Effect of anatomical variability on electric field characteristics of tES

A realistic head modeling study

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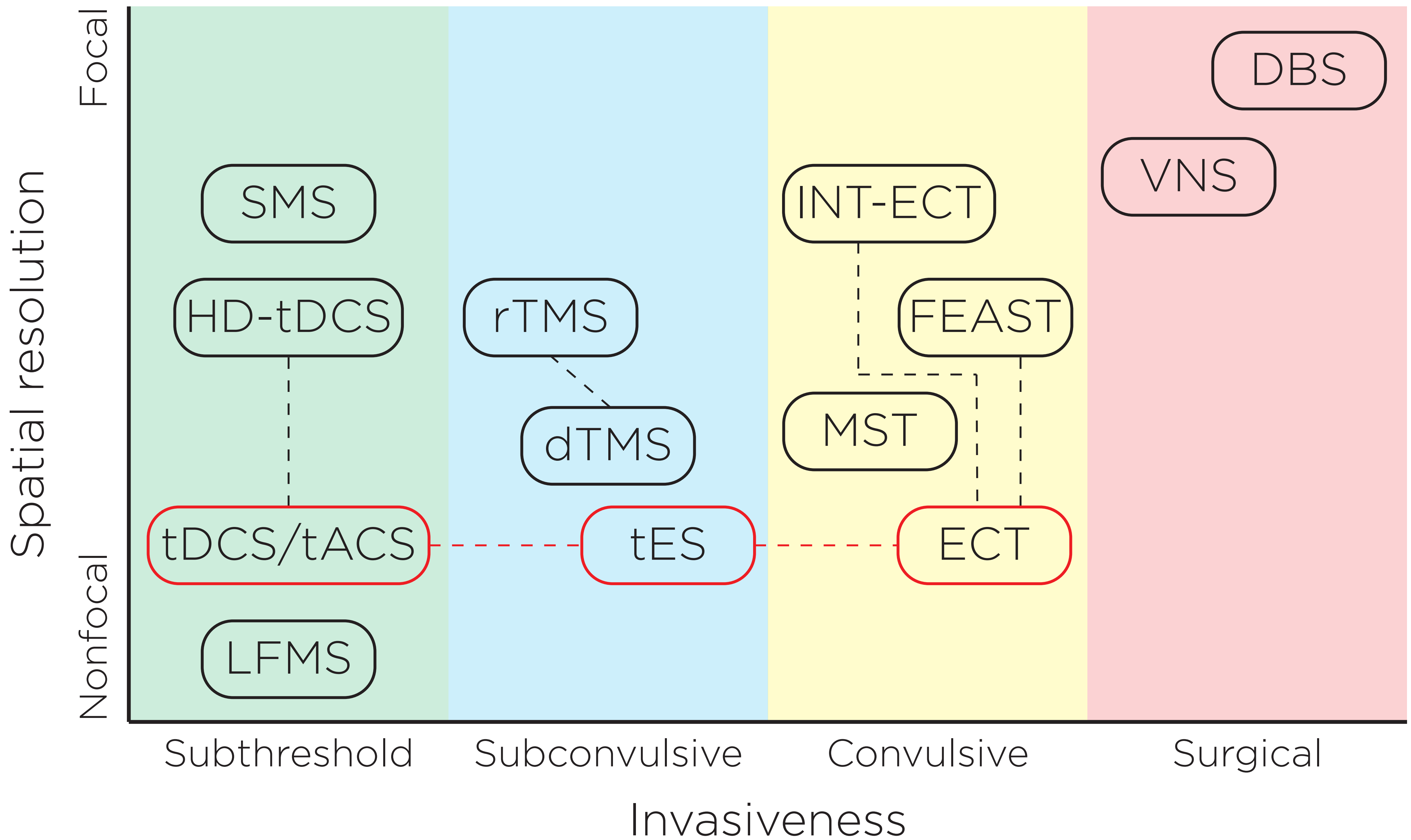
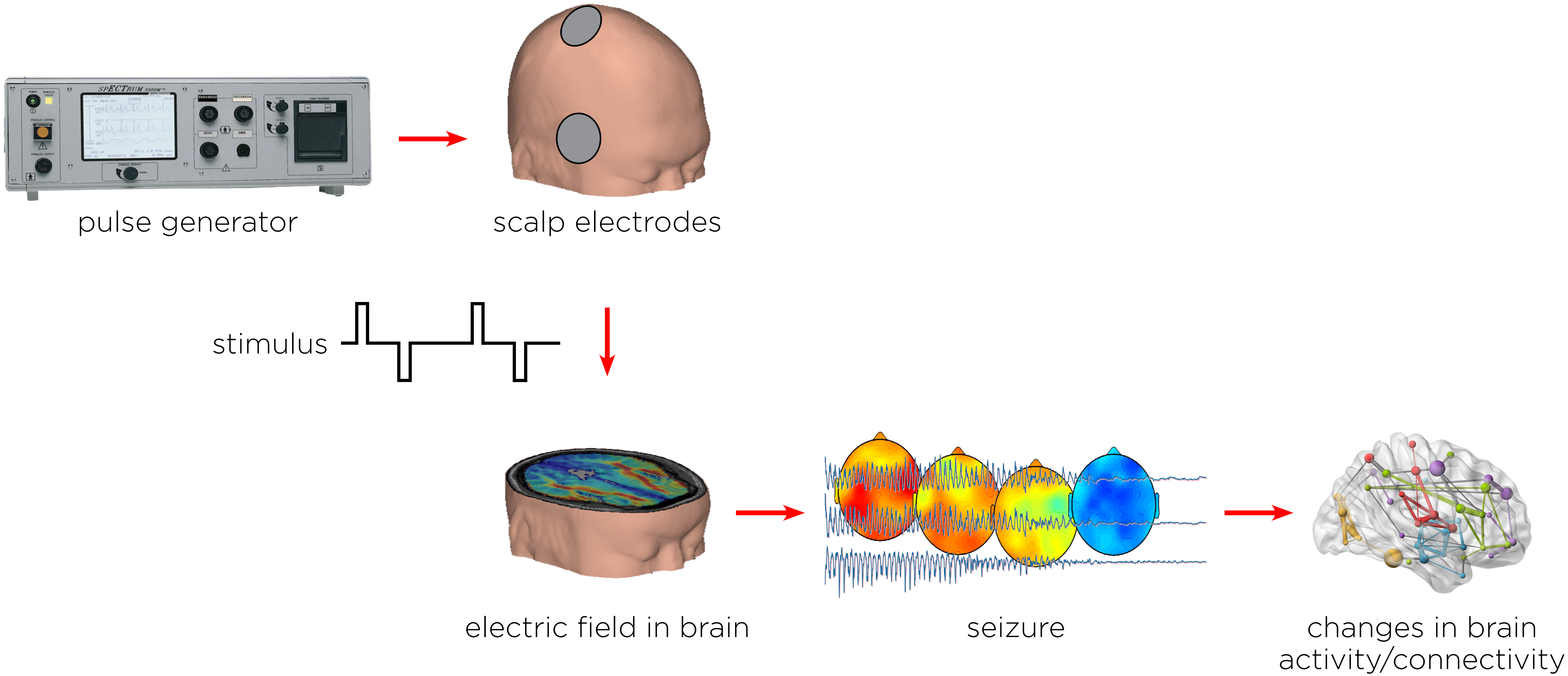
Brain stimulation landscape



