Individualized Neurotargeted Seizure Therapy

Reengineering ECT

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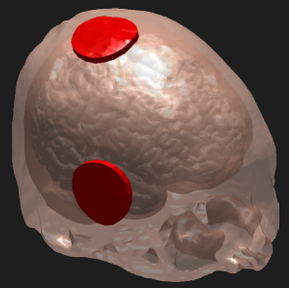
Disclosure

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.

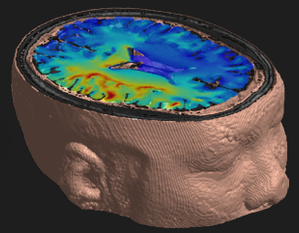
ECT in a nutshell

electrical stimulus

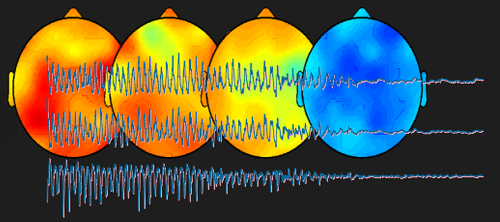
pulse generator



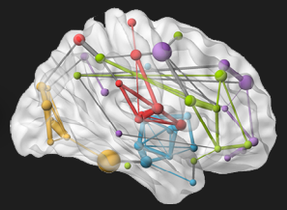
scalp electrodes



electric field in brain



generalized
tonic-clonic seizure



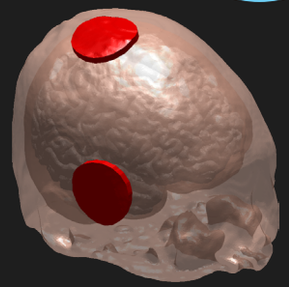
changes in brain
activity/connectivity

1

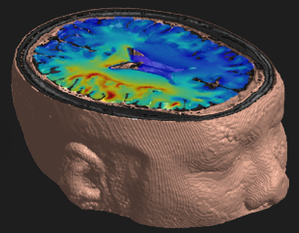
electrical stimulus

pulse generator

2

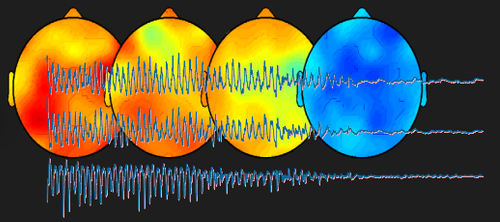


scalp electrodes



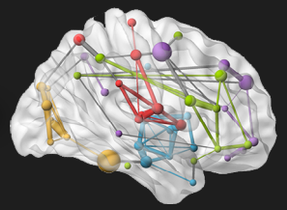
electric field in brain

3



generalized
tonic-clonic seizure

4



changes in brain
activity/connectivity

1

Current amplitude control

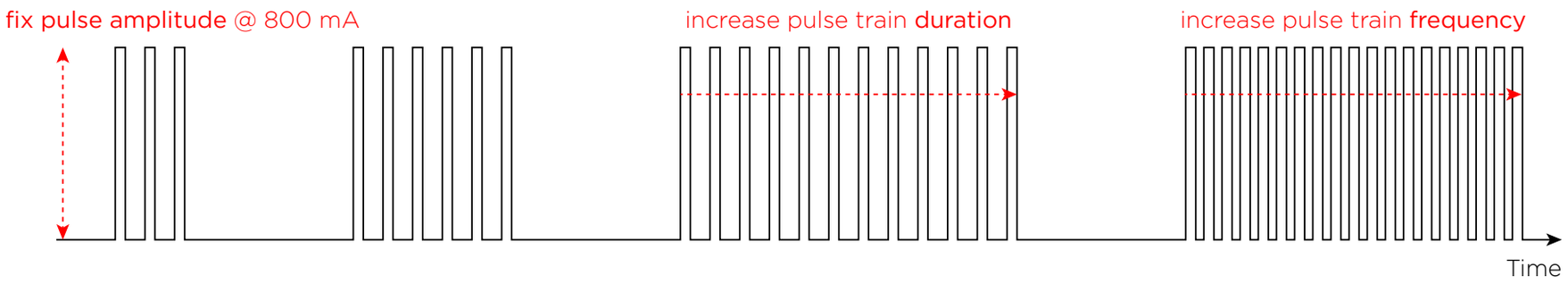
What current amplitude control?

1

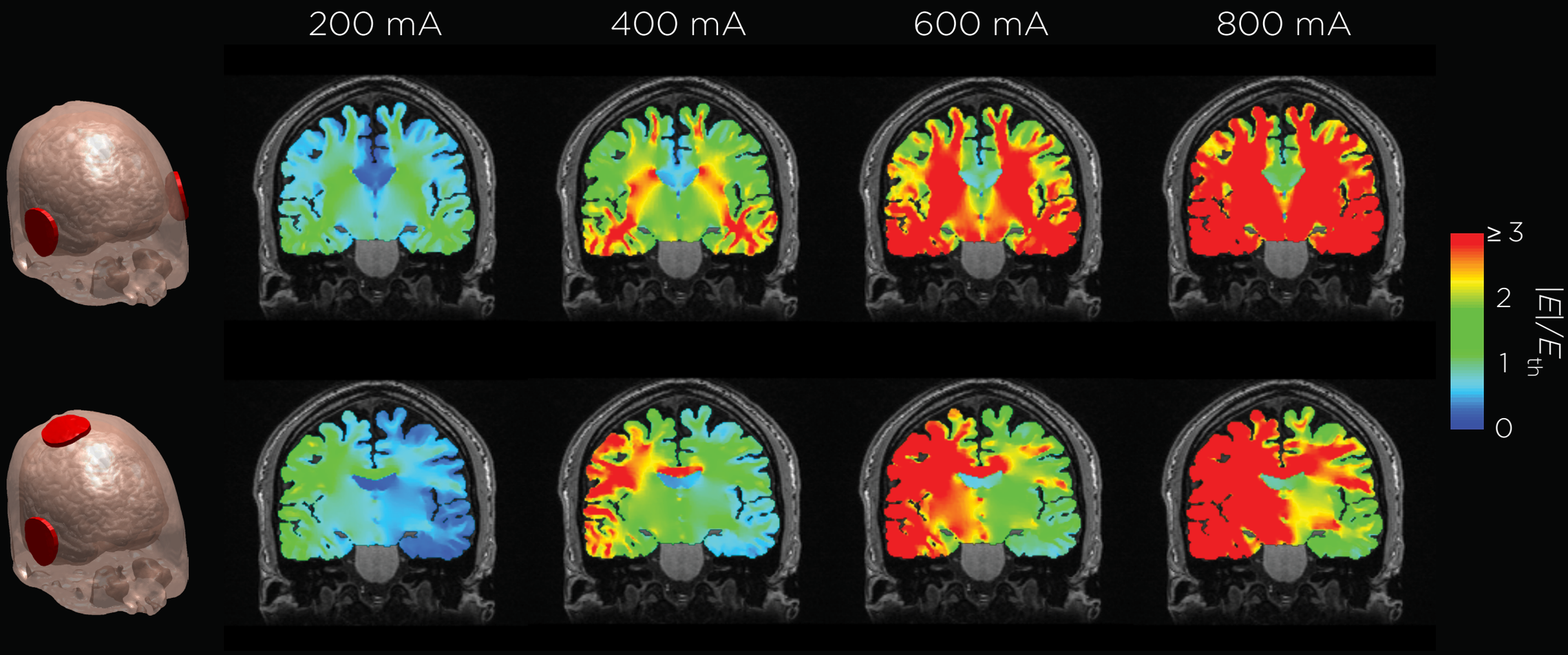
Conventional ECT titration

Increase train frequency and/or duration...

...with pulse amplitude fixed at 800 mA



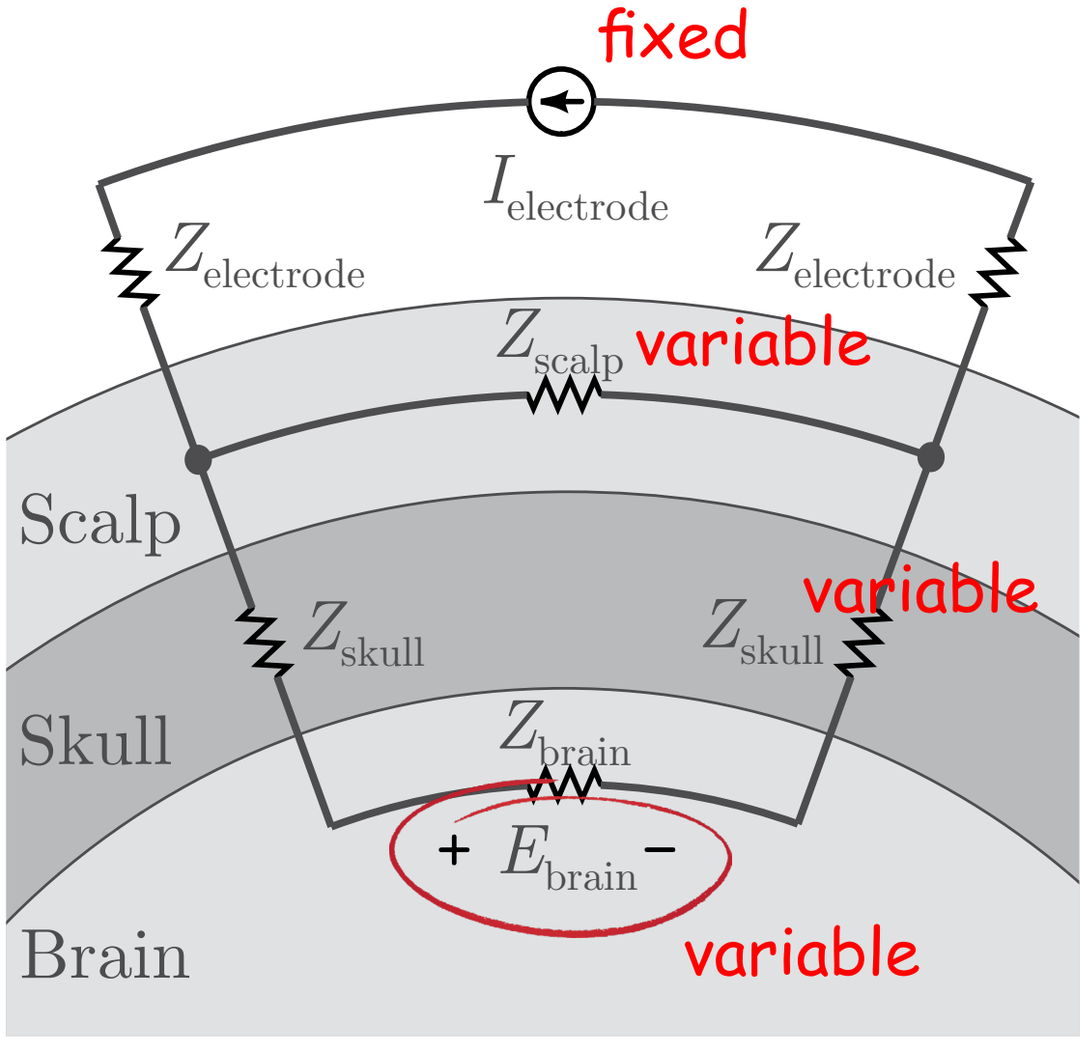
1 **High** current amplitude contributes to side effects



Deng et al., *J Neural Eng*, 2011; Lee at al., *Eur Psychiatry*, 2016

1

Fixed current amplitude
contributes to variability



1

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**."

