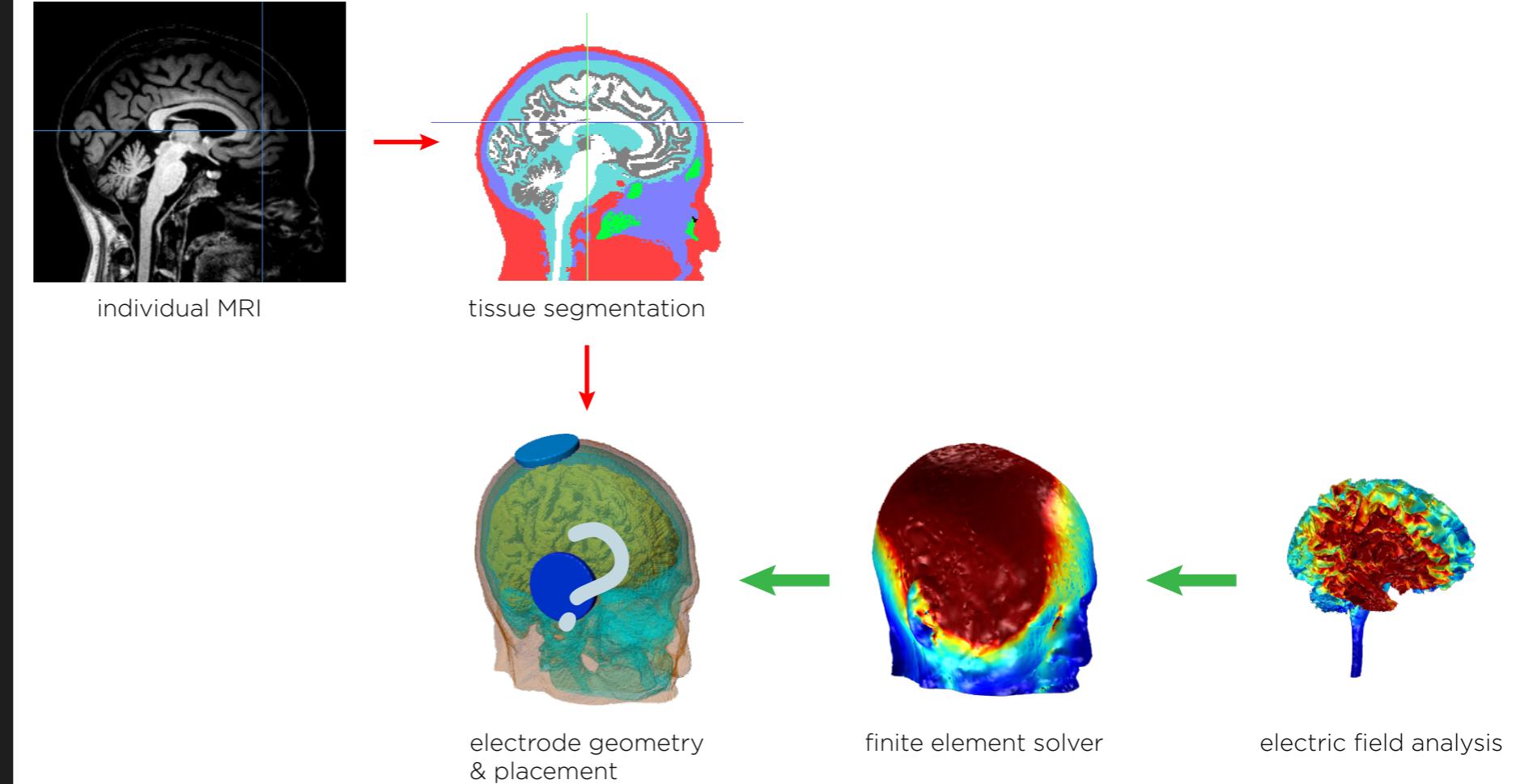
Global ECT-MRI Research Collaboration (GEMRIC) data

RUL ECT Responder
 Δ MADRS > 50%, N = 103
Nonresponder
 Δ MADRS < 30%, N = 68

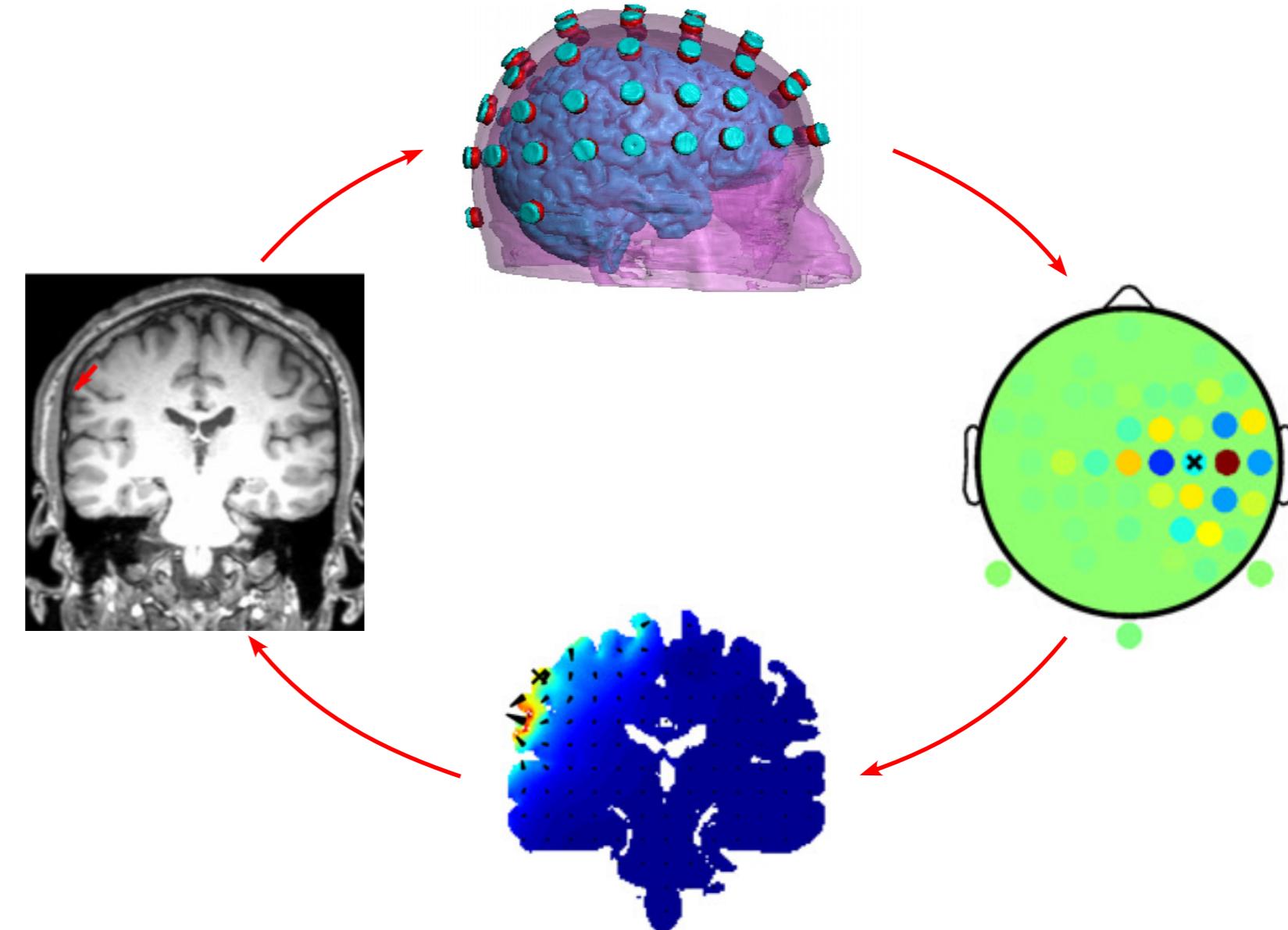
Responders showed increased E-field at cingulate cortex, left parahippocampal gyrus, and medial prefrontal cortex ($p < .005$)



Run this backwards...