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

ECT in a nutshell

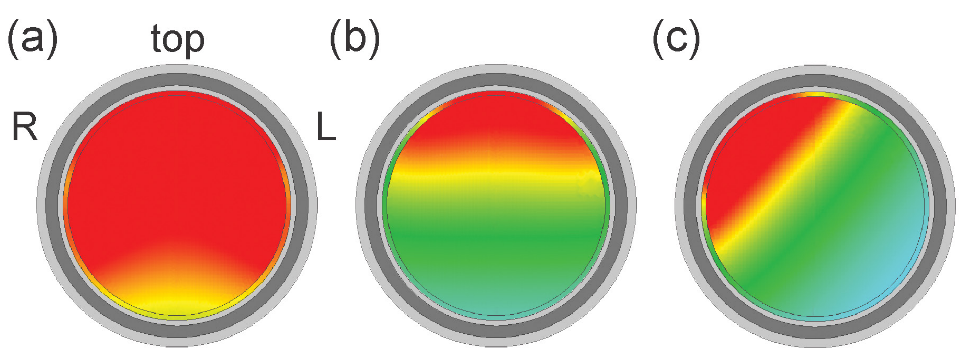


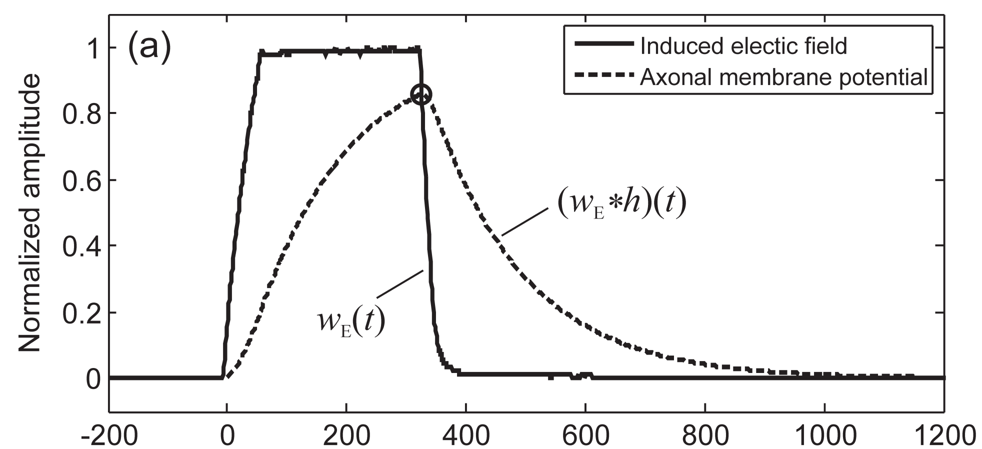
Quasistatic approximation

$$E(\mathbf{r}, t) = \underbrace{k(\mathbf{r})}_{\text{spatial}} \underbrace{I_{\mathrm{E}}(t)}_{\text{temporal}}$$

spatial

temporal





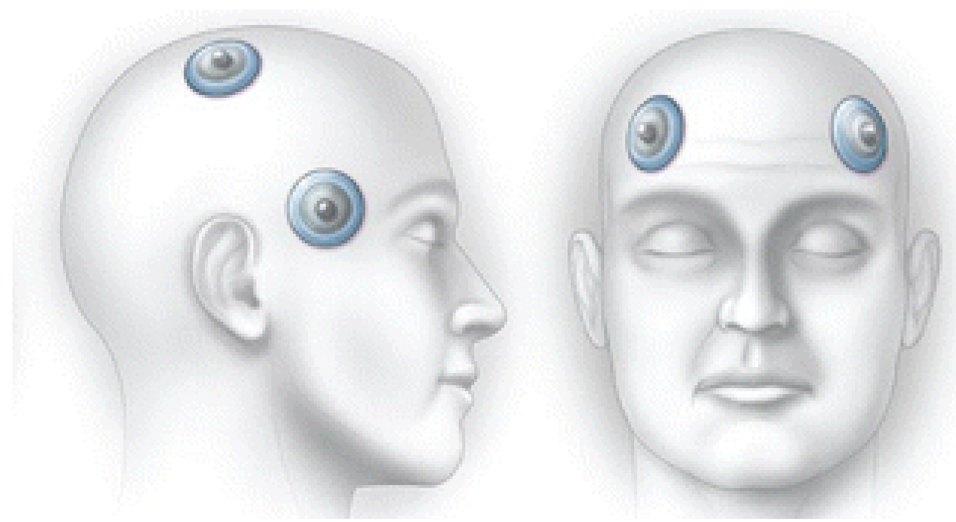
Bossetti et al., *J Neurl Eng*, 2008; Deng et al., *J Neural Eng*, 2011