1

“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.brainstimjrnl.com

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

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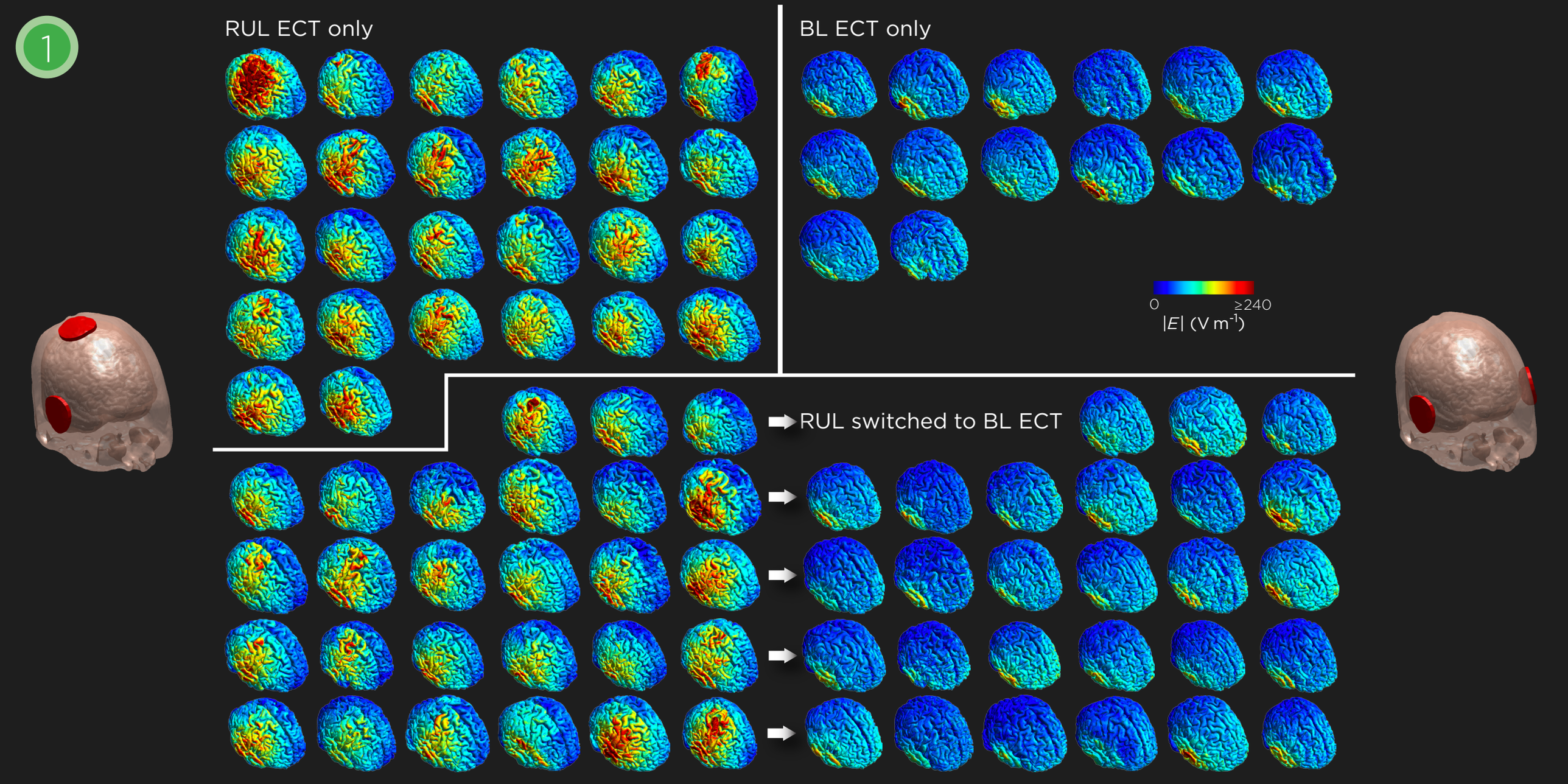
Facilitation

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 trans-cranial 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/cm^2). 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.

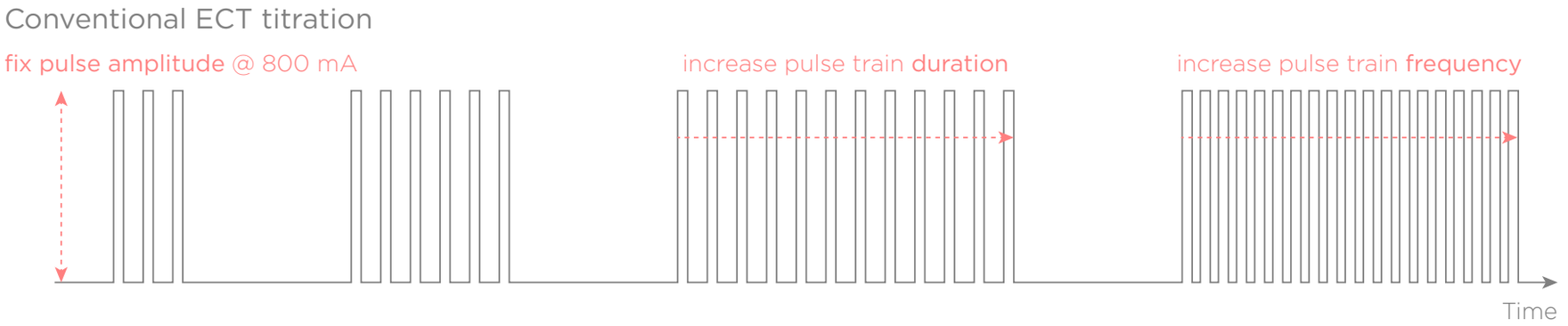

1
RUL ECT only
BL ECT only
0
≥240
|E| (V m-1)
RUL switched to BL ECT

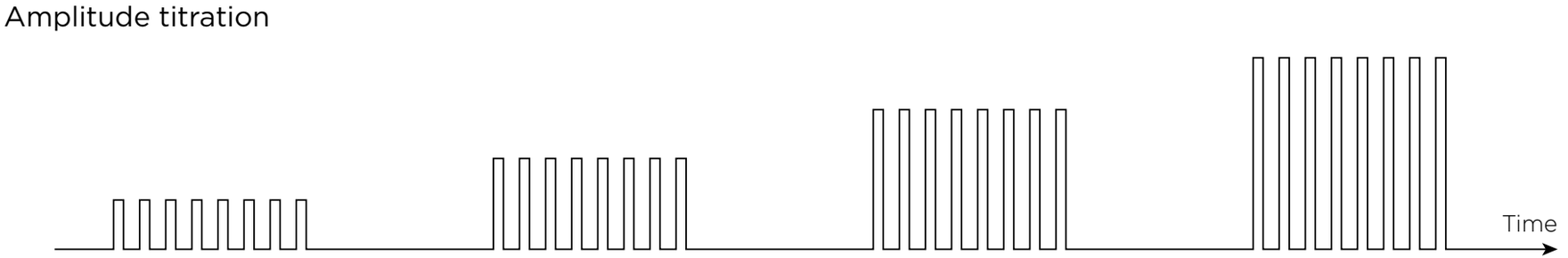
1

Titrate by current amplitude

Prevents overexposure of brain to suprathreshold stimulation

Compensates for variability in interindividual anatomy and excitability

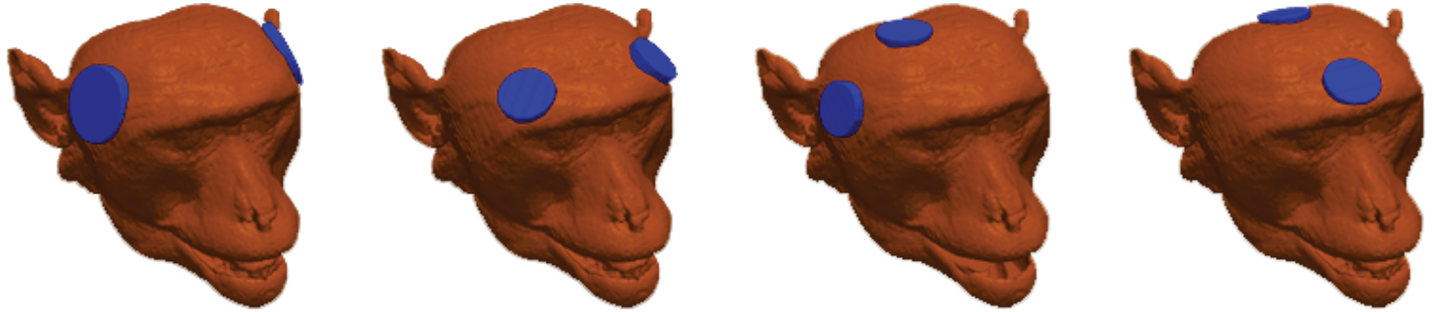


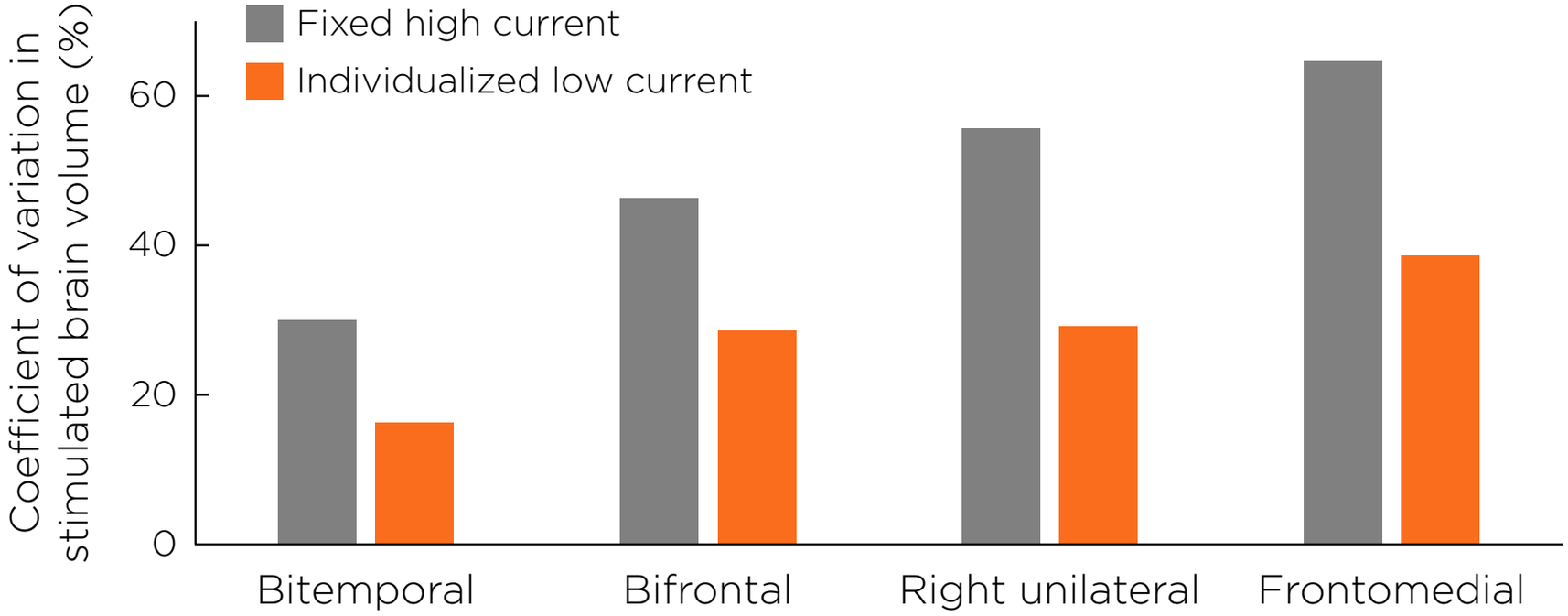


Deng et al. *JECT*, 2013

1

Individualized current ampltude titration: proof of concept





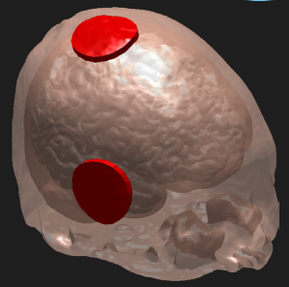
Recreate from Peterchev et al., *Neuropsychopharmacology*, 2015