Multielectrode optimization



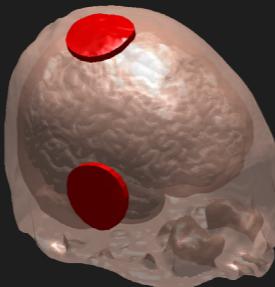
1

electrical stimulus



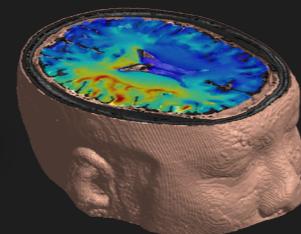
pulse generator

2



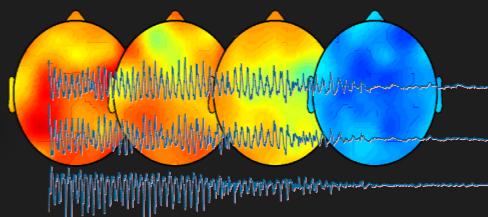
scalp electrodes

3

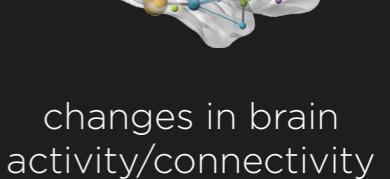


electric field in brain

4



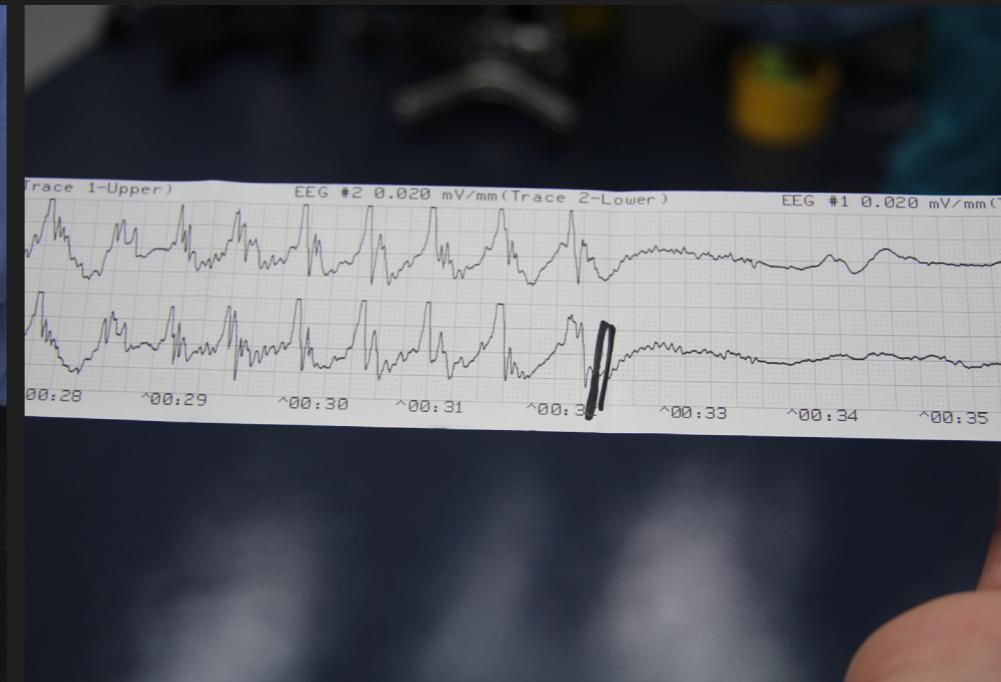
generalized
tonic-clonic seizure



changes in brain
activity/connectivity

3

Understanding seizure topography



3

State of the art

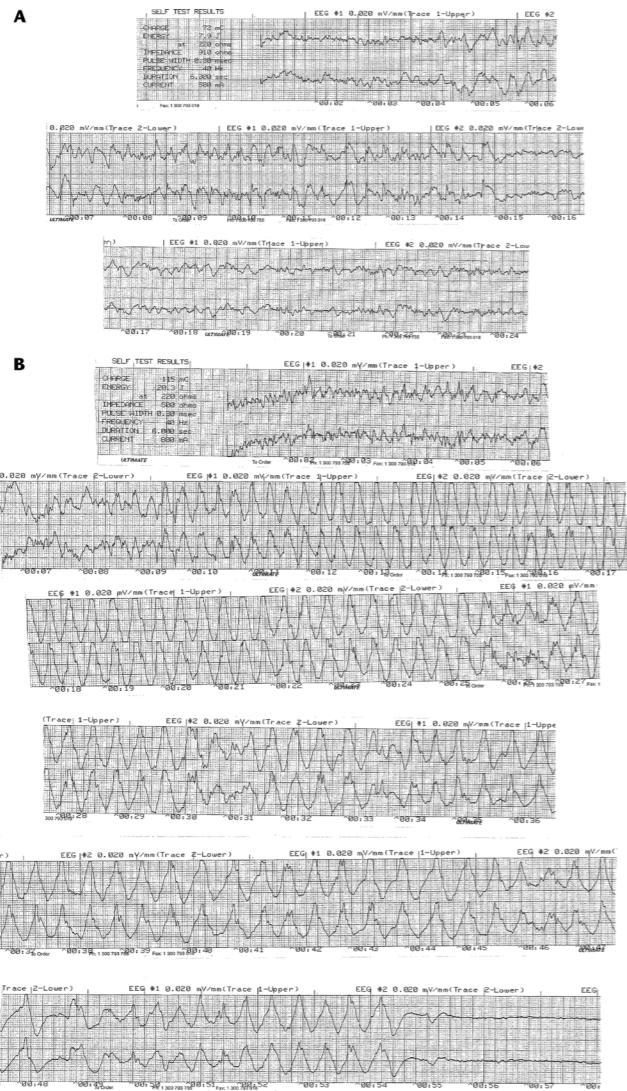


FIGURE 1. Electroencephalograms during ECT in patient 1.