Room for improvement: electrode placement

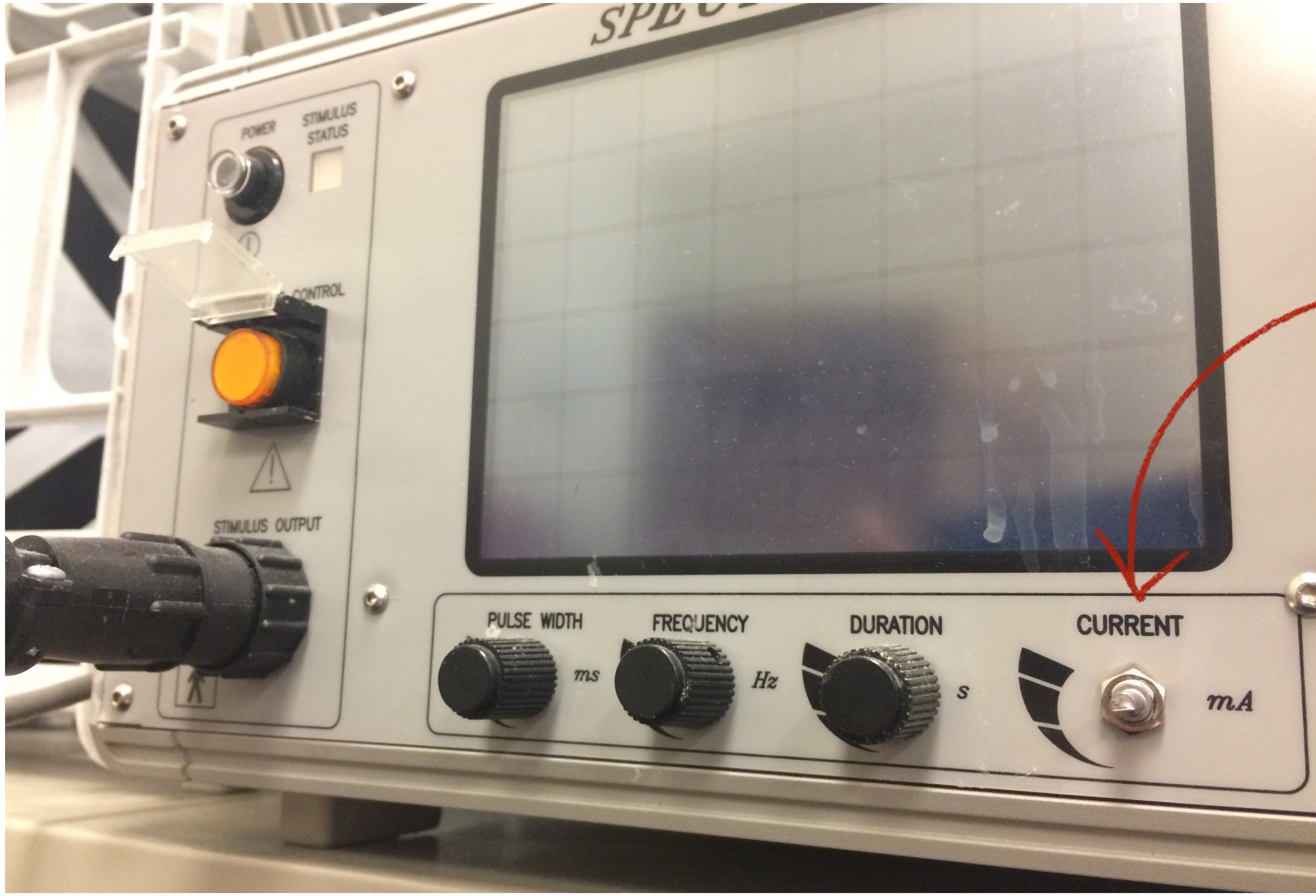
Cerletti 1930s

Modern day bilateral ECT

limited options
and imprecise

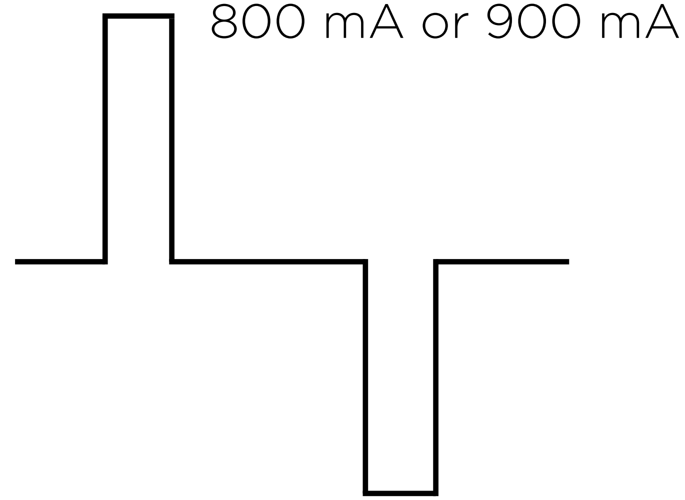


Room for improvement: current amplitude

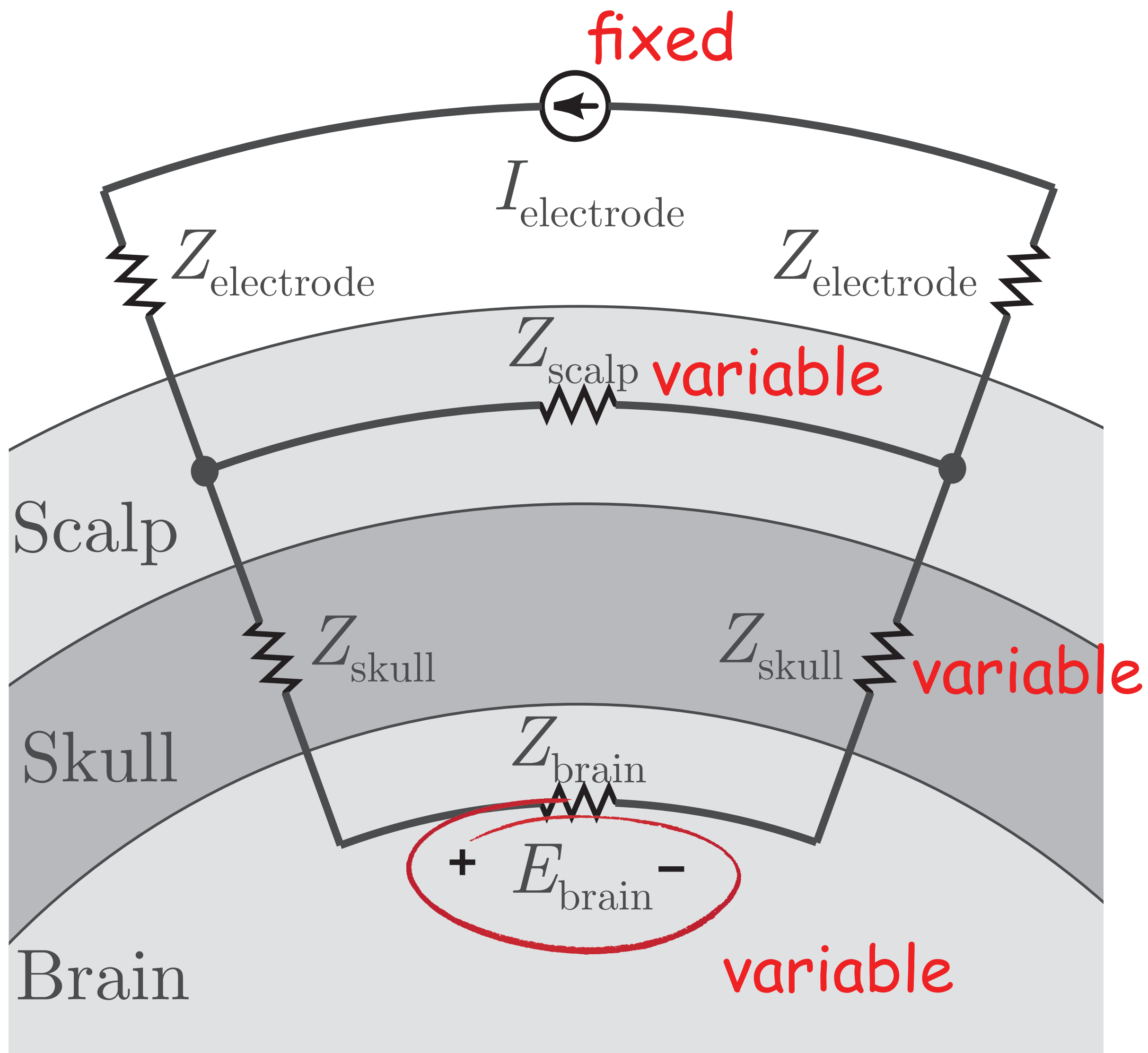


fixed

(... and probably way too high!)



Here's the problem...



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

Convulsive Therapy
10(2):93–123

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

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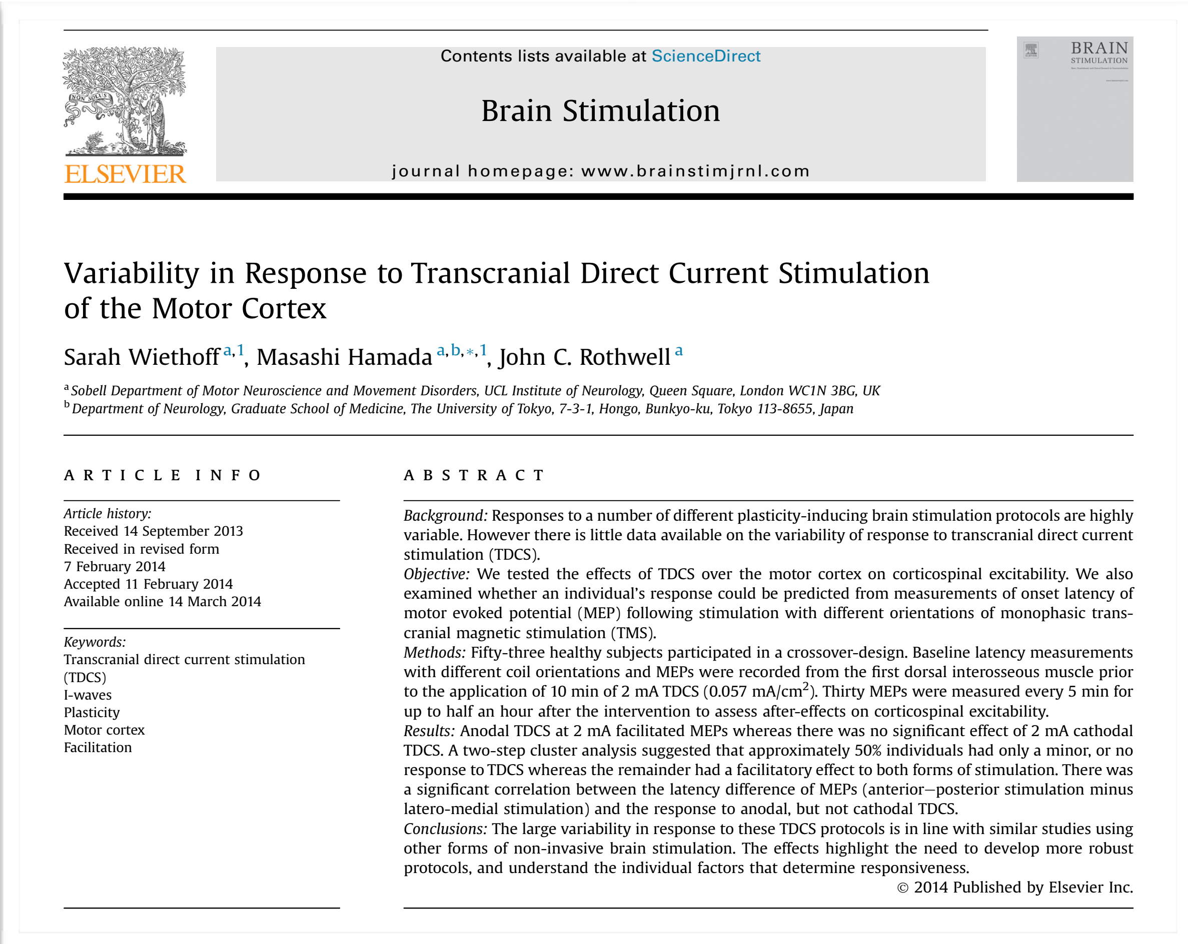
Summary: The physical properties of the electroconvulsive therapy (ECT) stimulus markedly affect both efficacy and side effects. We review basic principles in characterizing these physical properties and in quantifying the ECT stimulus. The topics discussed include the application of Ohm's law, alternative 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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Variability in Response to Transcranial Direct Current Stimulation of the Motor Cortex