1

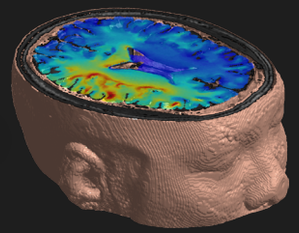
electrical stimulus

pulse generator

2

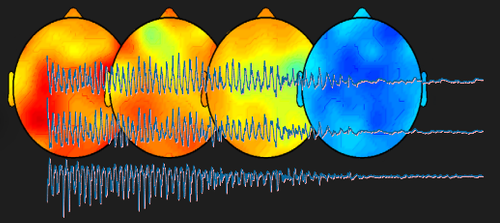


scalp electrodes



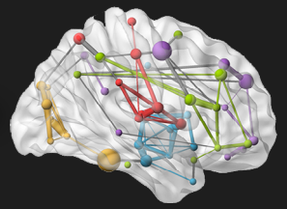
electric field in brain

3



generalized
tonic-clonic seizure

4

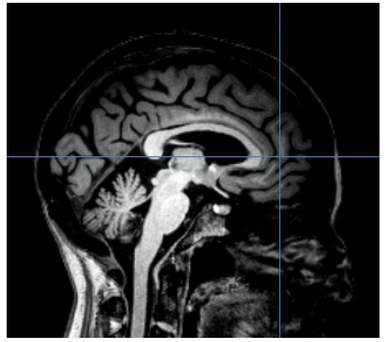


changes in brain
activity/connectivity

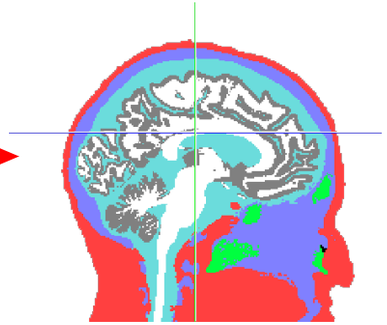
2

2

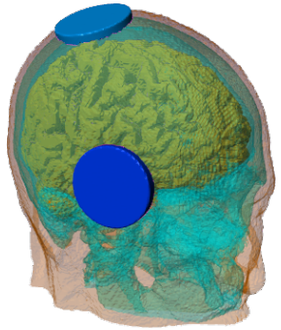
Computational electric field modeling



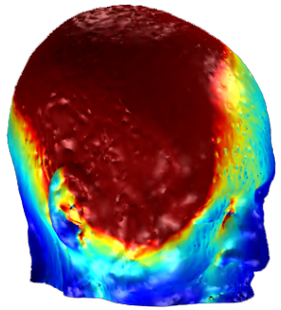
individual MRI



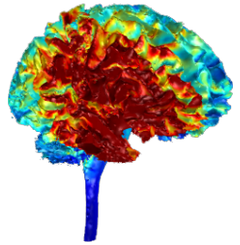
tissue segmentation



electrode geometry & placement

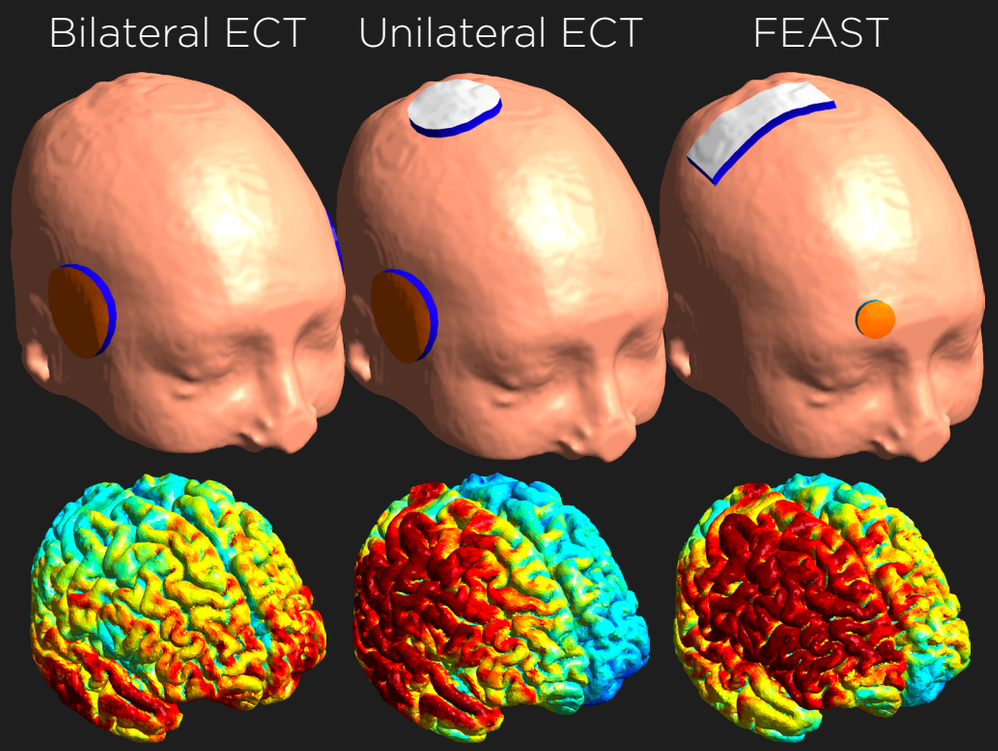


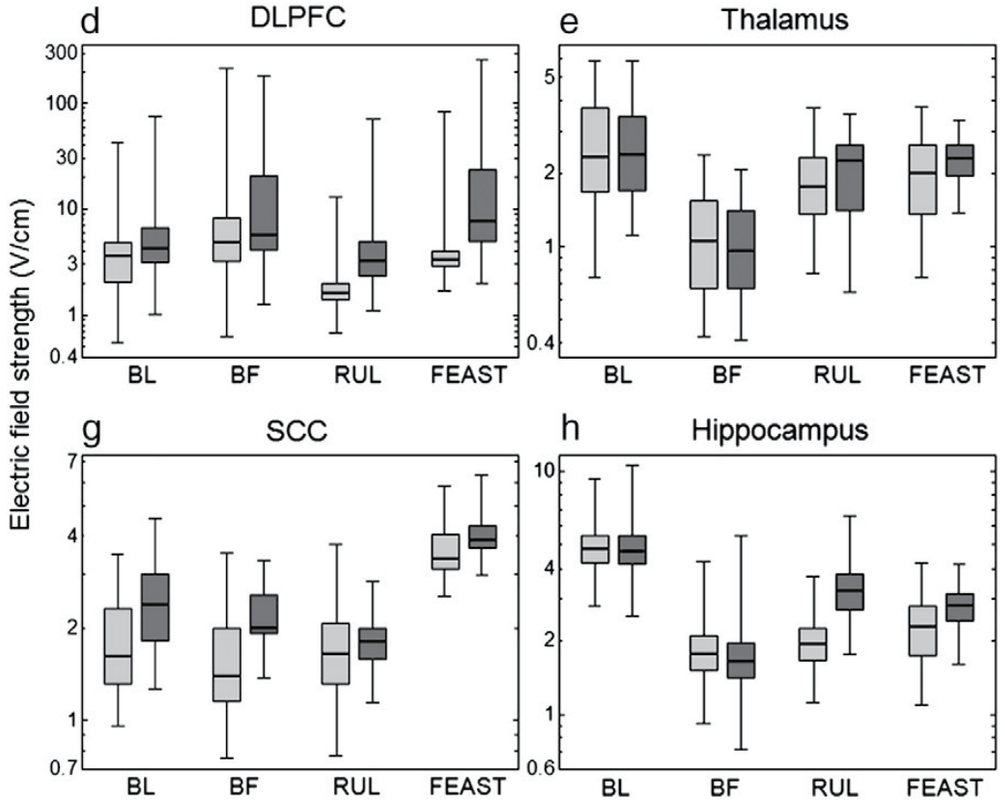
finite element solver



electric field analysis

2



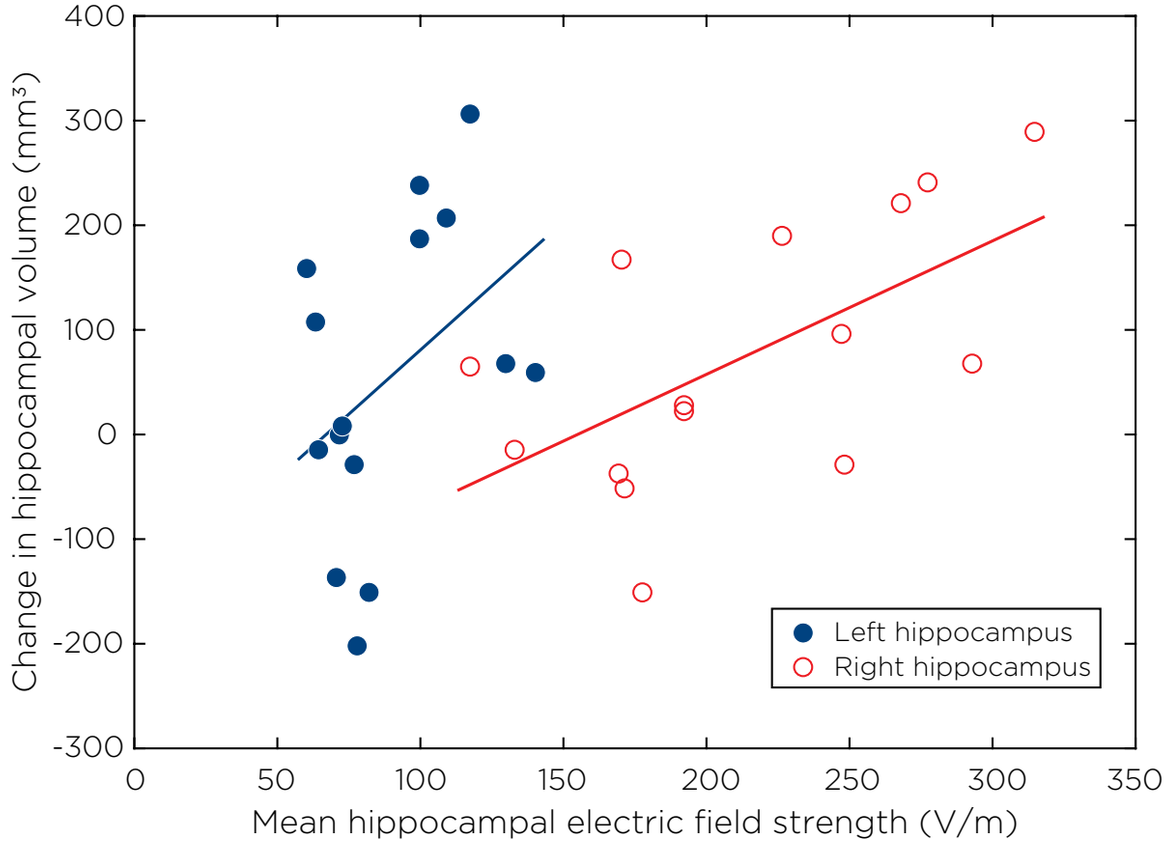


Deng et al. *ACNP*, 2009, Lee et al. *Neuroimage*, 2012

2

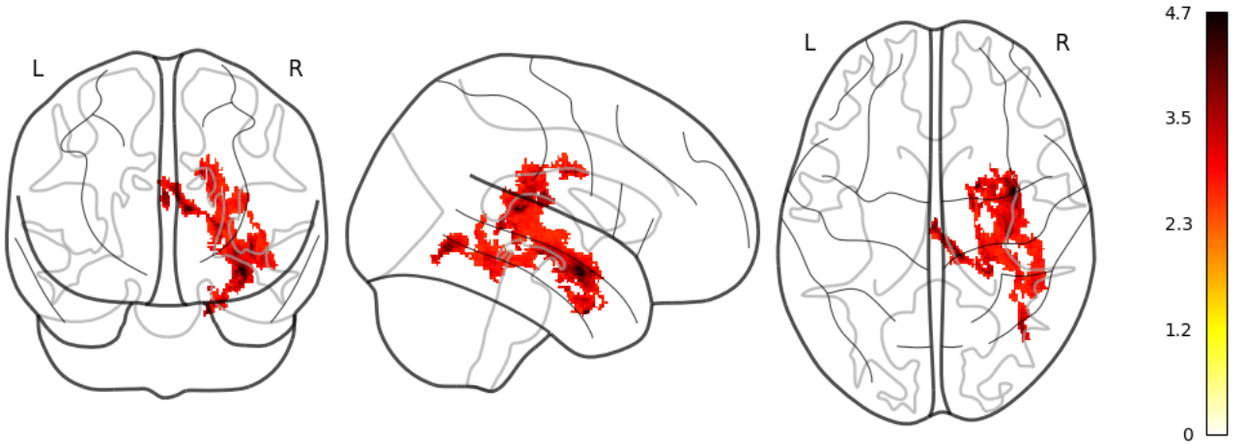