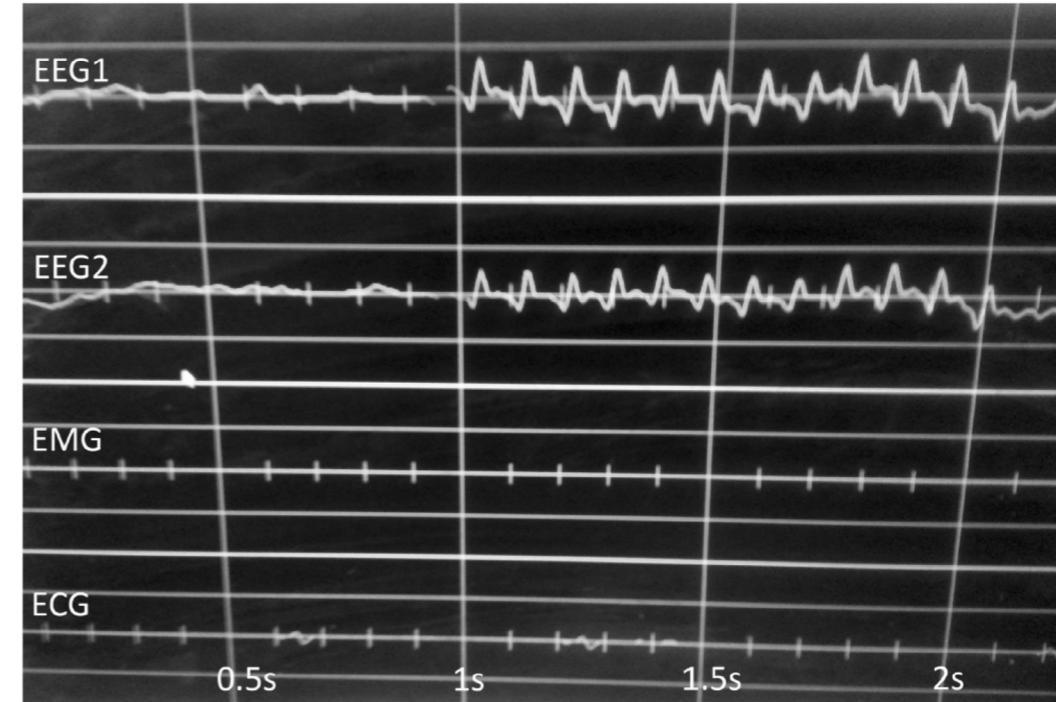
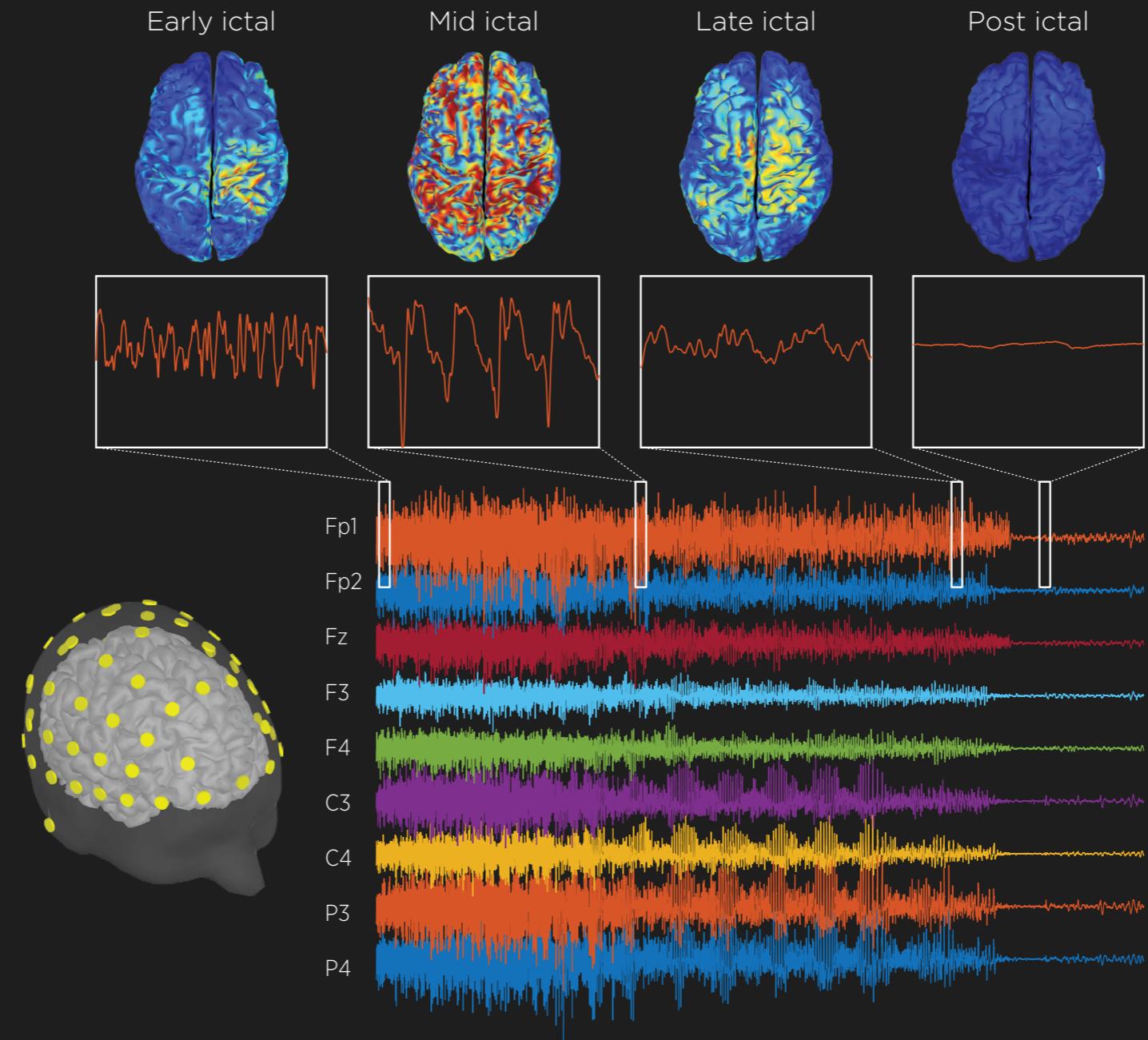
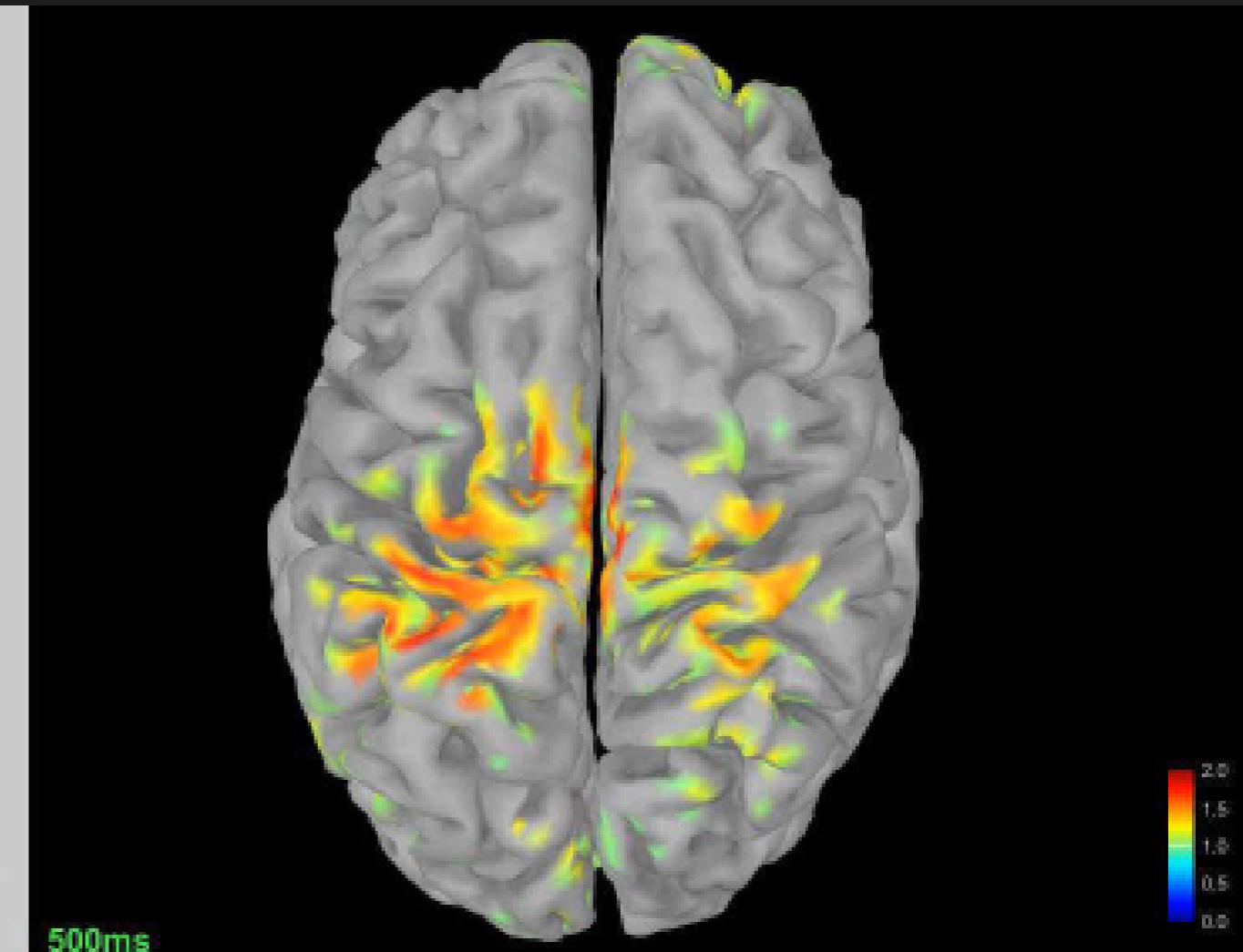
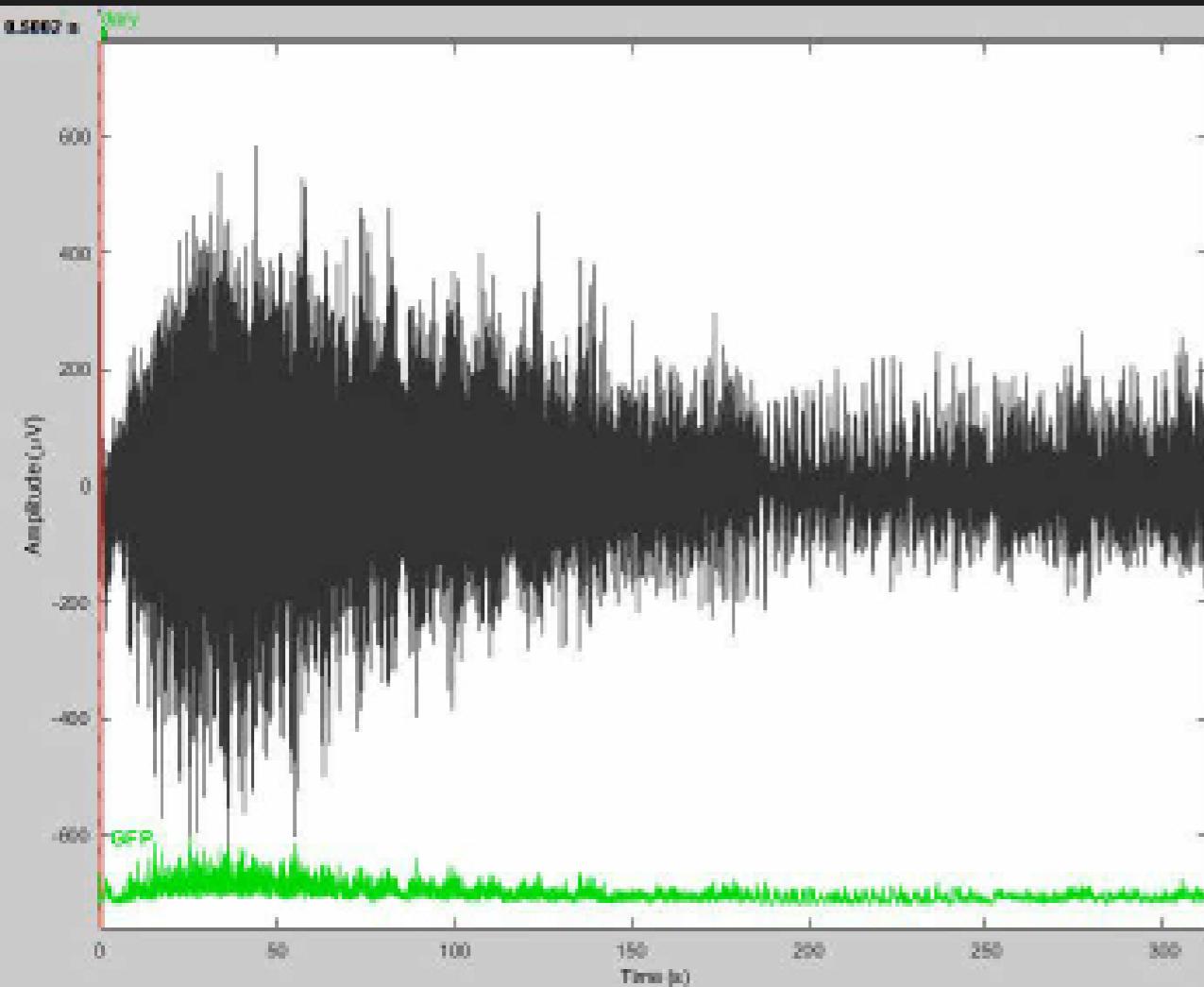


FIGURE 1. Real-time image on a computer monitor attached to the ECT device after resolution of seizure, with muscle artifact appearing on EEG1 and EEG2.