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A R T I C L E I N F O

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Keywords:
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I-waves
Plasticity
Motor cortex
Facilitation

A B S T R A C T

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/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.

“The effects of tDCS are **highly variable**, as in other plasticity-inducing protocols, with around 50% of individuals having poor or absent responses.”

Classic spherical head model

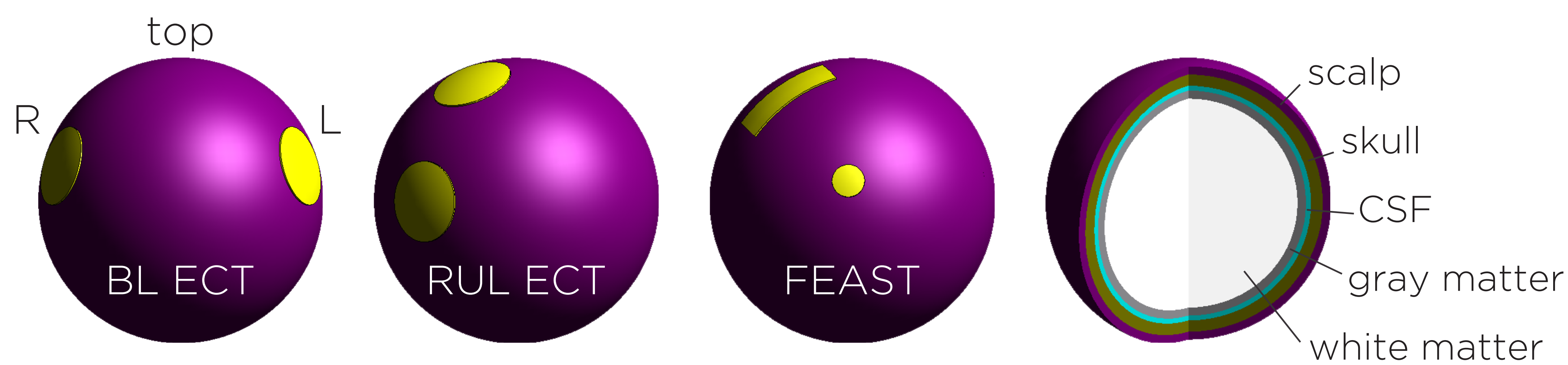
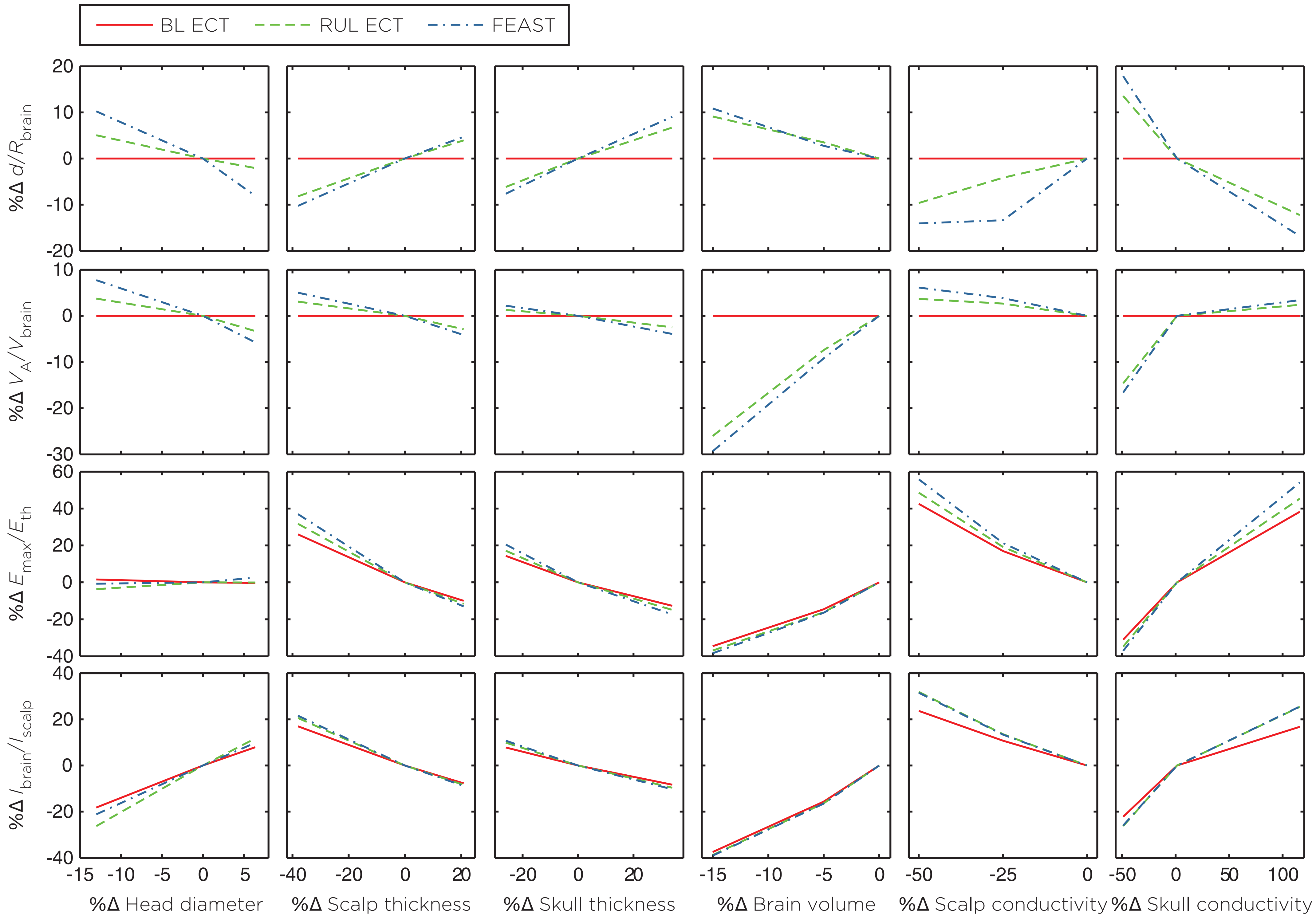
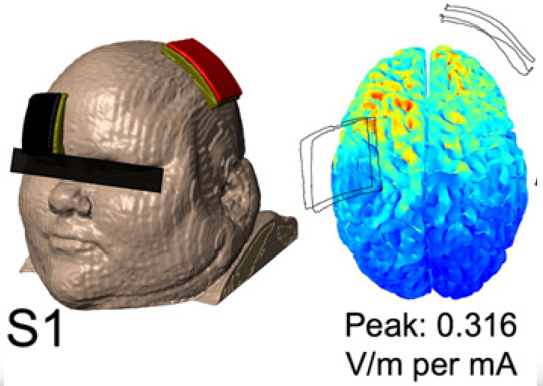