In actual ECT patients now…

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



Deng and Abbott, *ACNP*, 2016; U01 MH111826 (PI=Abbott)

2



67 bilateral ECT patients
@ Rijinstate Hospital in Arnhem, Netherlands

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

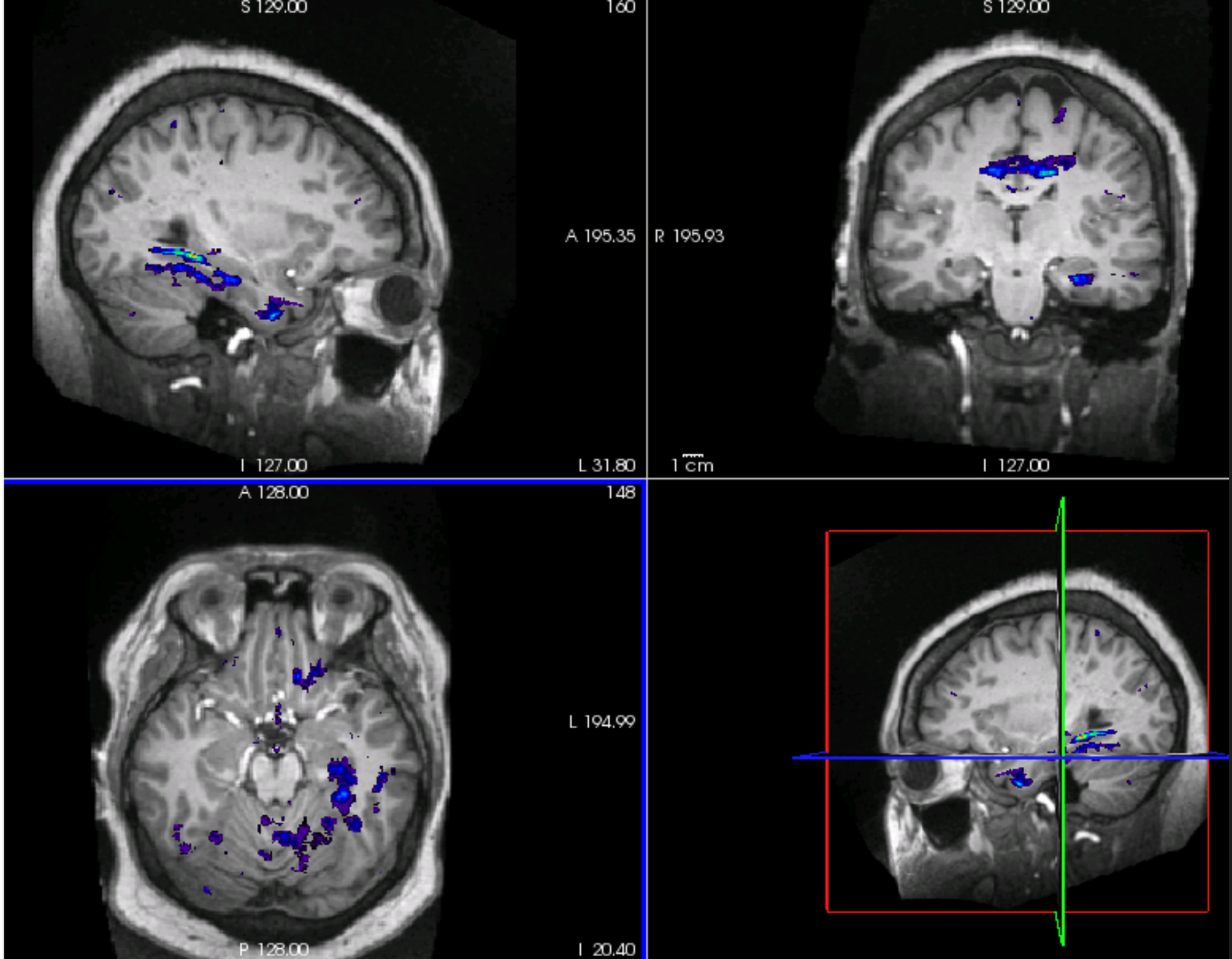
Deng, Axfjörð Fridgeirsson, Lilien, van Wingen, van Waarde, in submission

2

Global ECT-MRI Research Collaboration (GEMRIC) data

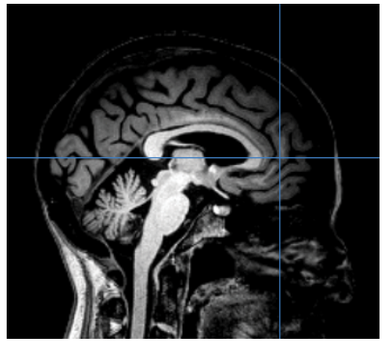
RUL ECT Responder
ΔMADRS > 50%, N = 103
Nonresponder
ΔMADRS < 30%, N = 68

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

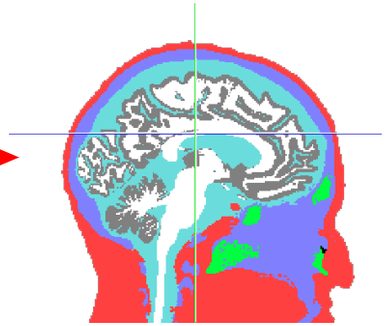


2

Run this backwards...



individual MRI



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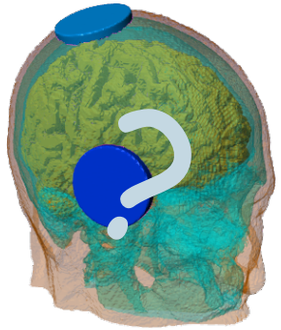
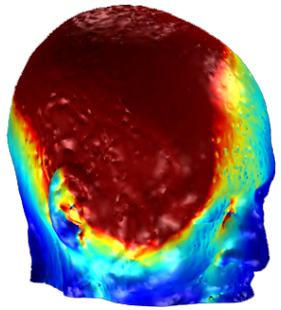
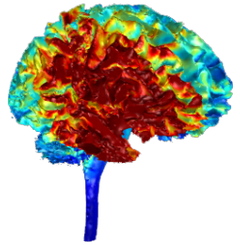