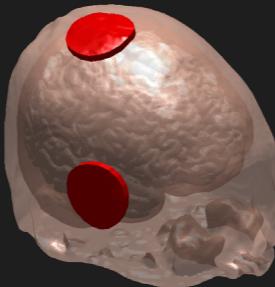
1

electrical stimulus



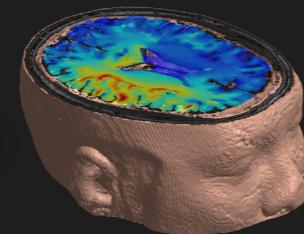
pulse generator

2



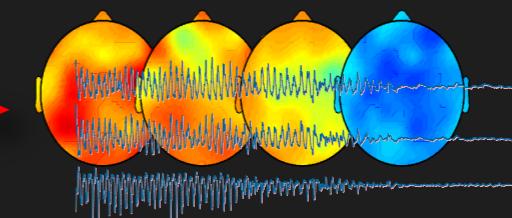
scalp electrodes

3



electric field in brain

4



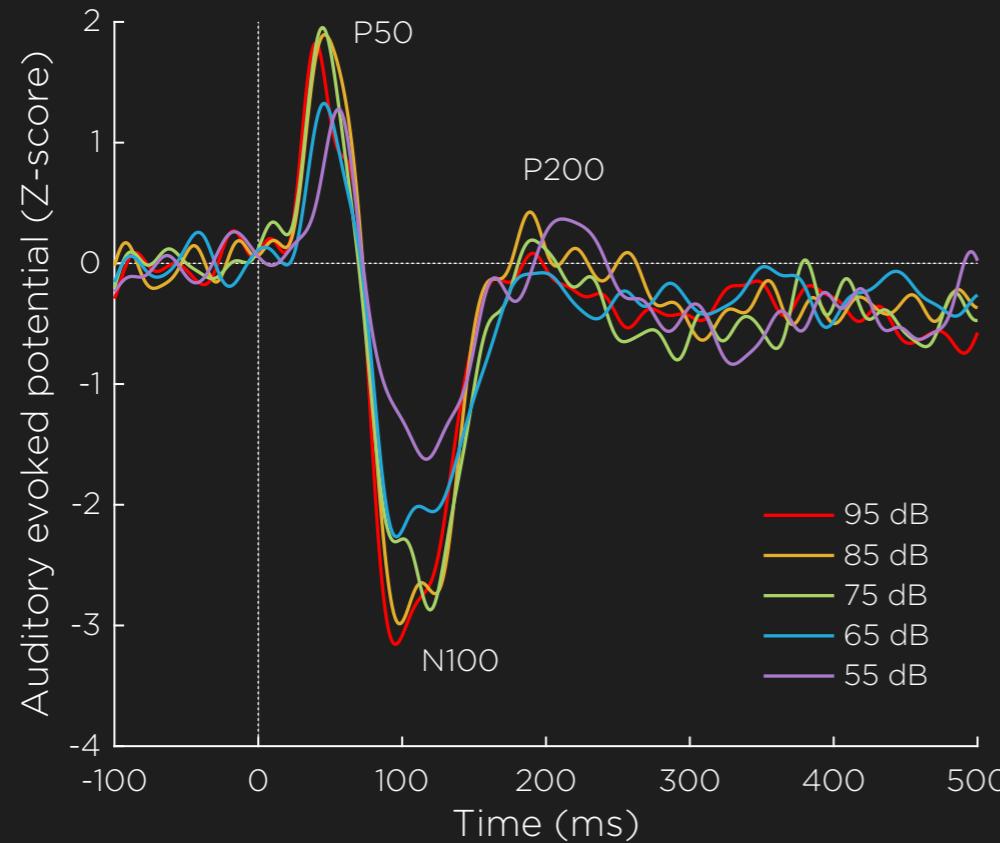
generalized
tonic-clonic seizure



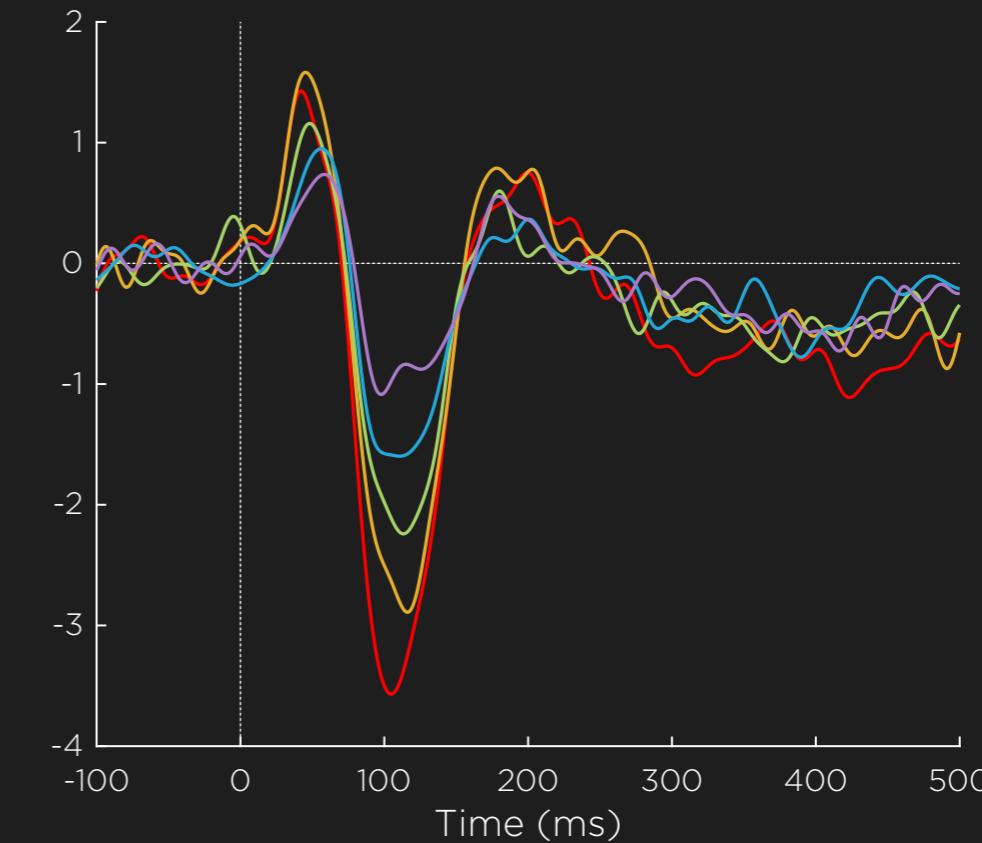
changes in brain
activity/connectivity