TABLE I
NOMINAL HEAD MODEL PARAMETERS

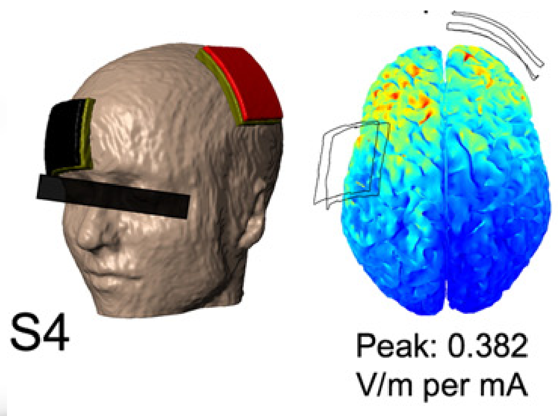
Anatomical parameter	Human	
	Female	Male
Head diameter (cm)	17.3	17.5
Scalp thickness (mm)	5.60	5.53
Skull thickness (mm)	7.08	6.50
CSF thickness (mm)	3.00	3.00
Gray matter thickness (mm)	3.00	3.00
White matter thickness (mm)	67.8	69.6
Brain volume (cm^3)	1486.6	1602.9
Scalp conductivity ($S\,m^{-1}$)	0.33	0.33
Skull conductivity ($S\,m^{-1}$)	0.0083	0.0083
CSF conductivity ($S\,m^{-1}$)	1.79	1.79
Gray matter conductivity ($S\,m^{-1}$)	0.33	0.33
White matter conductivity ($S\,m^{-1}$)	0.14	0.14

Deng et al., *J Neural Eng*, 2011; *J ECT*, 2013; *IEEE Trans Neural Syst Rehabil Eng* 2015

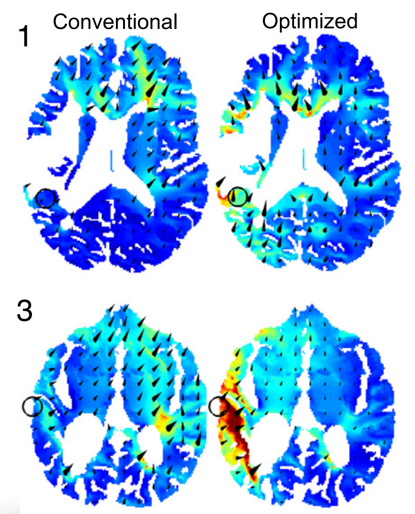

BL ECT
RUL ECT
FEAST
%Δ d/R_brain
%Δ V_A/V_brain
%Δ E_max/E_th
%Δ I_brain/I_scalp
20
10
0
-10
-20
-30
60
40
-40
-15 -10 -5 0 5
-40 -20 0 20
-20 0 20
-15 -10 -5 0
-50 -25 0
-50 0 50 100
%Δ Head diameter
%Δ Scalp thickness
%Δ Skull thickness
%Δ Brain volume
%Δ Scalp conductivity
%Δ Skull conductivity