electrode geometry
& placement



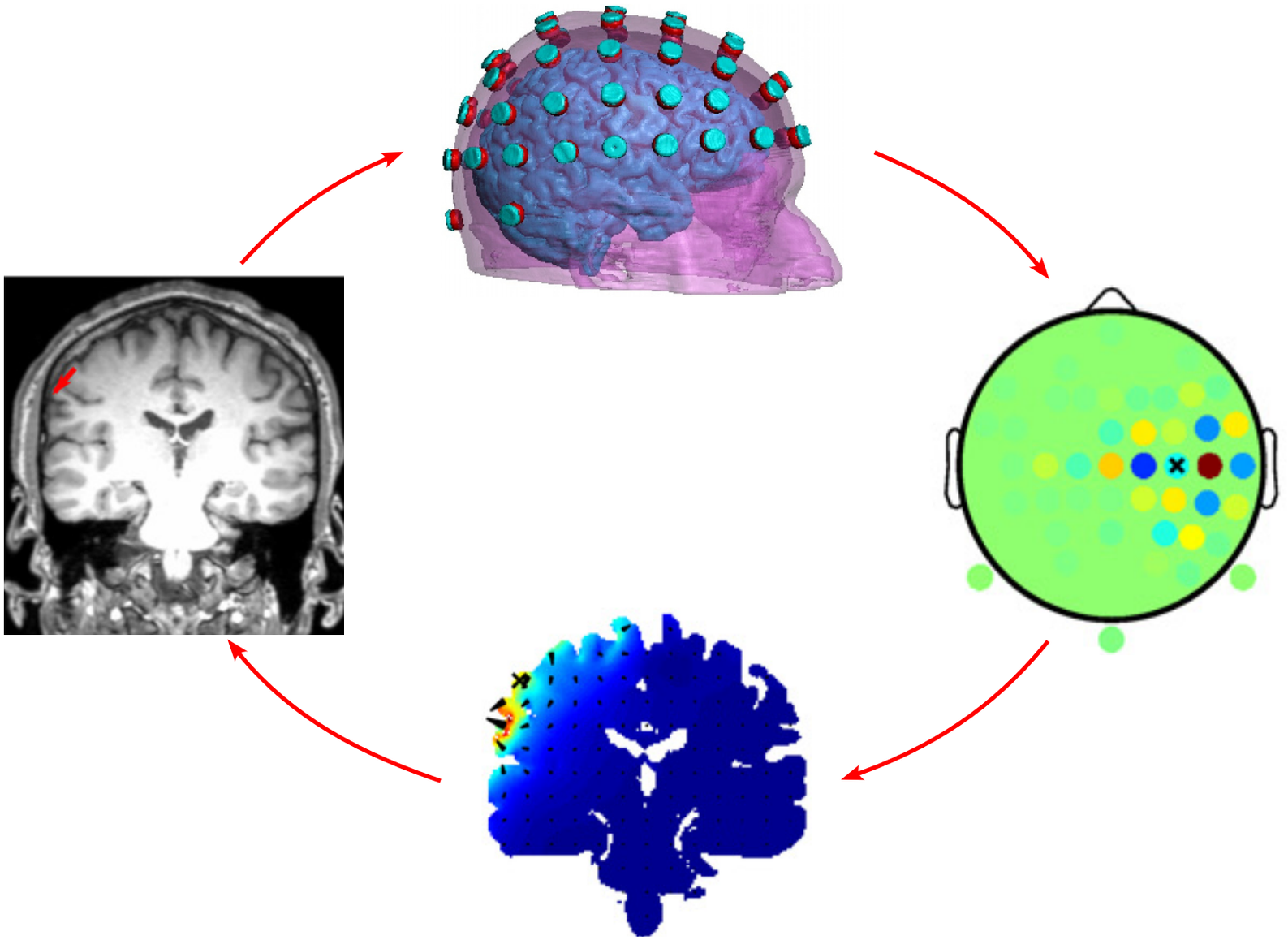
finite element solver



electric field analysis

2

Multielectrode optimization



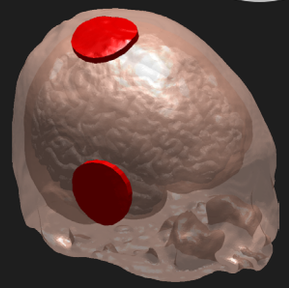
Dmochowski et al., *J Neural Eng*, 2011

1

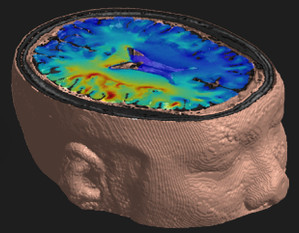
electrical stimulus

pulse generator

2

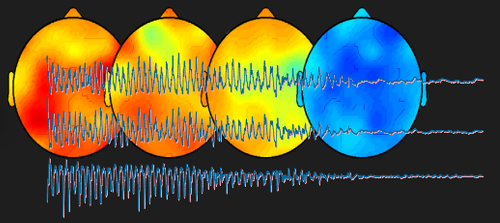


scalp electrodes



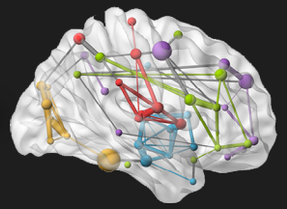
electric field in brain

3



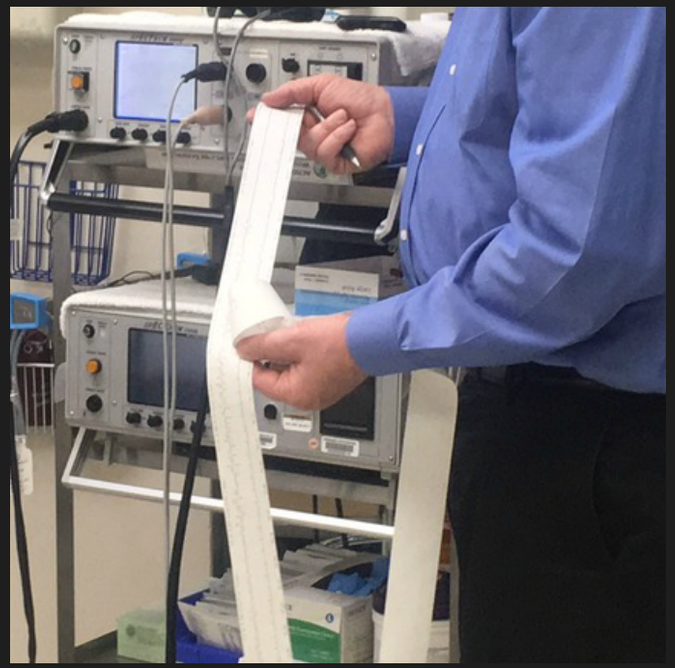
generalized
tonic-clonic seizure

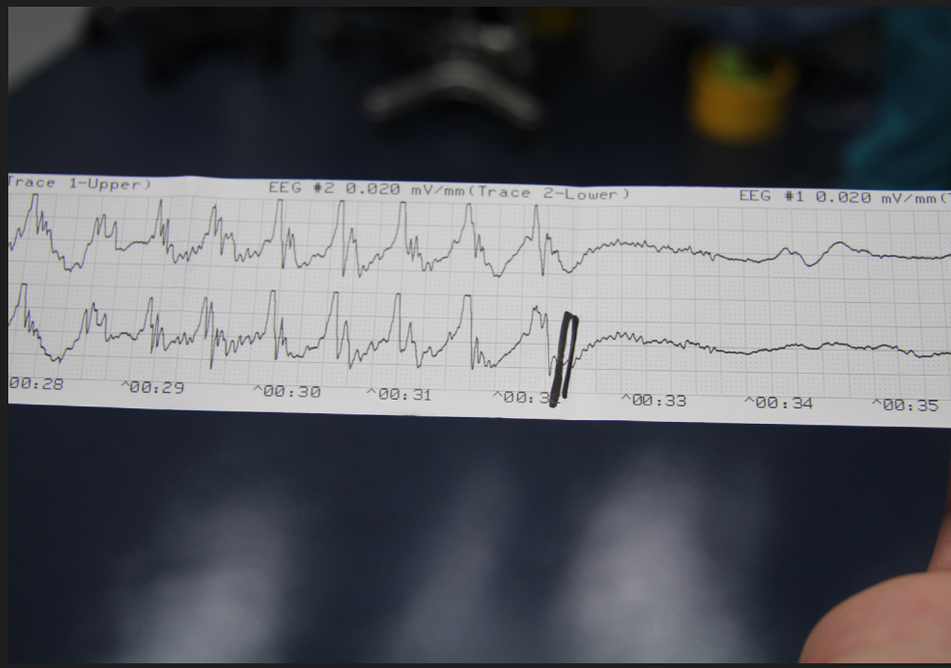
4



changes in brain
activity/connectivity

3 Understanding seizure topography





3 Really?

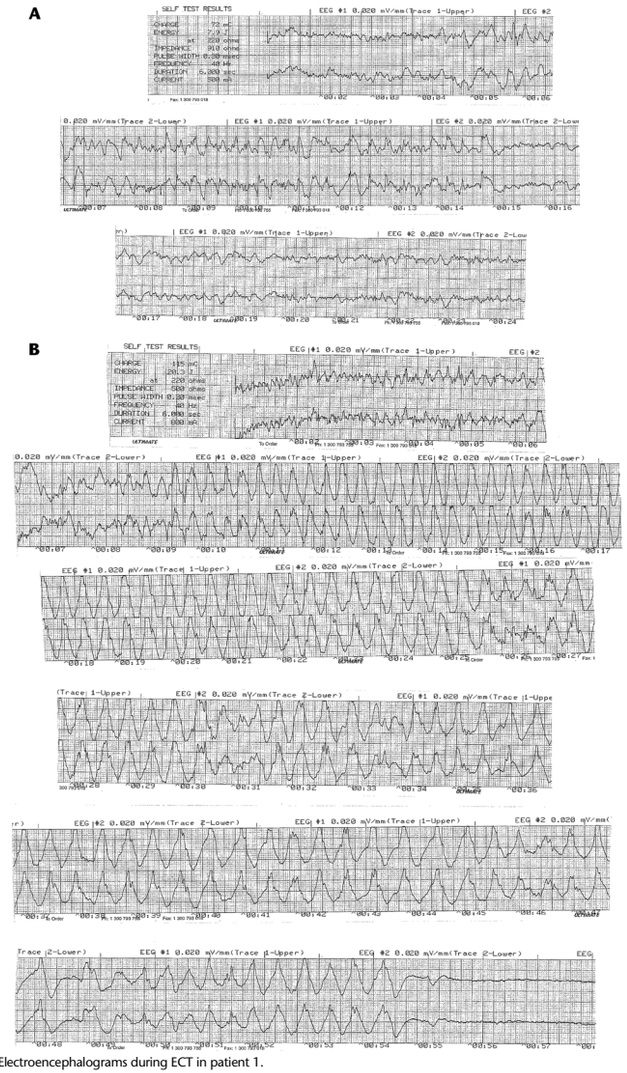


FIGURE 1. Electroencephalograms during ECT in patient 1.

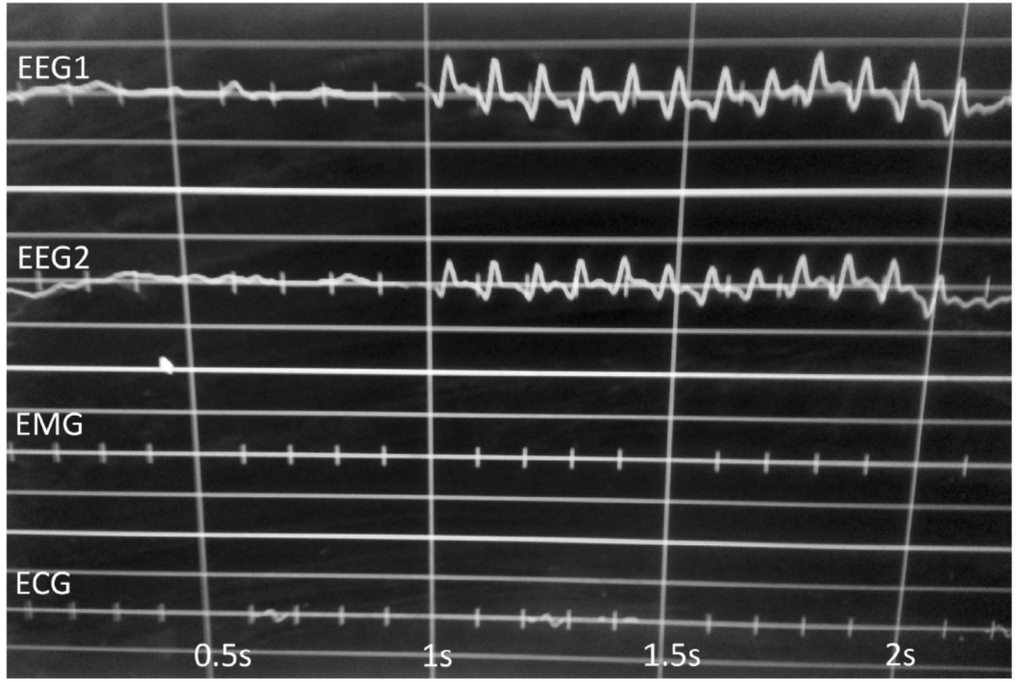
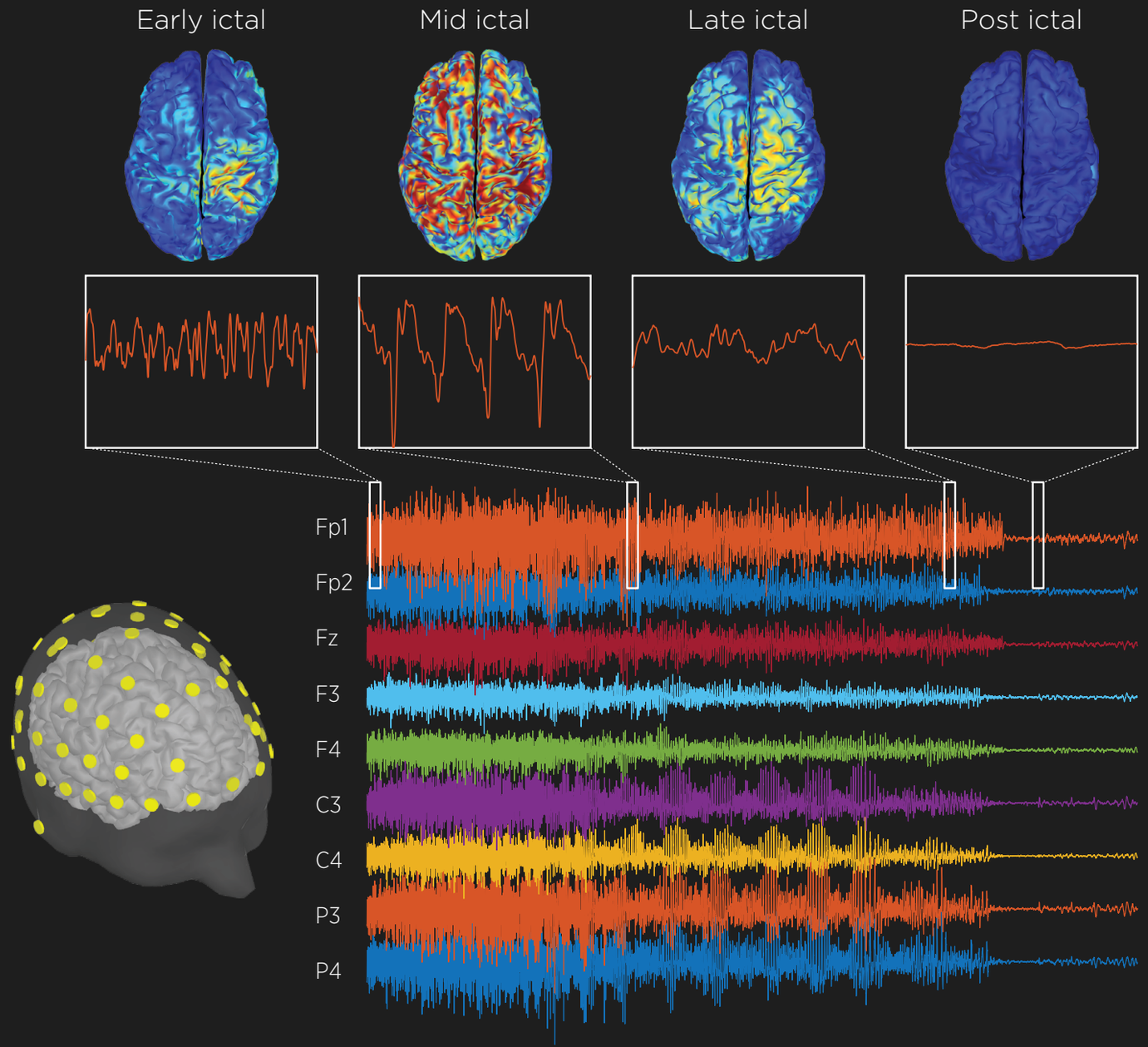