Loudness Dependence of Auditory Evoked Potentials

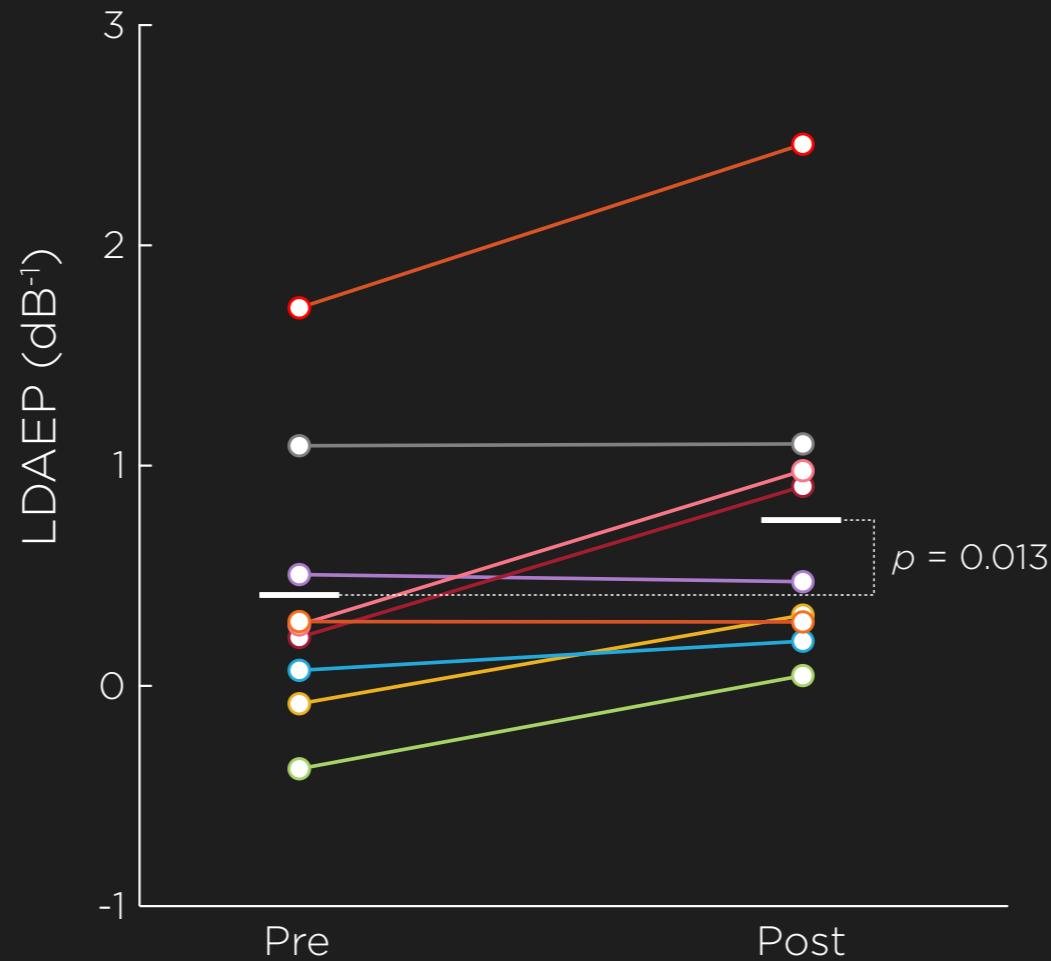
A. Baseline



B. Post ECT



Loudness Dependence of Auditory Evoked Potentials



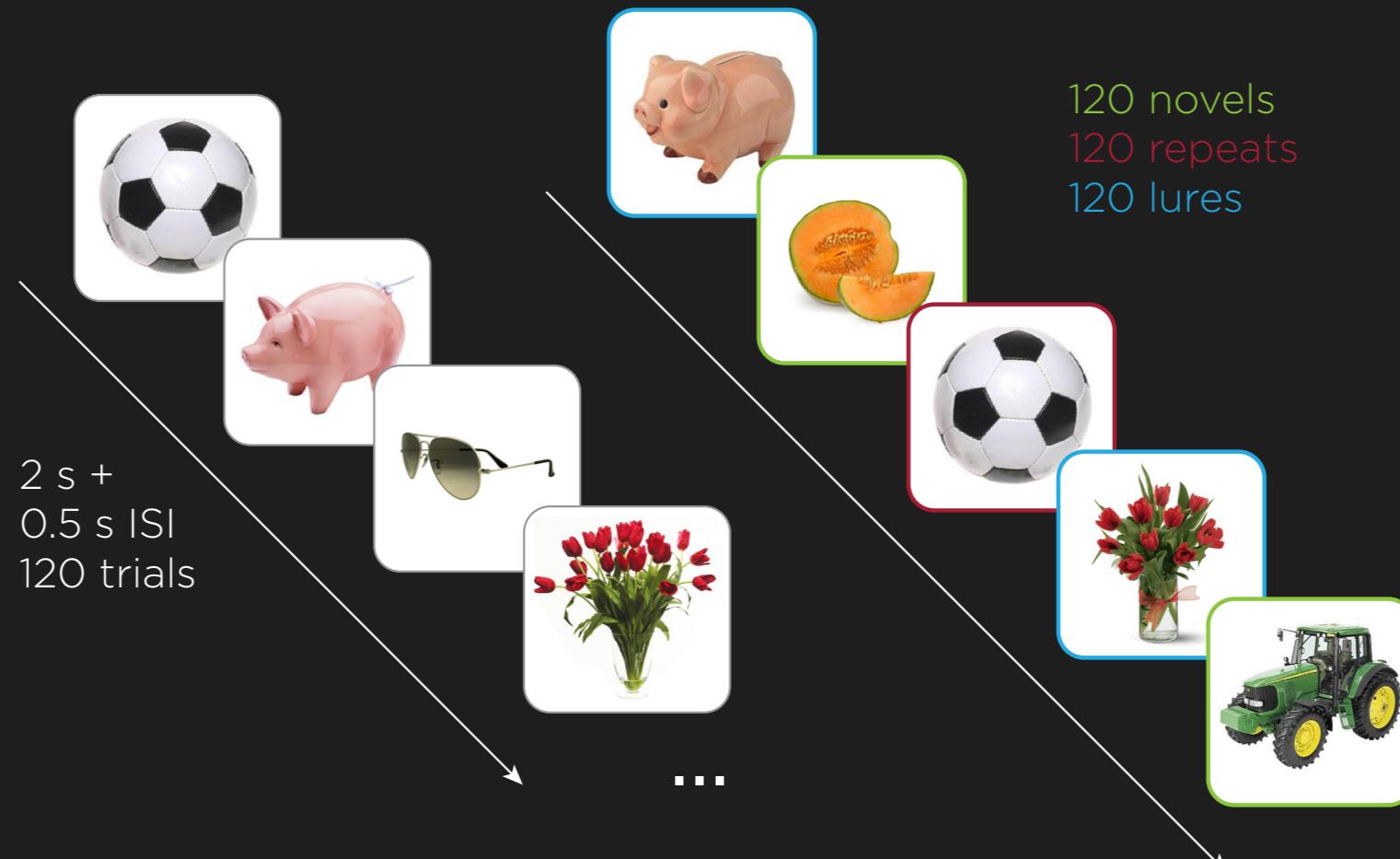
Mnemonic Similarity Task to Assess Hippocampal Function

Encoding phase

Indoor or Outdoor?

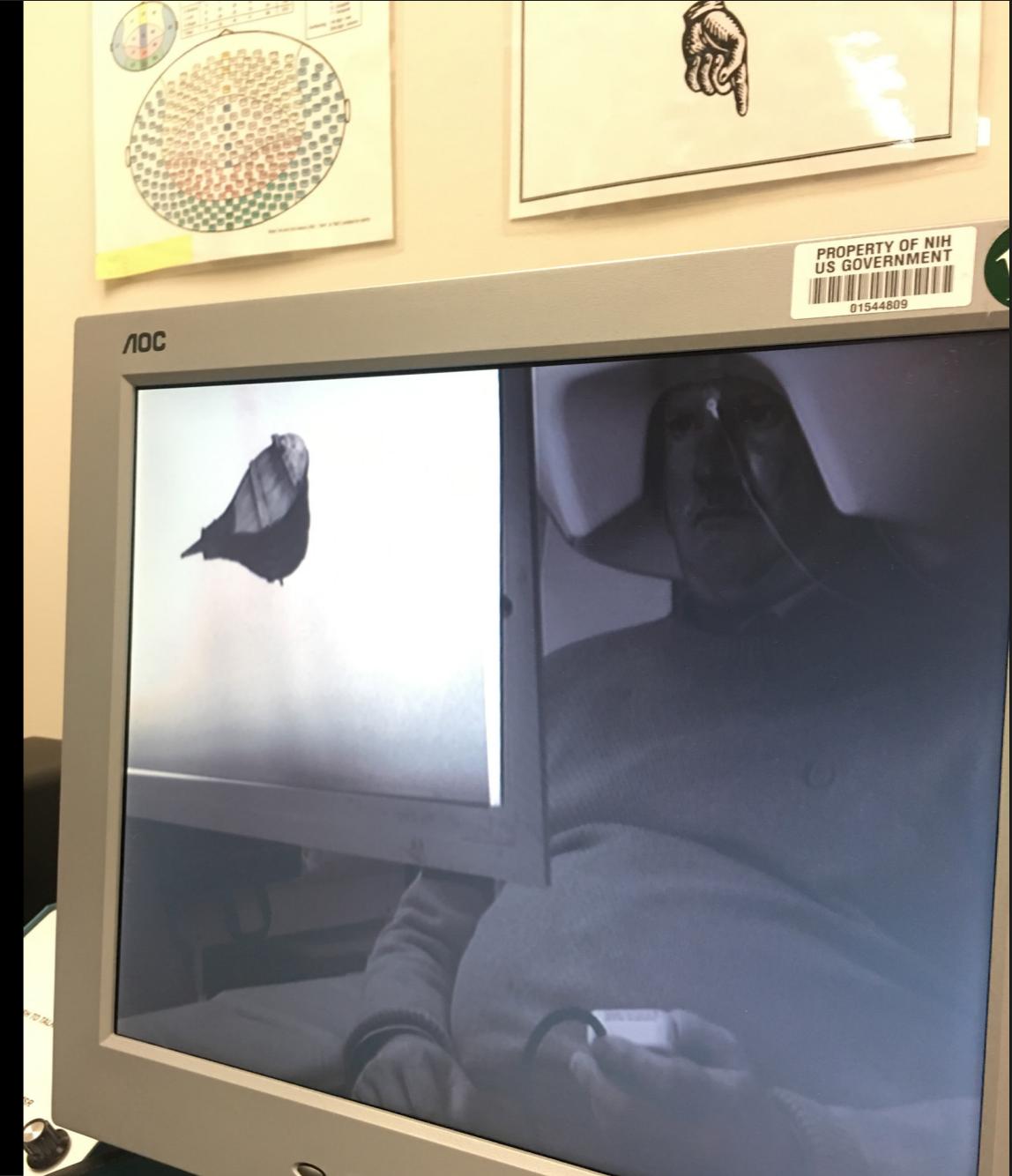
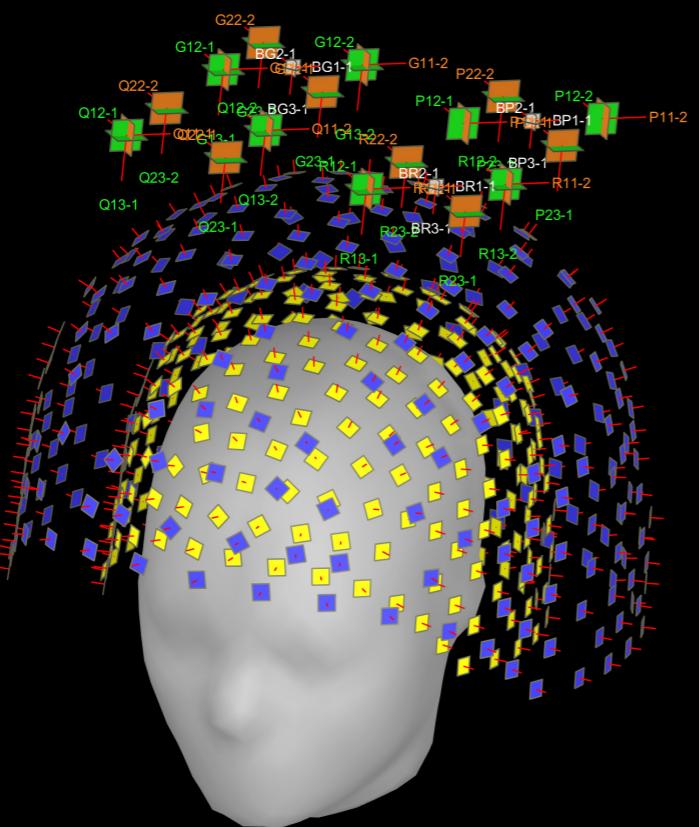
Retrieval phase