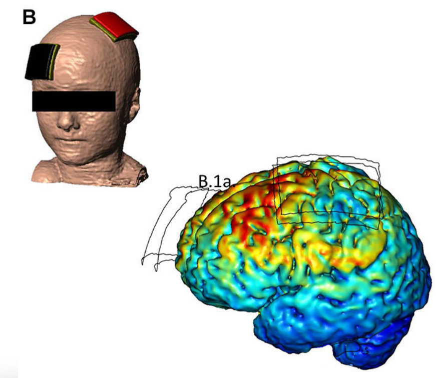
Troung et al., 2013
tDCS in obesity



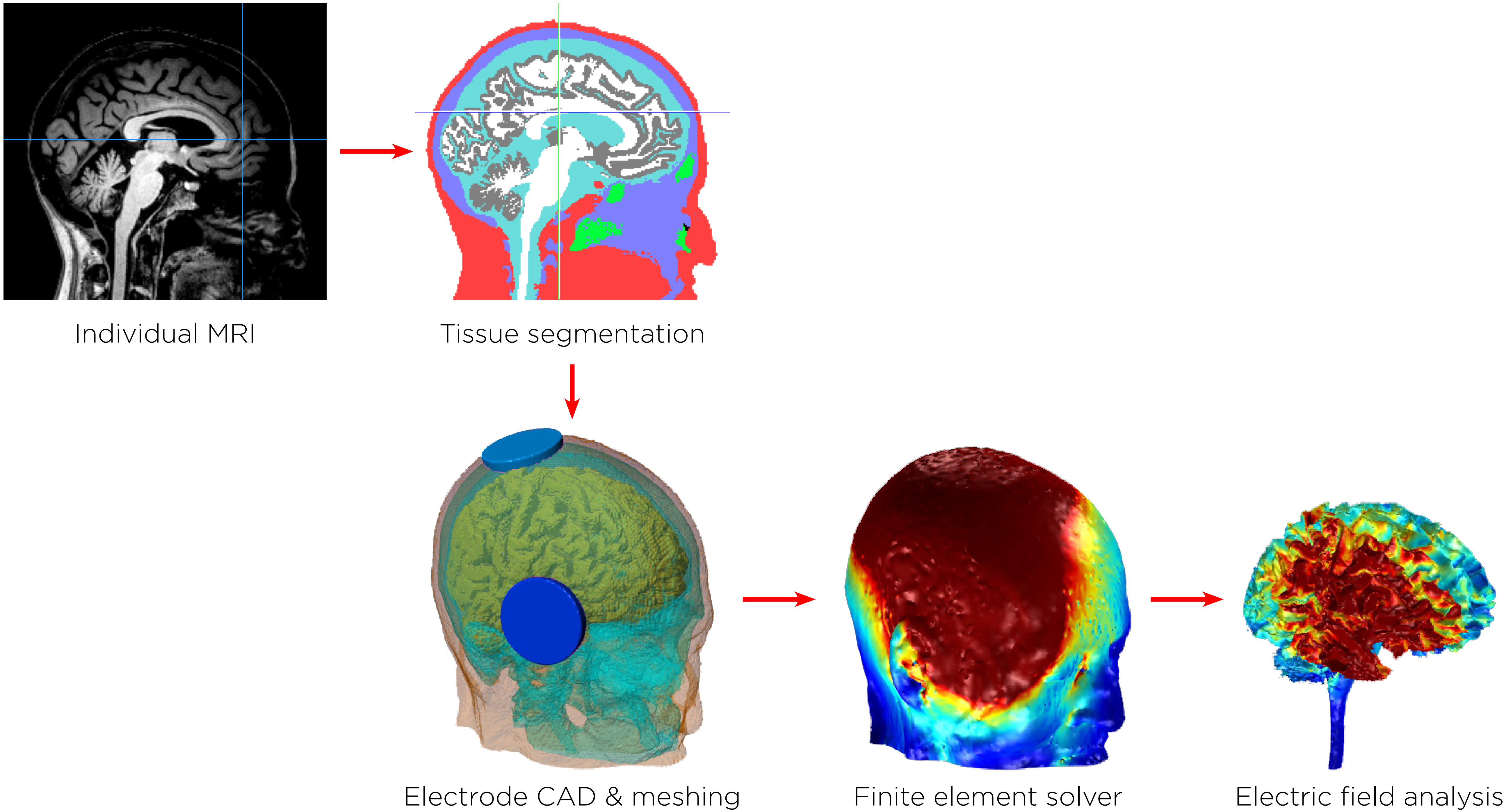
Troung et al., 2013
tDCS in pediatric

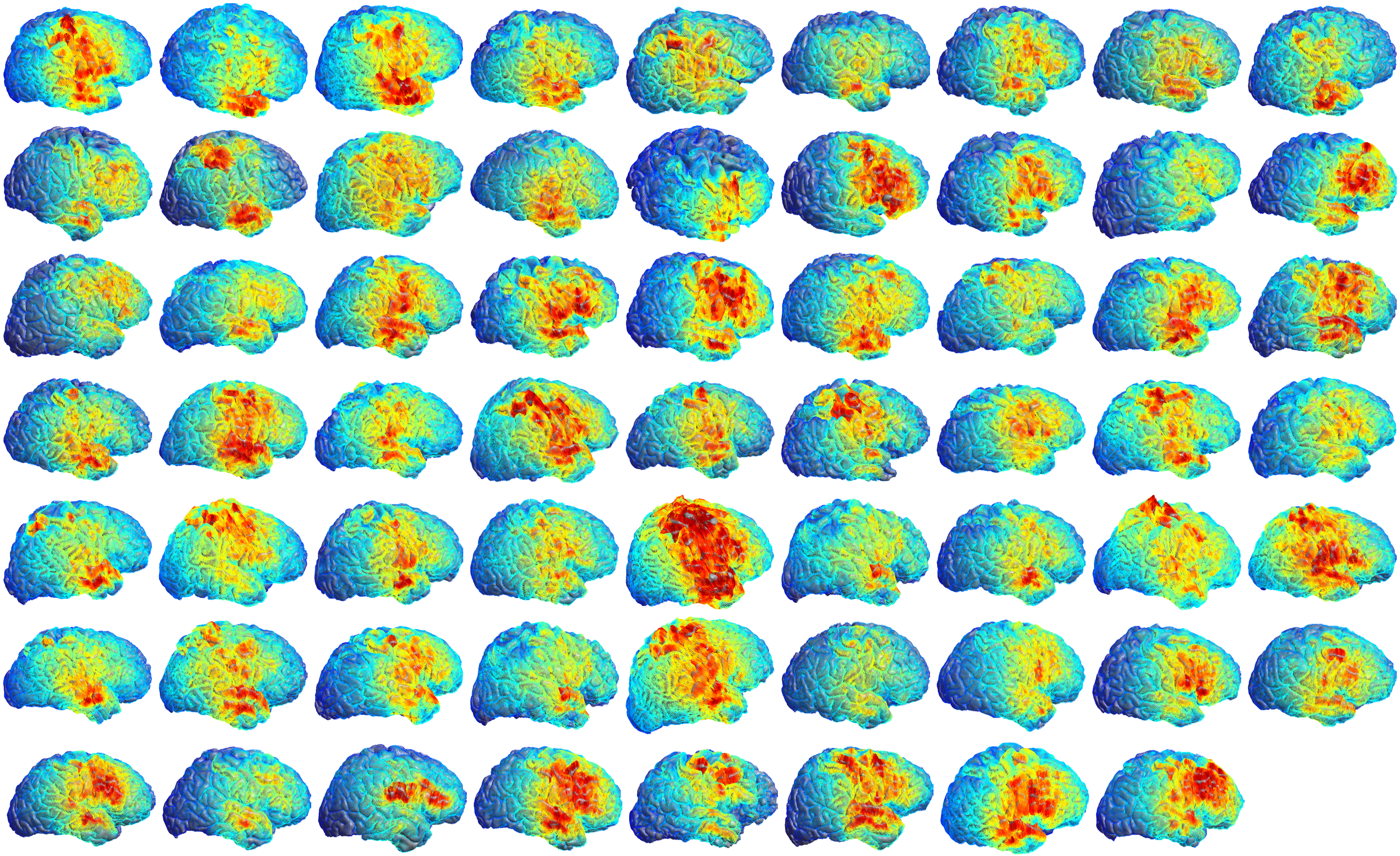


Dmochowski et al., 2013
tDCS in stroke

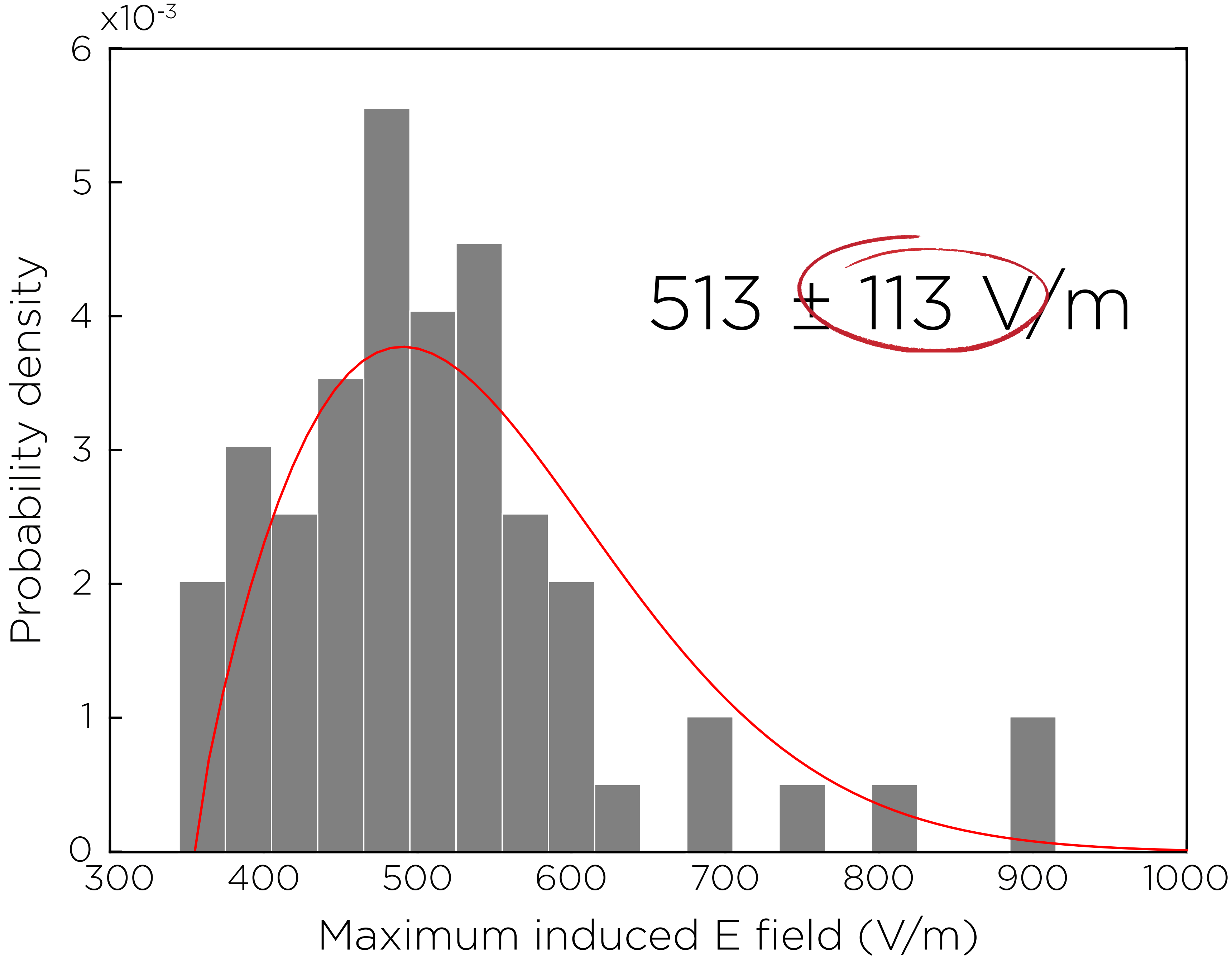


Gillick et al., 2014
tDCS in pediatric stroke

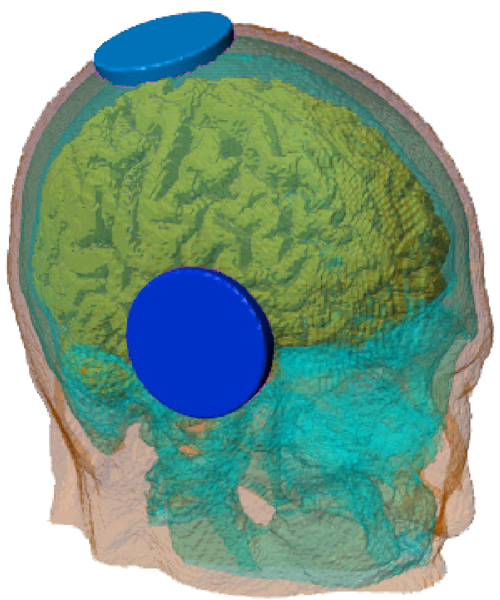