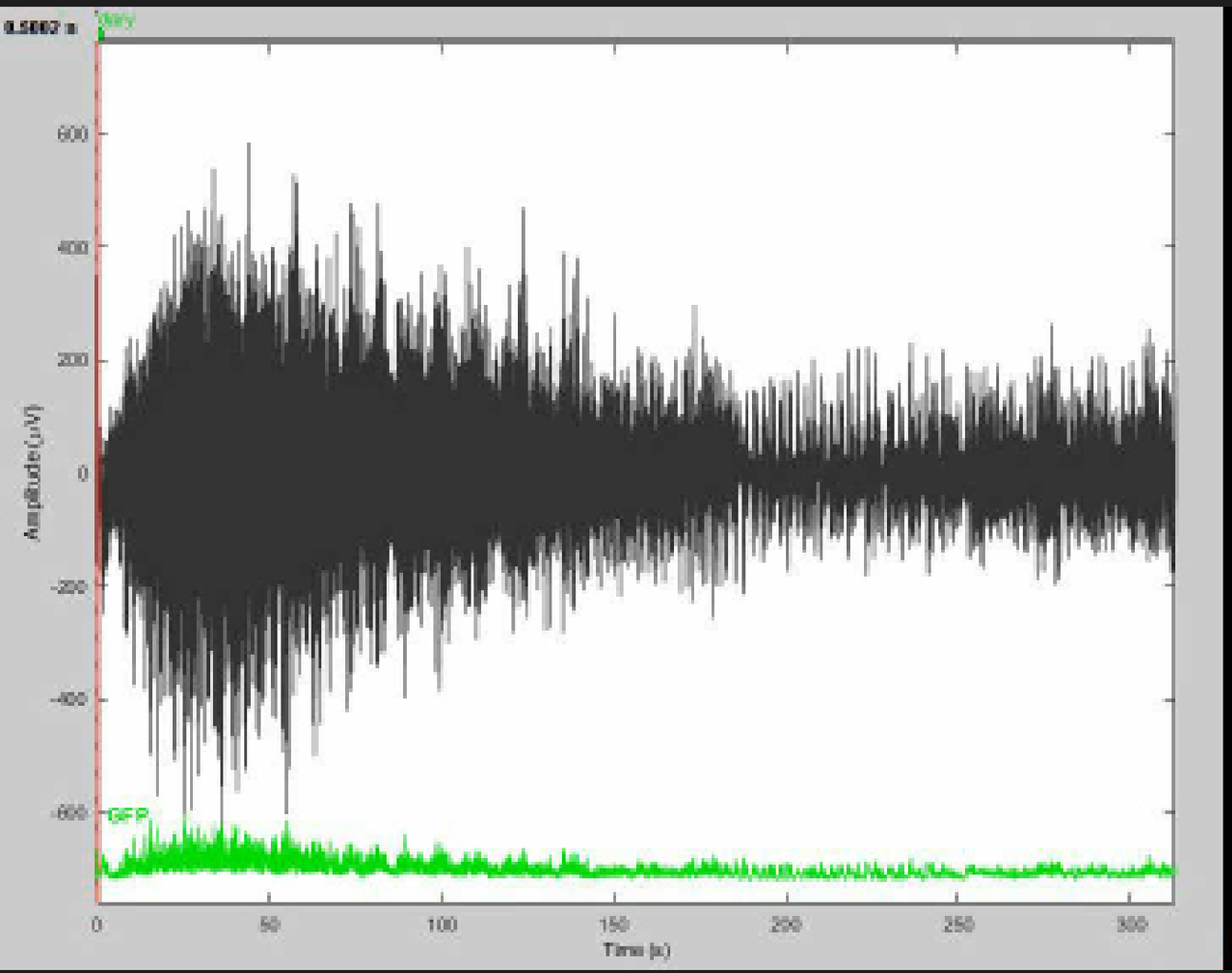
FIGURE 1. Real-time image on a computer monitor attached to the ECT device after resolution of seizure, with muscle artifact appearing on EEG1 and EEG2.