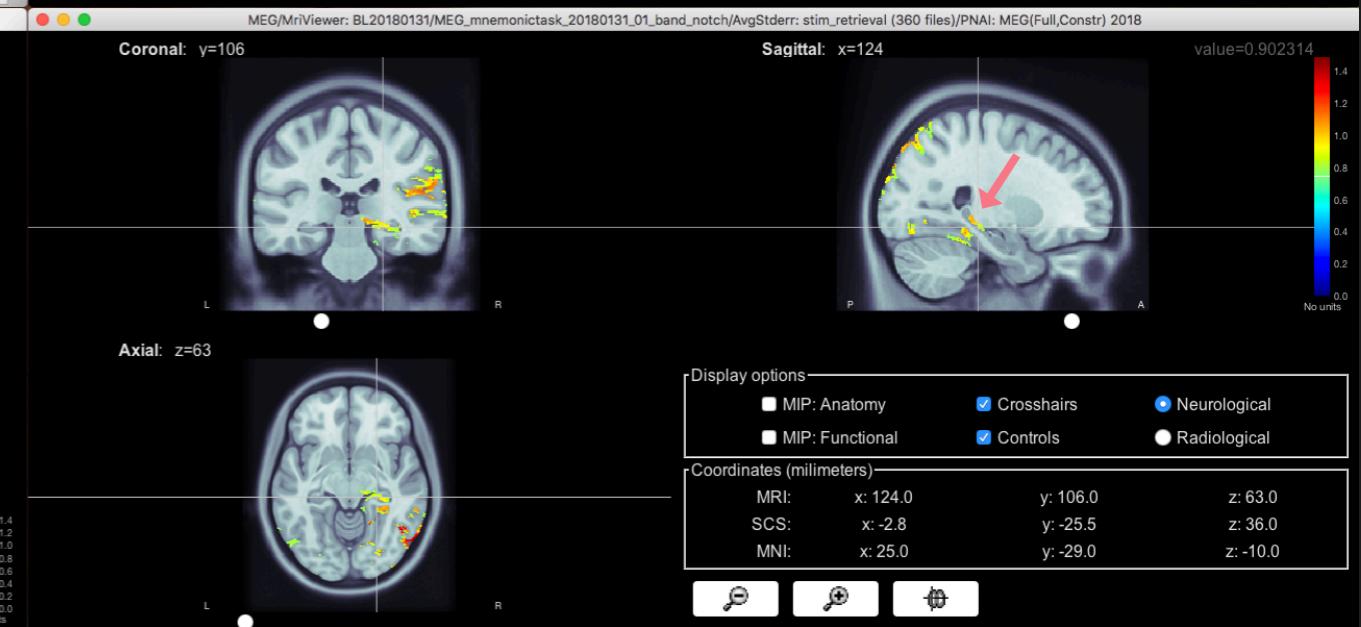
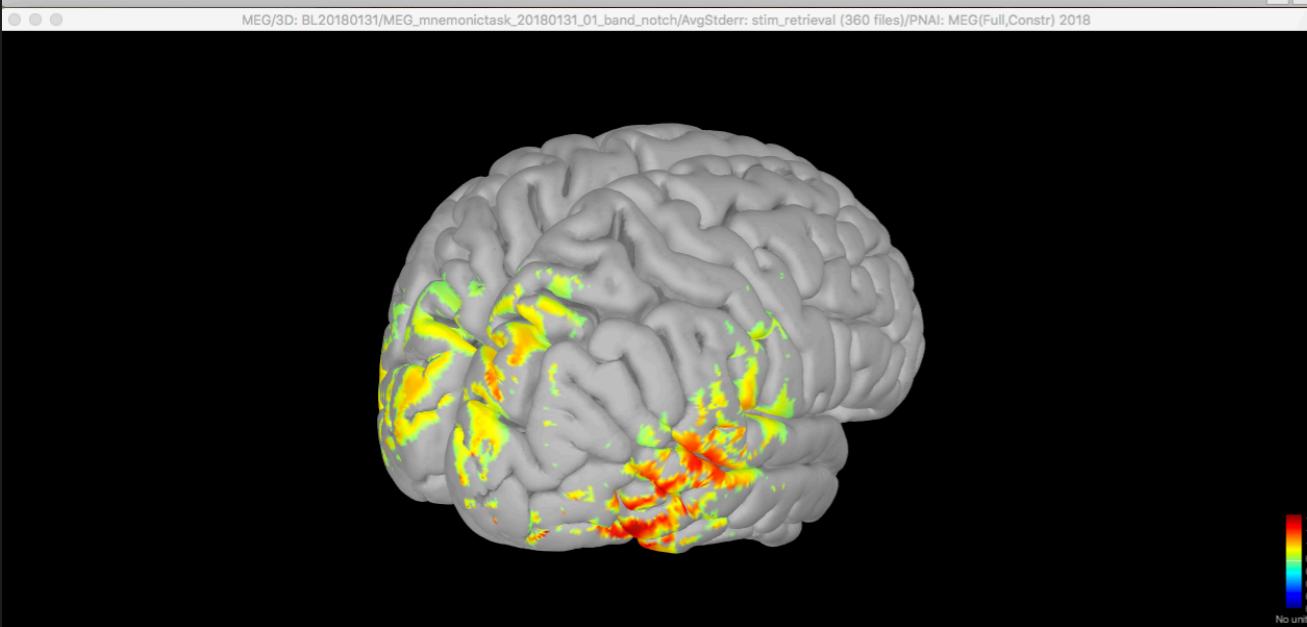
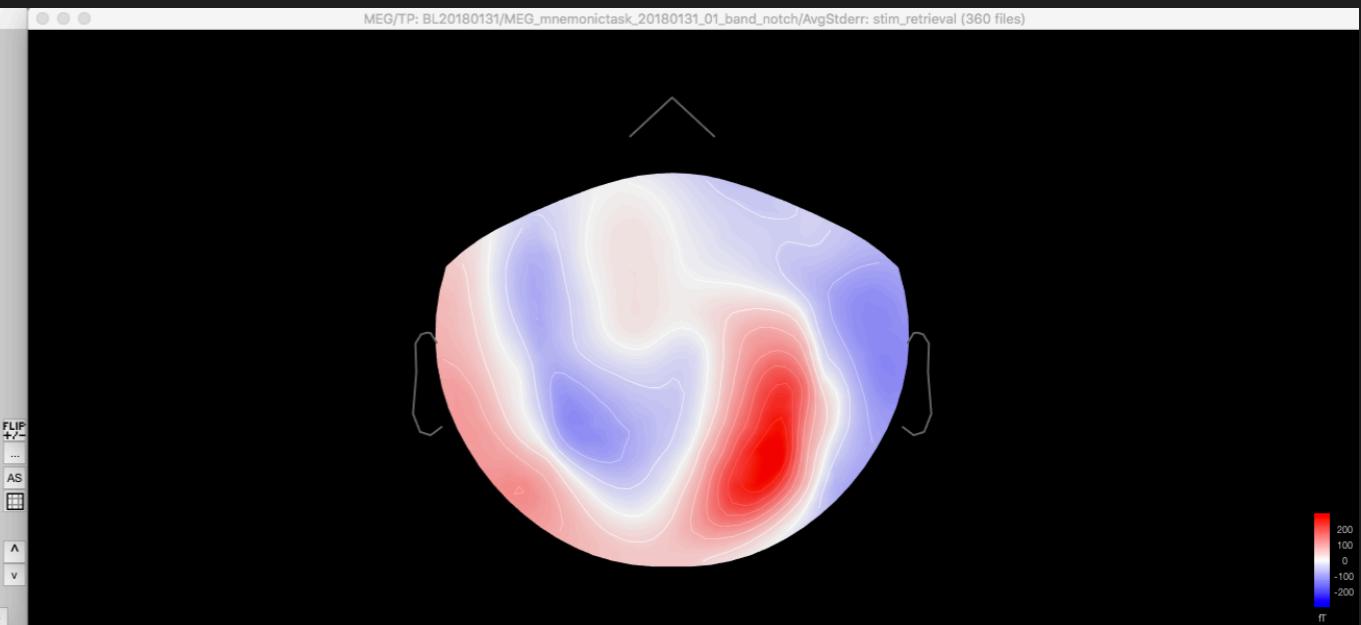
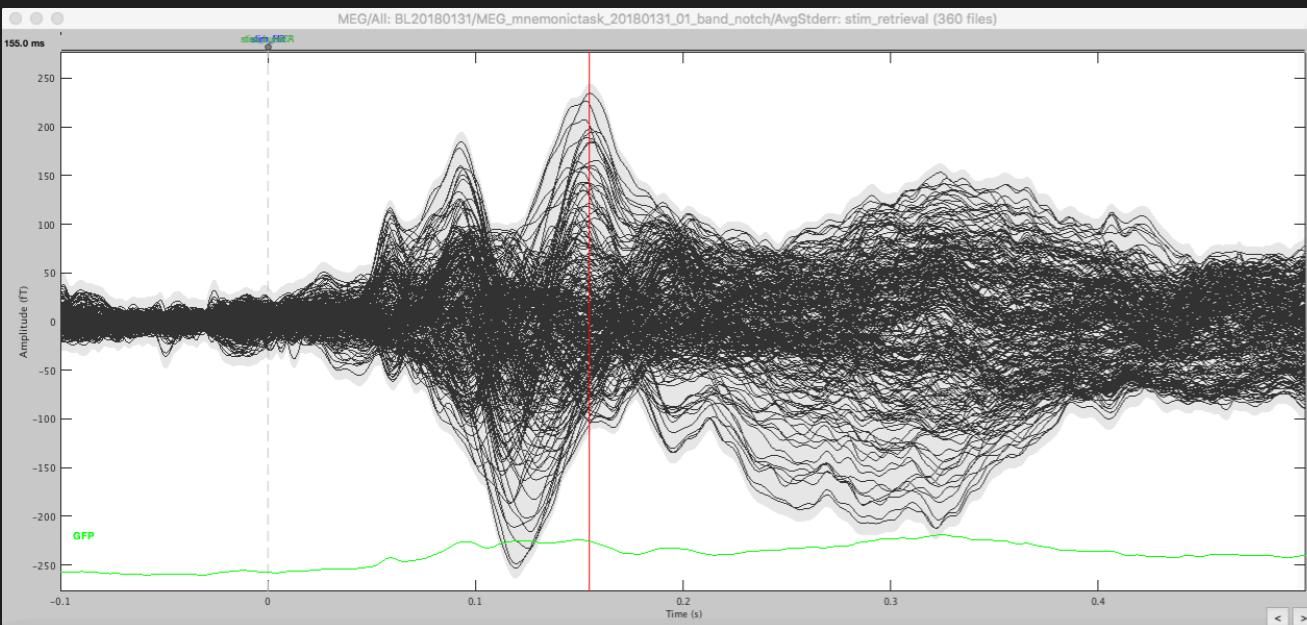
Old, New, or Similar?