Individual MRI
Tissue segmentation
Electrode CAD & meshing
Finite element solver
Electric field analysis

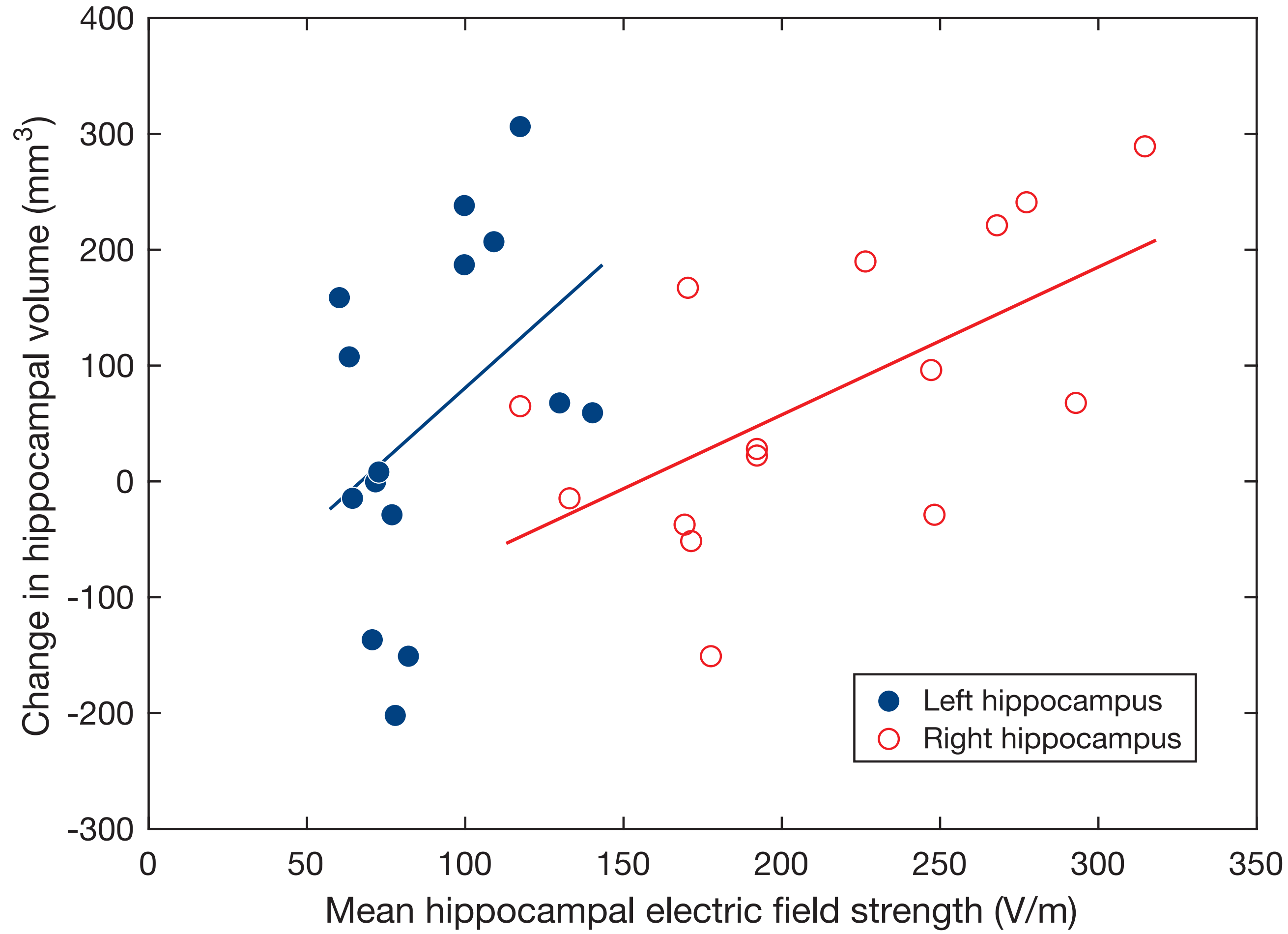


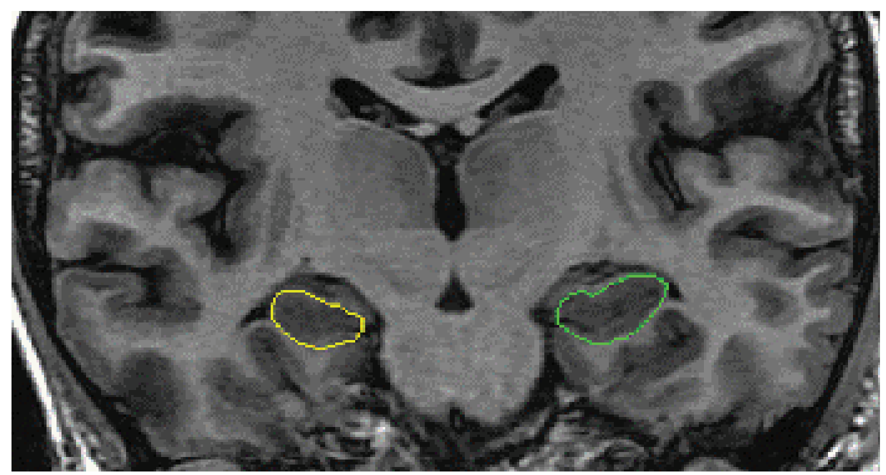
Unpublished, collaboration with J. van Waarde (Netherlands)


x10-3
6
5
4
3
2
1
0
Probability density
513 ± 113 V/m
300
400
500
600
700
800
900
1000
Maximum induced E field (V/m)