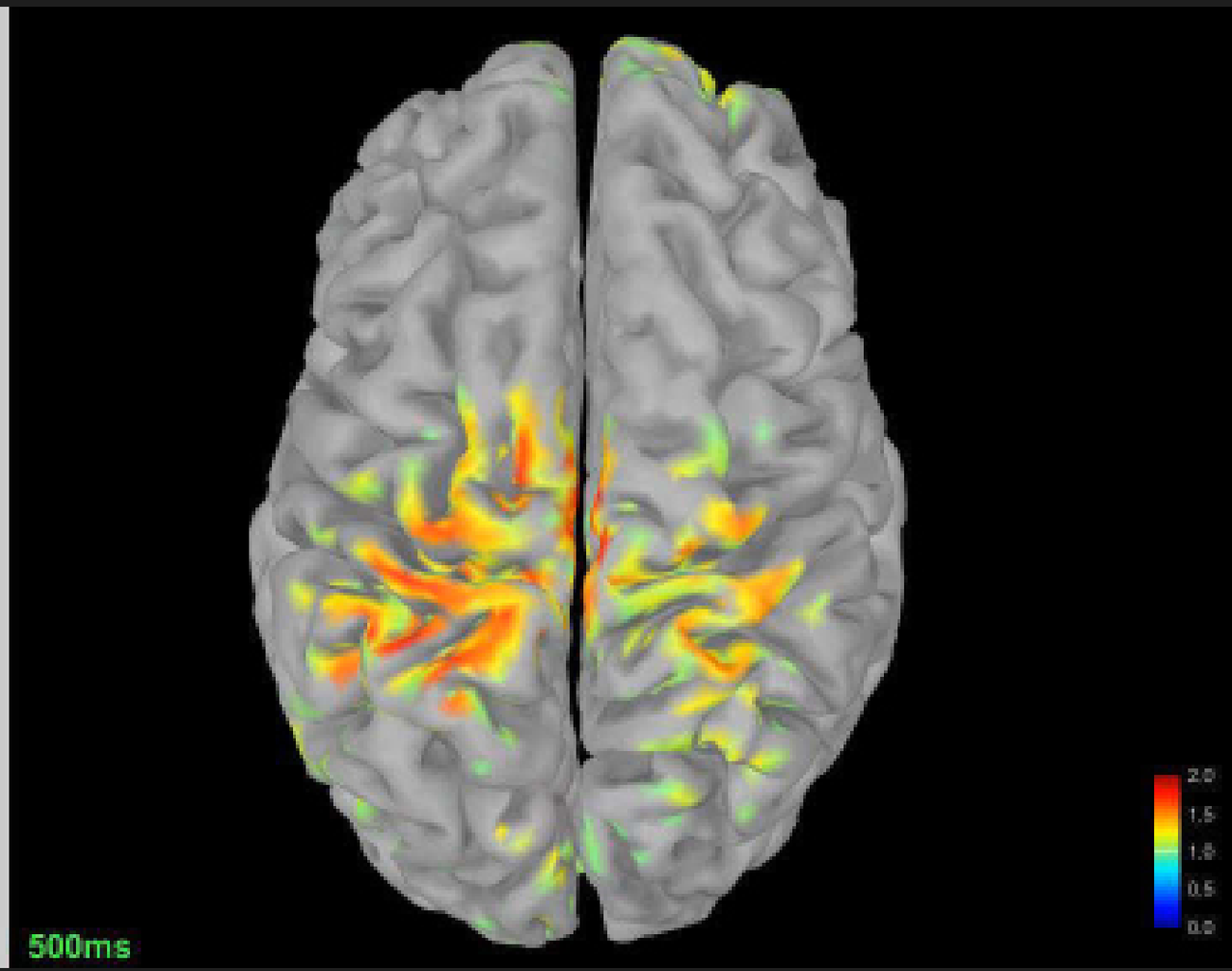
3



Deng et al., *unpublished*

3





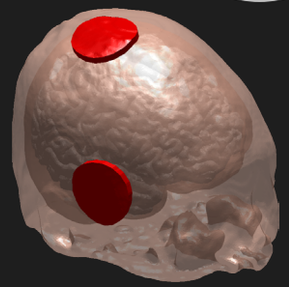
Deng et al., *unpublished*

1

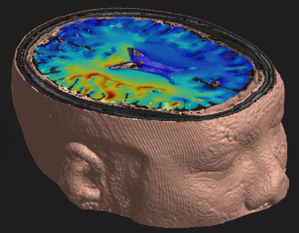
electrical stimulus

pulse generator

2

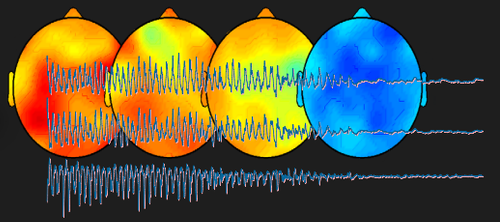


scalp electrodes



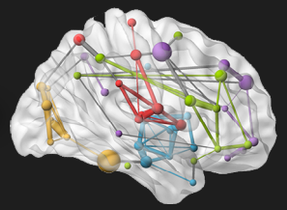
electric field in brain

3



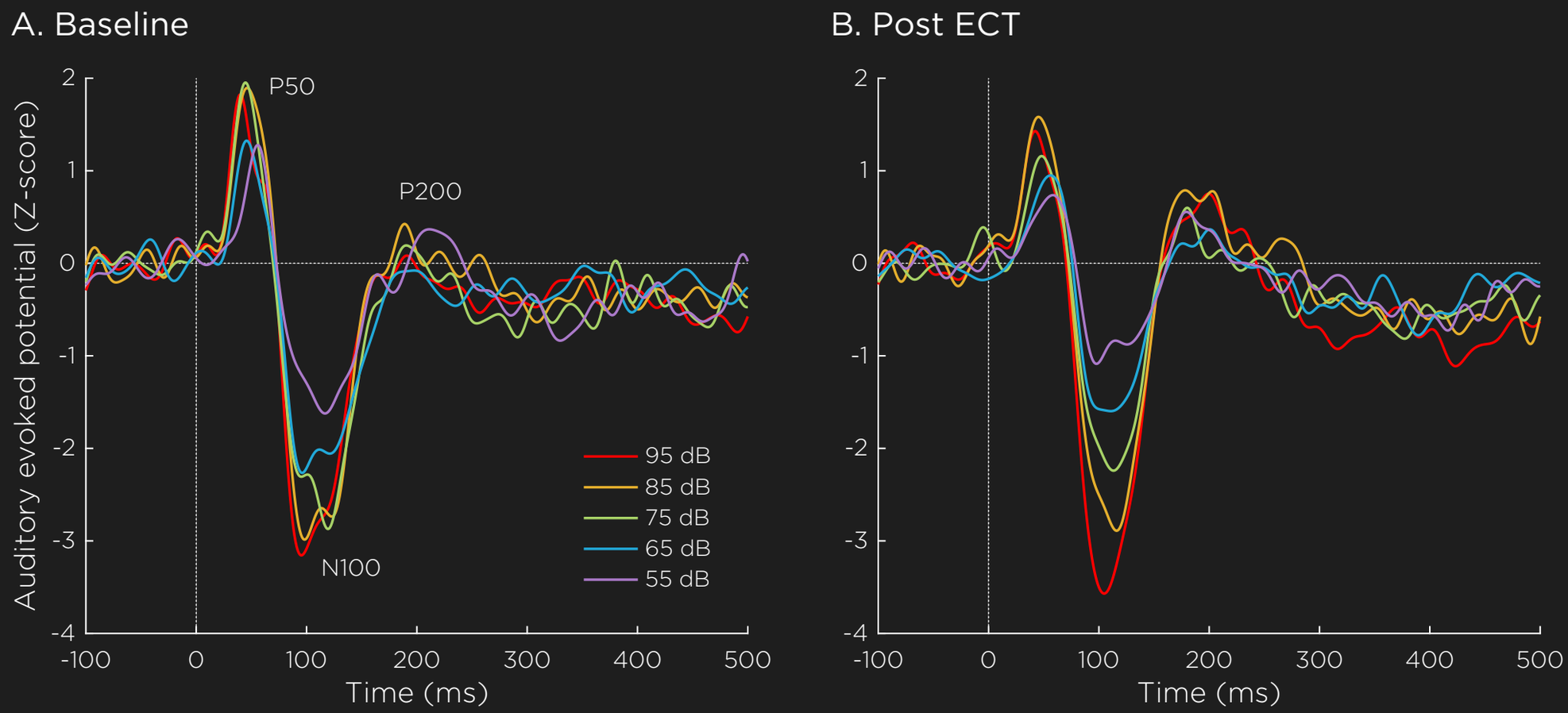
generalized
tonic-clonic seizure

4



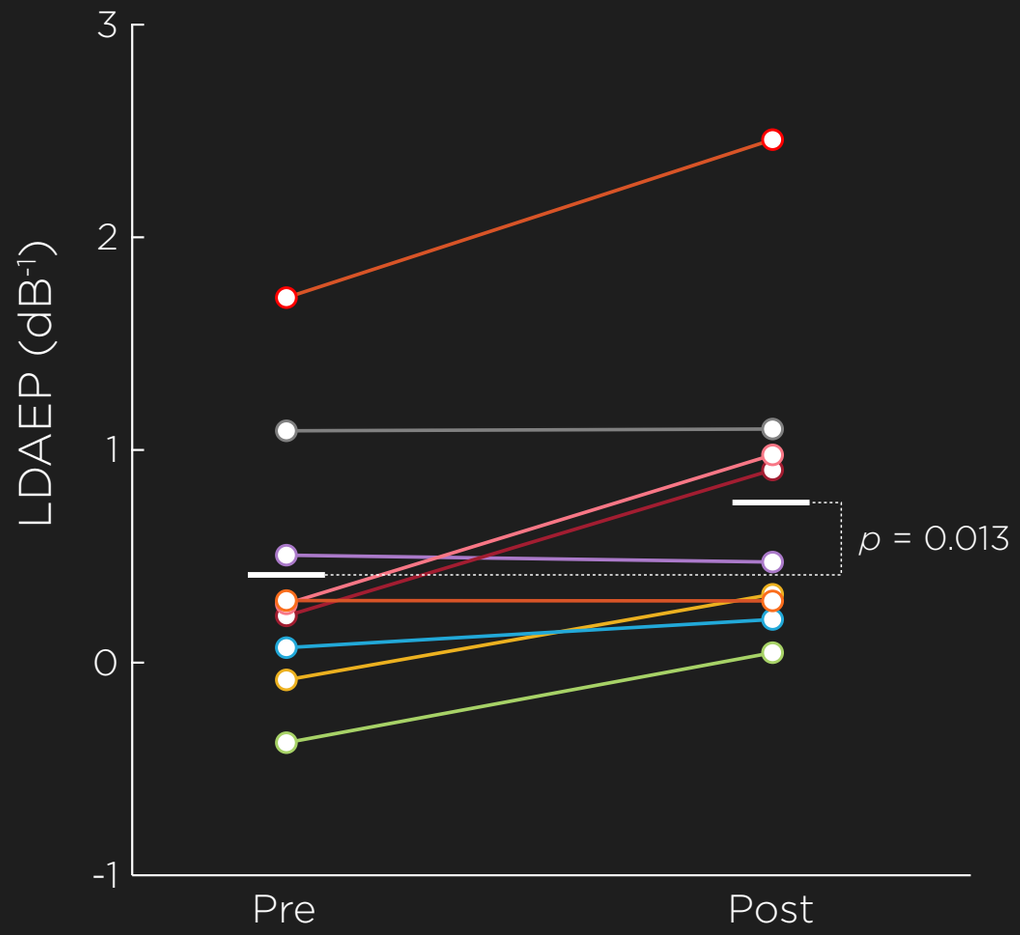
changes in brain
activity/connectivity

4 Loudness Dependence of Auditory Evoked Potentials

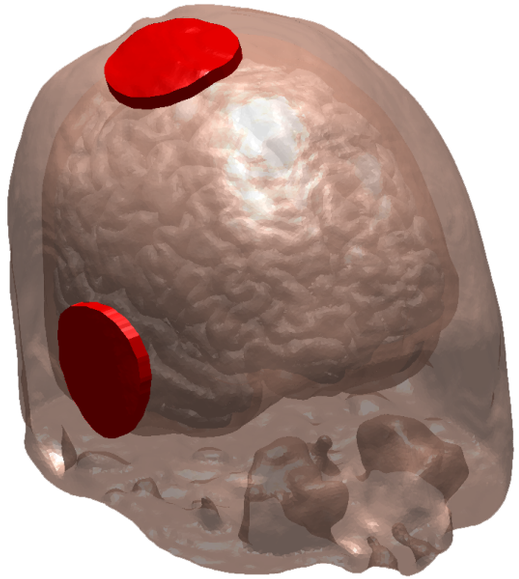


Deng et al., *ACNP*, 2018

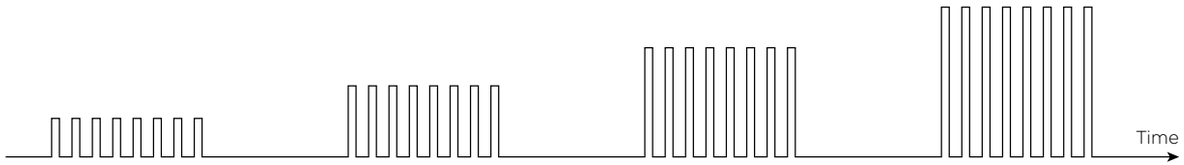
4 Loudness Dependence of Auditory Evoked Potentials