Modified from Stark et al., *Neuropsychologia*, 2013

Subject 1: BL20180131

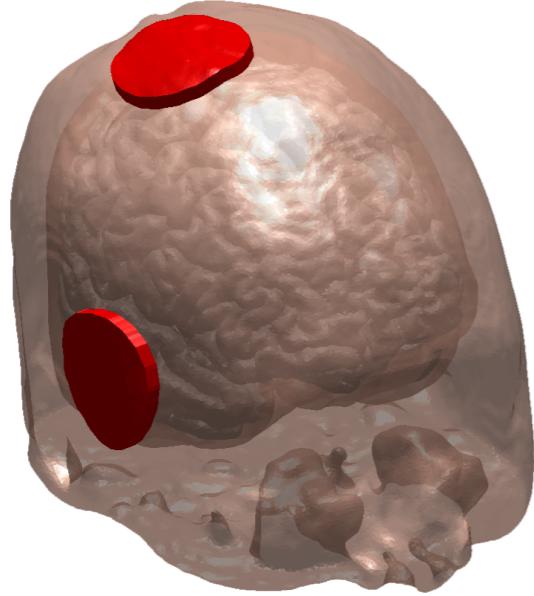




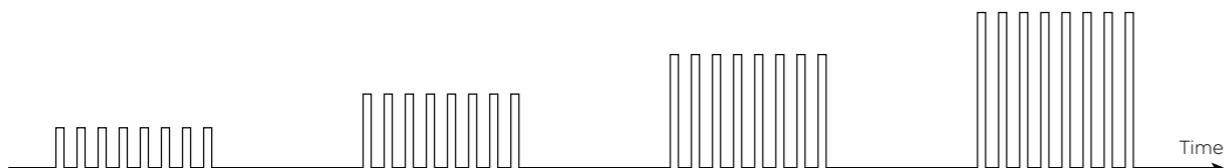
Next generation ECT

Individualized

- § subject-specific head model
- § pulse amplitude titration



Amplitude titration





Next generation ECT

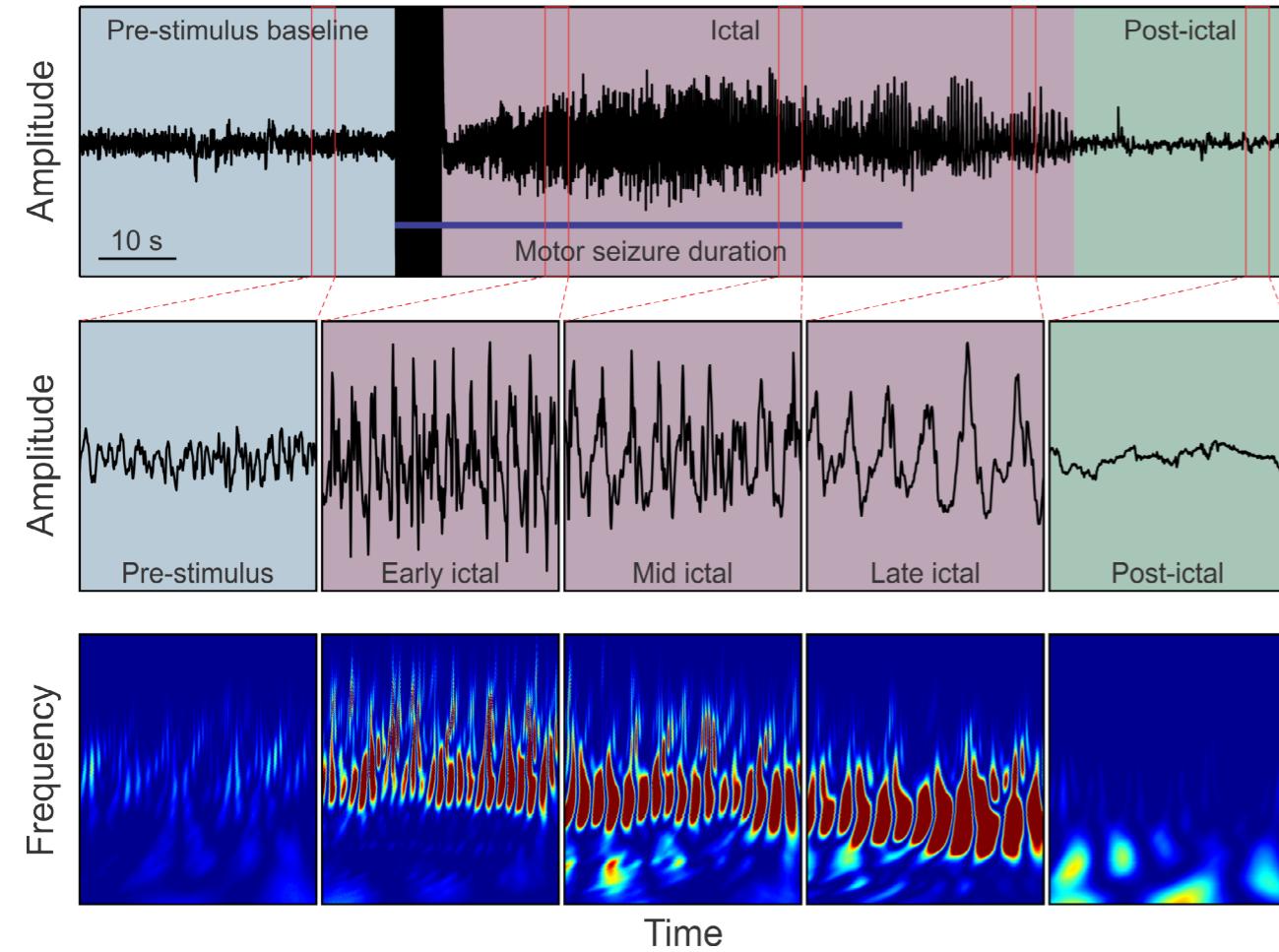
Individualized

- § subject-specific head model
- § pulse amplitude titration

Neurotargeted

- § multichannel stimulation device
- § multi-stim electrode array
- § electrode optimization

Next generation ECT



Individualized

- § subject-specific head model
- § pulse amplitude titration

Neurotargeted

- § multichannel stimulation device
- § multi-stim electrode array
- § electrode optimization

Dynamic seizure sculpting

- § topographical seizure analysis
- § online modulation of seizure

iLAST: First-in-human trial, Fall 2018

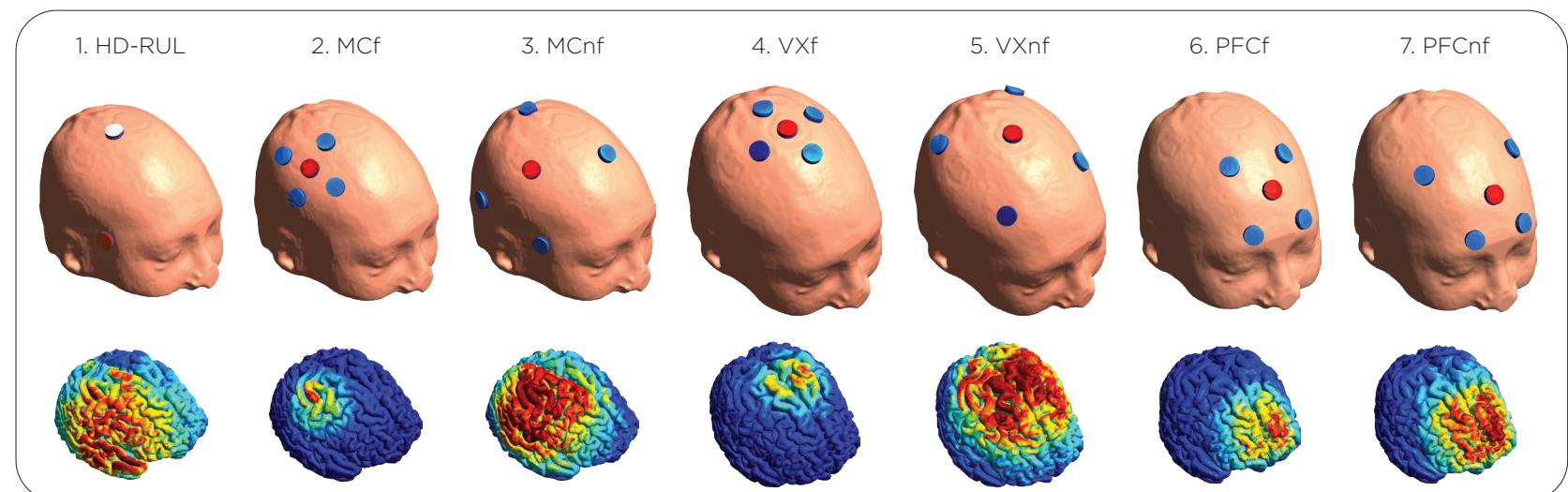
n = 10 completers

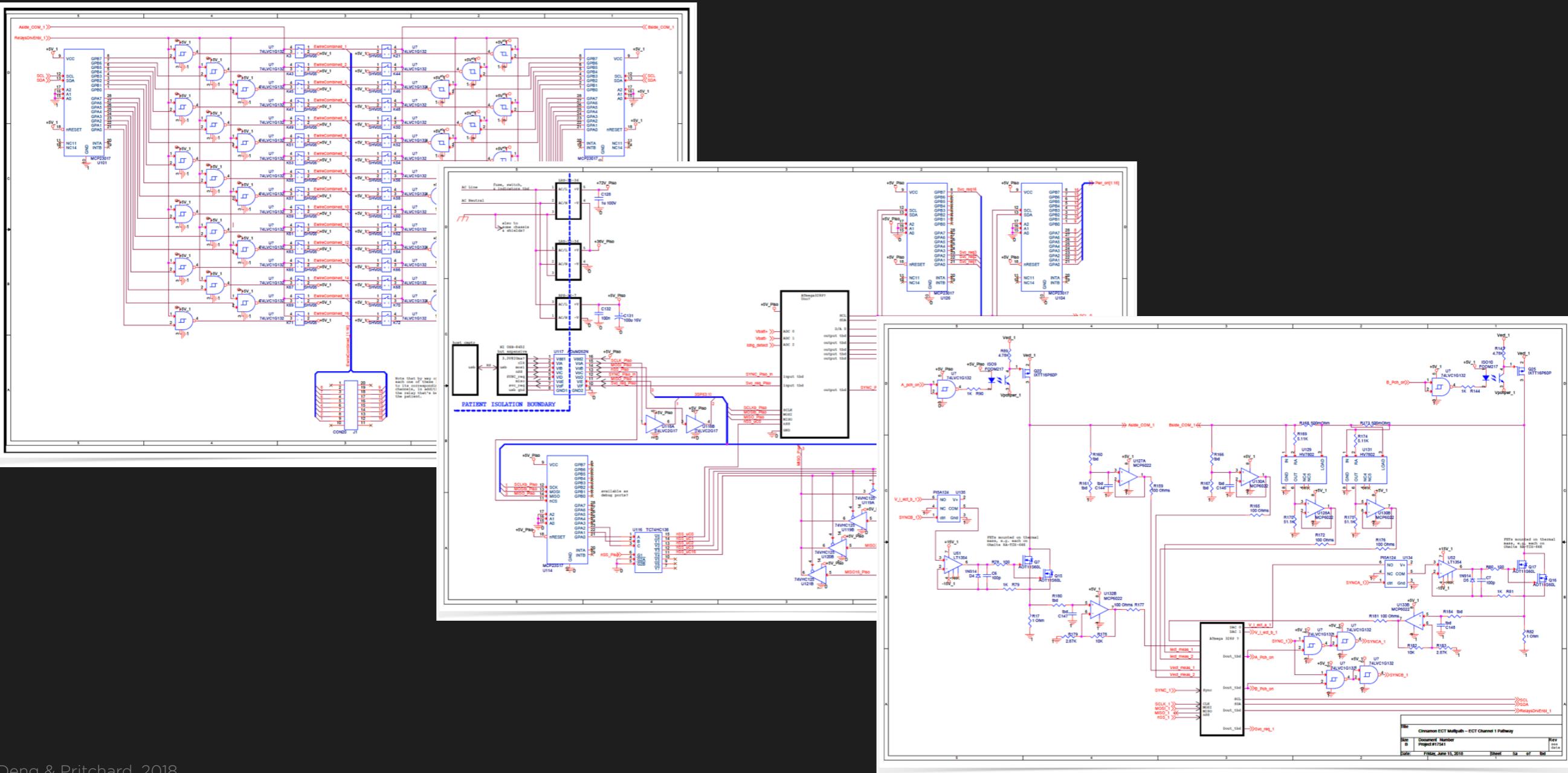
	Phase I: Baseline	Phase II: iLAST	Phase III: RUL ECT
Screening	Clinical & neurocognitive assessment with *video recording	Session 1-7: HD-RUL × 1, iECT-MC × 2, iECT-VX × 2, iECT-PFC × 2 (random order)	Standard course of RUL ECT + *full montage ictal EEG
Informed consent	Neuroimaging (MRI, DTI, *EEG-fMRI resting and task, *TMS-fMRI, *MEG) *Cortical excitability/plasticity assessment	Peri treatment assessment -Acute neurocog battery -Acute clinical assessment -*Video recording of neurocog/clinical assessment -resting EEG, *TMS-EP	Pre & Post acute course clinical/neurocog/ *neuroimaging/ *plasticity assessment Relapse prevention/maintainence

5 electrode adaptor



iLAST



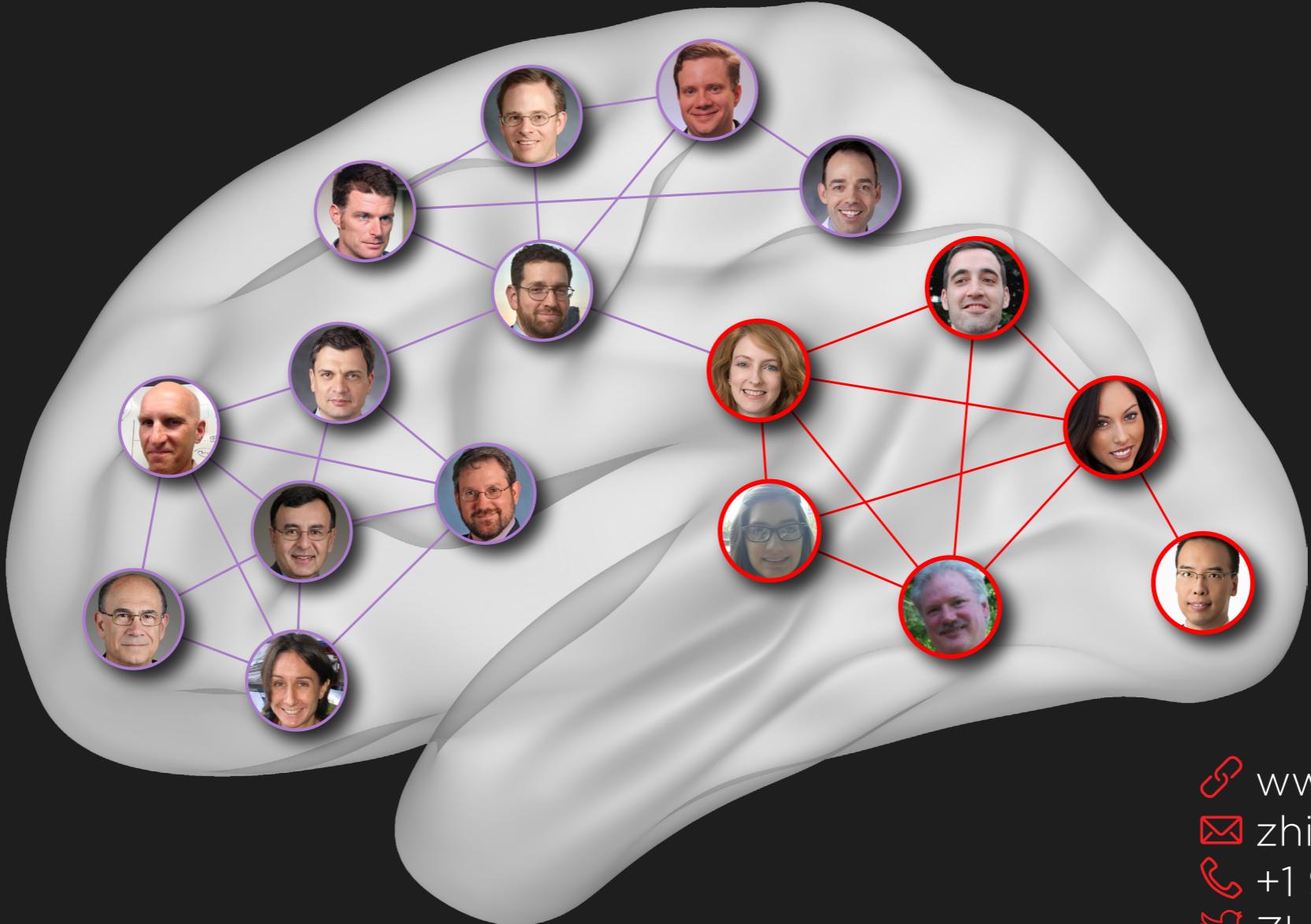


ECT 2.0

ECT X

~~ECT X~~ *ECT-Z*

...trademark pending...



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