Deng et al., *ACNP*, 2018



Amplitude titration



Next generation ECT

Individualized

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

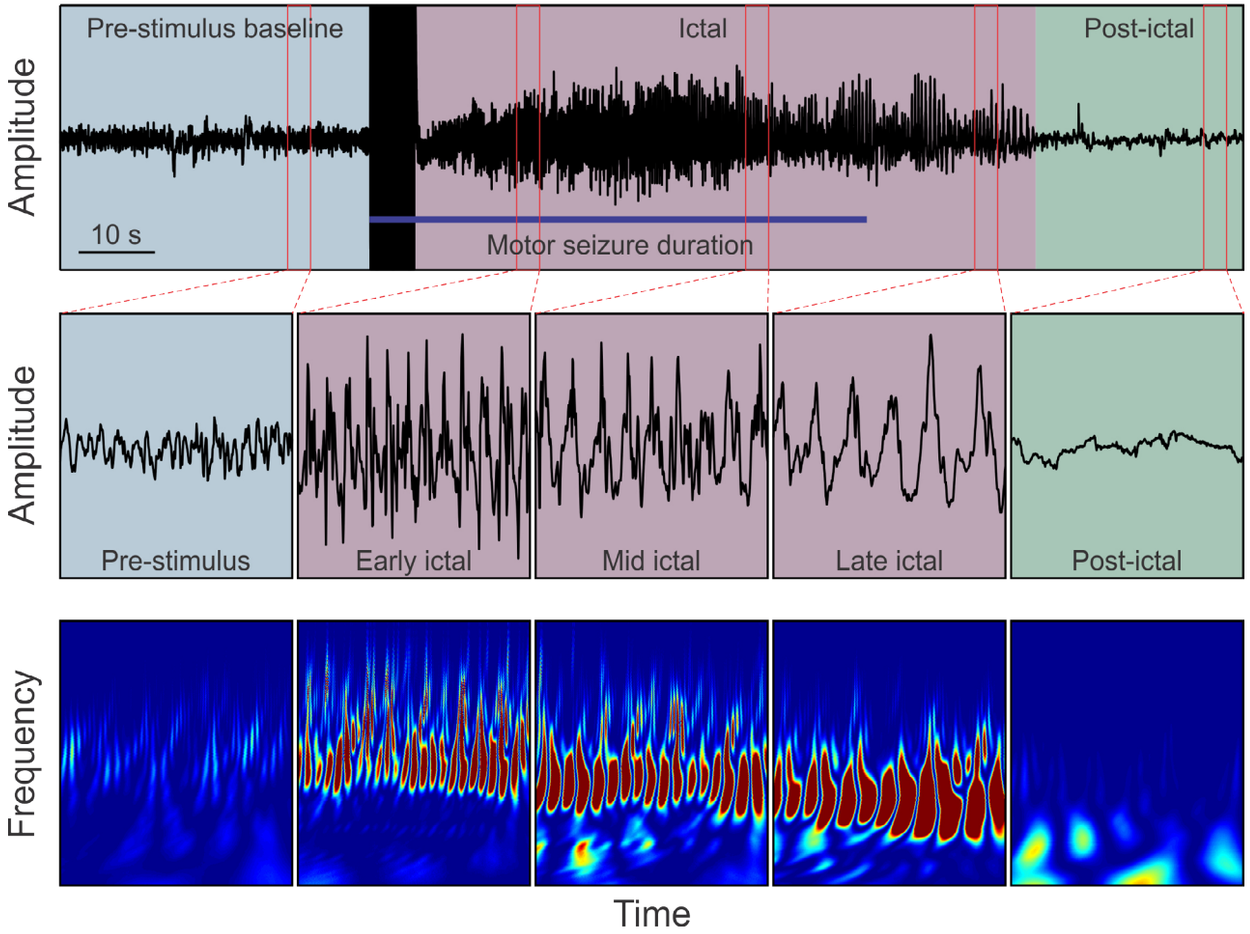
Next generation ECT

Individualized

- subject-specific head model
- pulse amplitude titration

Neurotargeted

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



Next generation ECT

Individualized

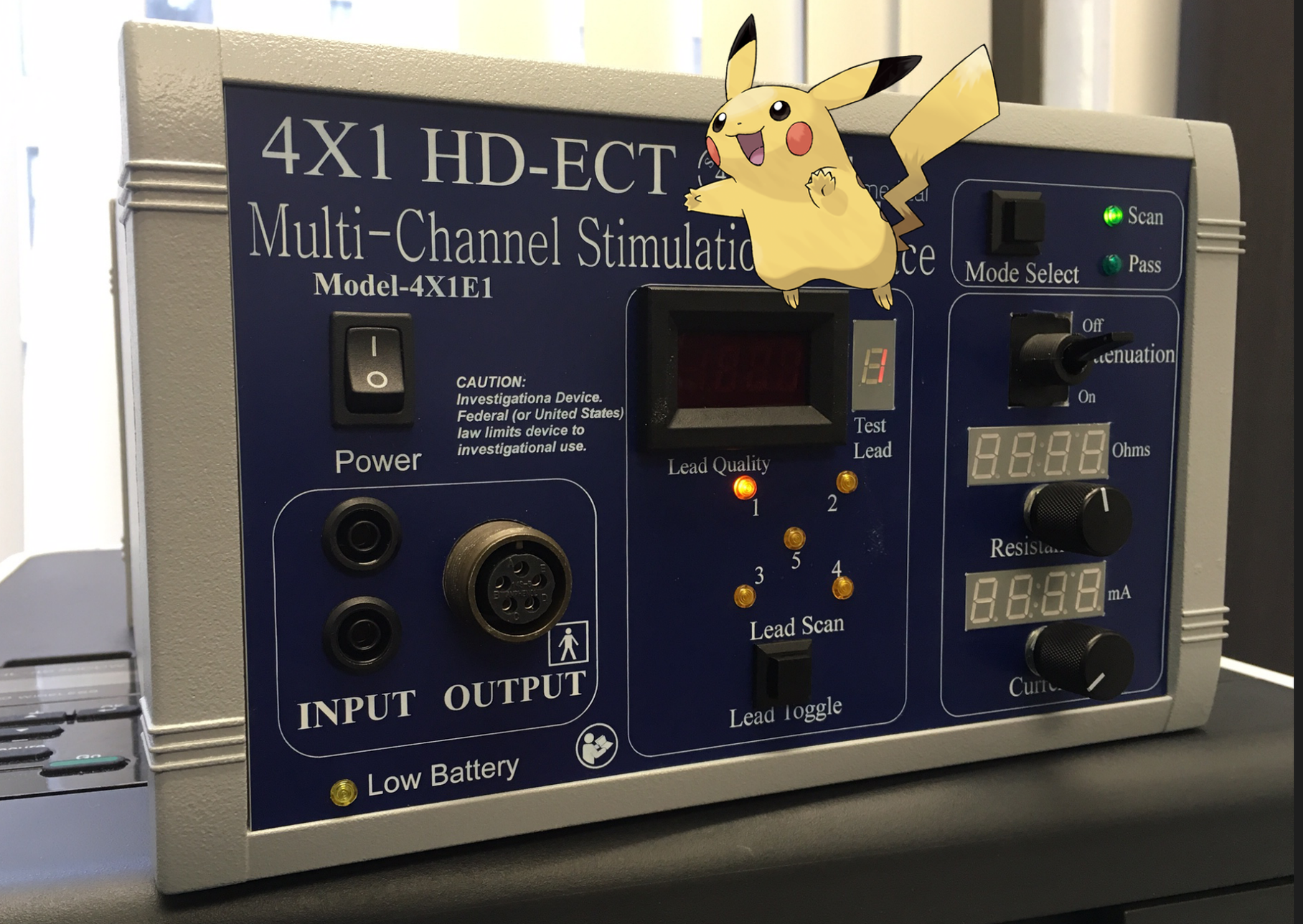
- § subject-specific head model
- § pulse amplitude titration

Neurotargeted

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

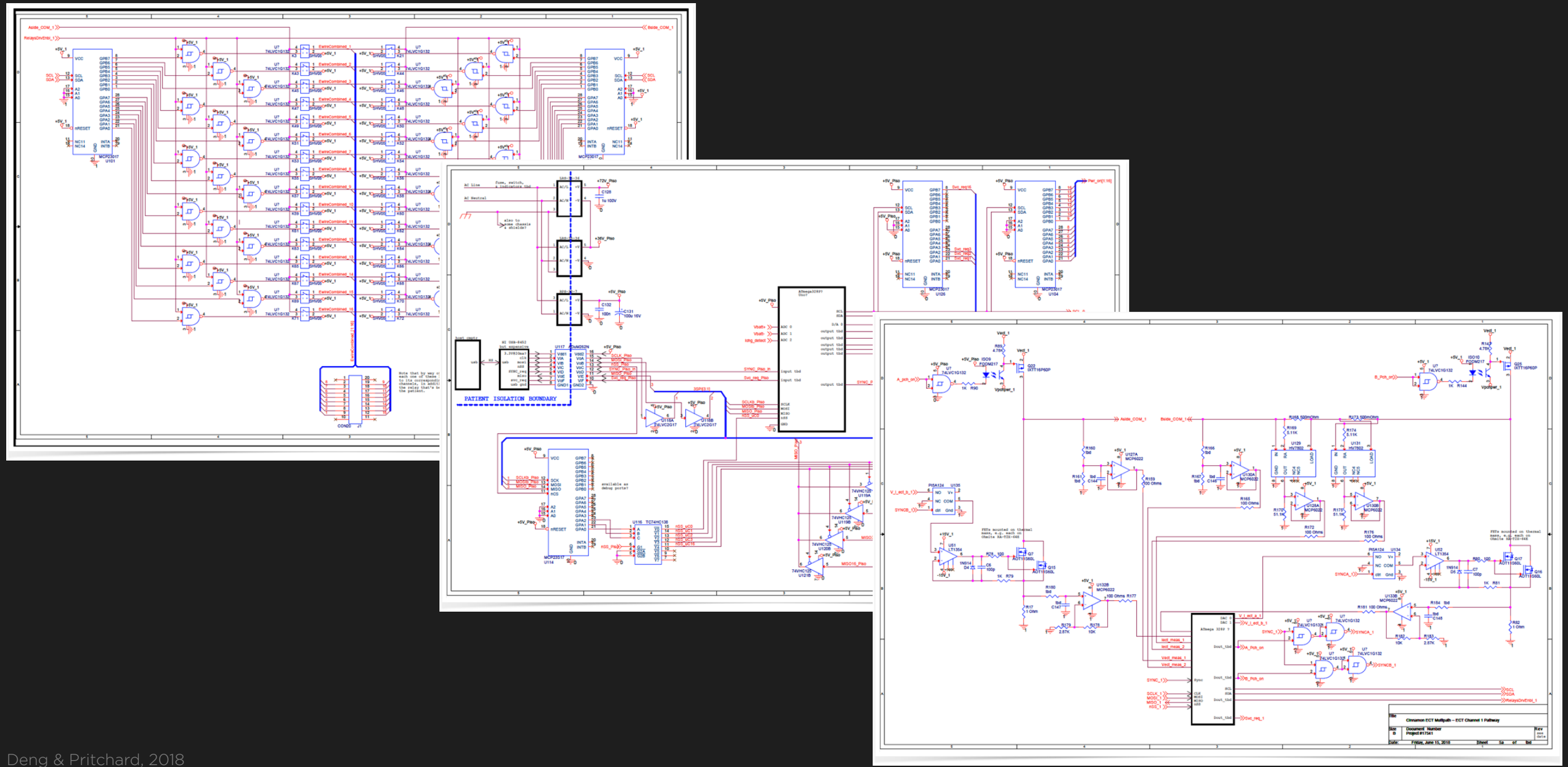
Dynamic seizure sculpting

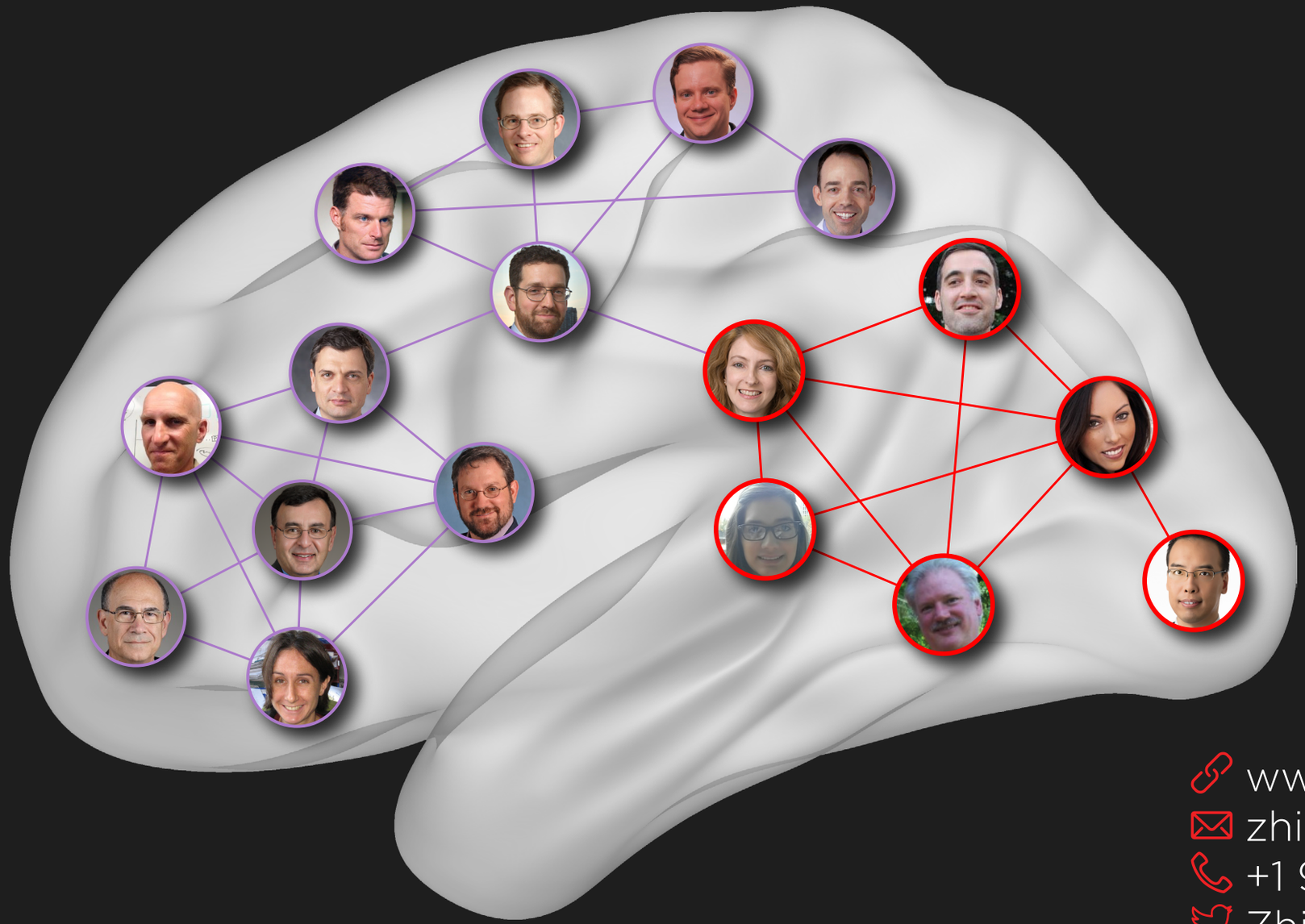
- § topographical seizure analysis
- § online modulation of seizure



4x1 adaptor, passively splits current

First-in-human trial this fall @ NIH


PATIENT ISOLATION BOUNDARY
Cinnamon ECT Multipath – ECT Channel 1 Pathway



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