Electric field and hippocampal plasticity

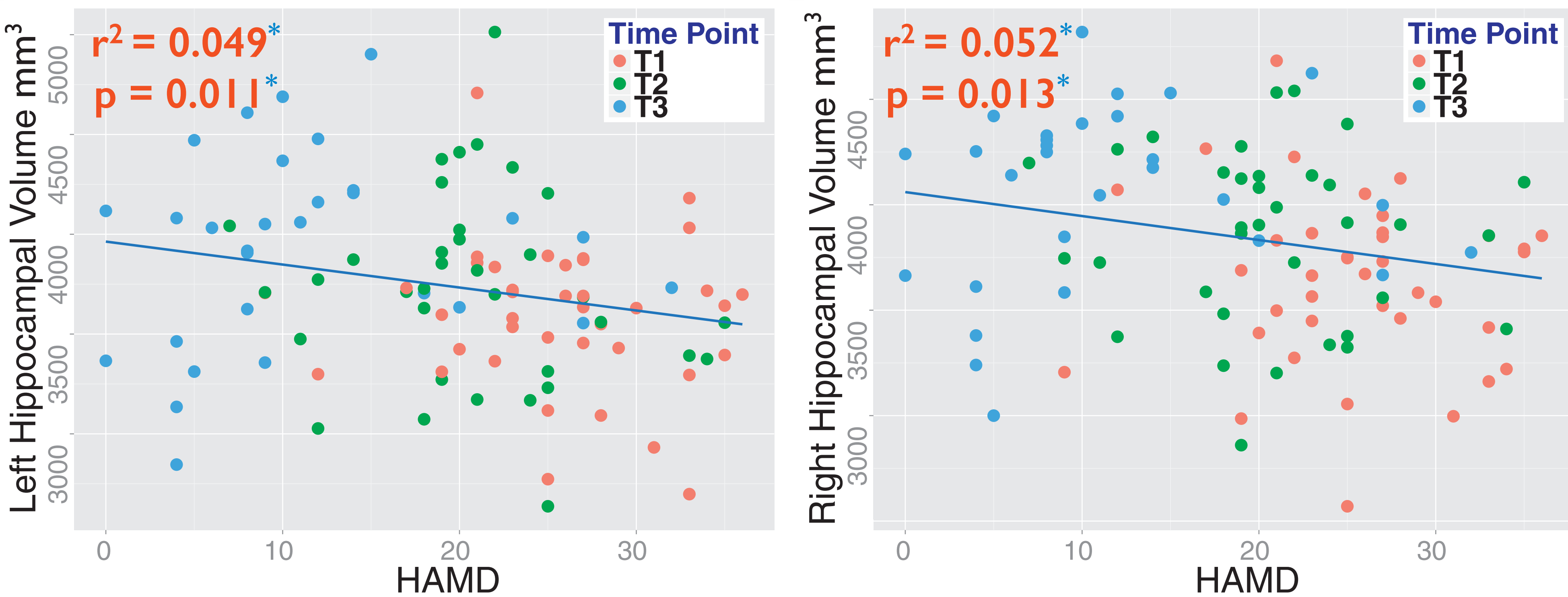




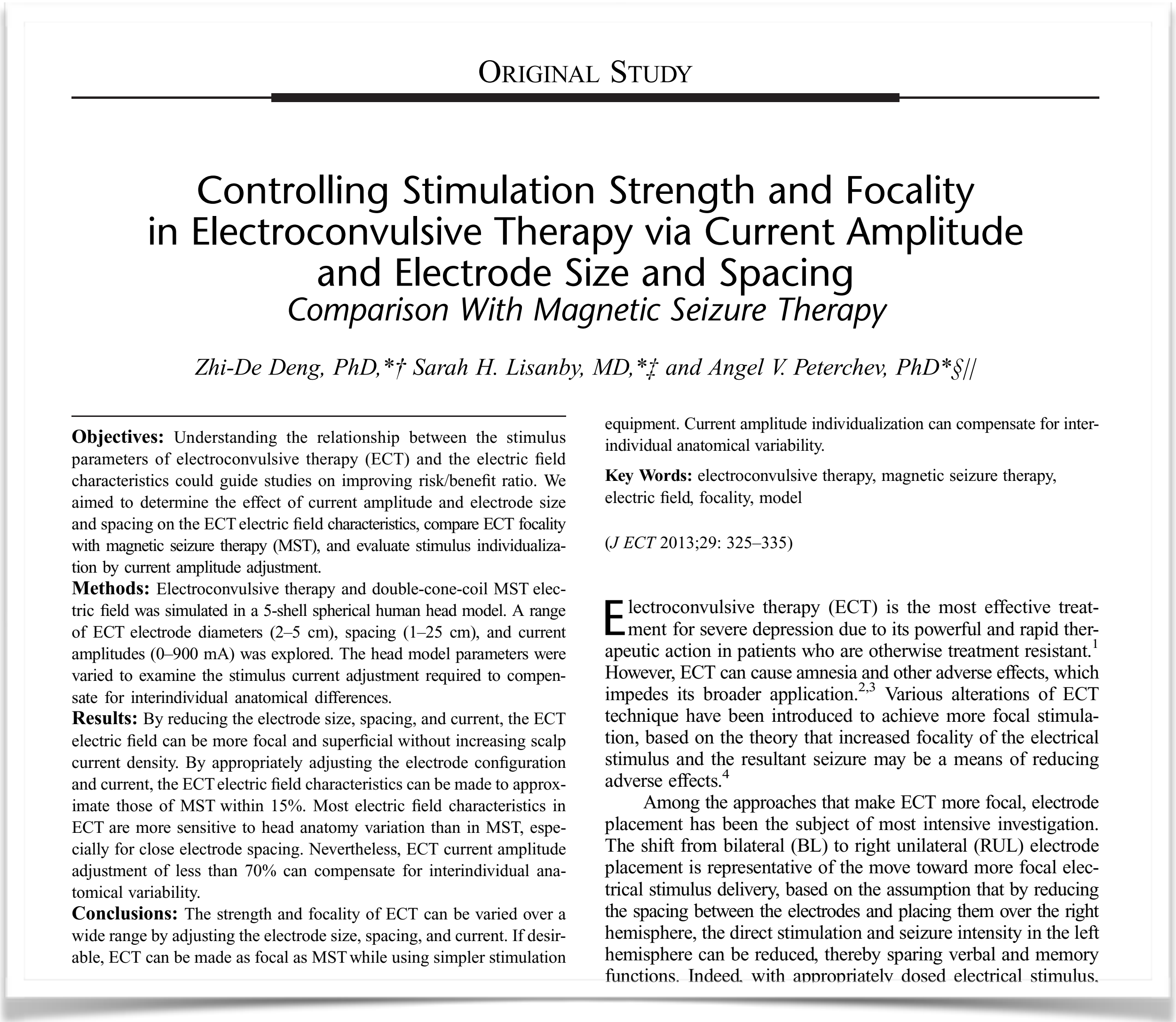


Deng and Abbott, *ACNP*, 2016

Hippocampal plasticity in ECT



Joshi et al., *Biol Psychiatr*, 2016



ORIGINAL STUDY

Controlling Stimulation Strength and Focality in Electroconvulsive Therapy via Current Amplitude and Electrode Size and Spacing

Comparison With Magnetic Seizure Therapy

Zhi-De Deng, PhD,† Sarah H. Lisanby, MD,*‡ and Angel V. Peterchev, PhD*§||*

Objectives: Understanding the relationship between the stimulus parameters of electroconvulsive therapy (ECT) and the electric field characteristics could guide studies on improving risk/benefit ratio. We aimed to determine the effect of current amplitude and electrode size and spacing on the ECT electric field characteristics, compare ECT focality with magnetic seizure therapy (MST), and evaluate stimulus individualization by current amplitude adjustment.

Methods: Electroconvulsive therapy and double-cone-coil MST electric field was simulated in a 5-shell spherical human head model. A range of ECT electrode diameters (2–5 cm), spacing (1–25 cm), and current amplitudes (0–900 mA) was explored. The head model parameters were varied to examine the stimulus current adjustment required to compensate for interindividual anatomical differences.

Results: By reducing the electrode size, spacing, and current, the ECT electric field can be more focal and superficial without increasing scalp current density. By appropriately adjusting the electrode configuration and current, the ECT electric field characteristics can be made to approximate those of MST within 15%. Most electric field characteristics in ECT are more sensitive to head anatomy variation than in MST, especially for close electrode spacing. Nevertheless, ECT current amplitude adjustment of less than 70% can compensate for interindividual anatomical variability.

Conclusions: The strength and focality of ECT can be varied over a wide range by adjusting the electrode size, spacing, and current. If desirable, ECT can be made as focal as MST while using simpler stimulation equipment. Current amplitude individualization can compensate for interindividual anatomical variability.

Key Words: electroconvulsive therapy, magnetic seizure therapy, electric field, focality, model

(*J ECT* 2013;29: 325–335)

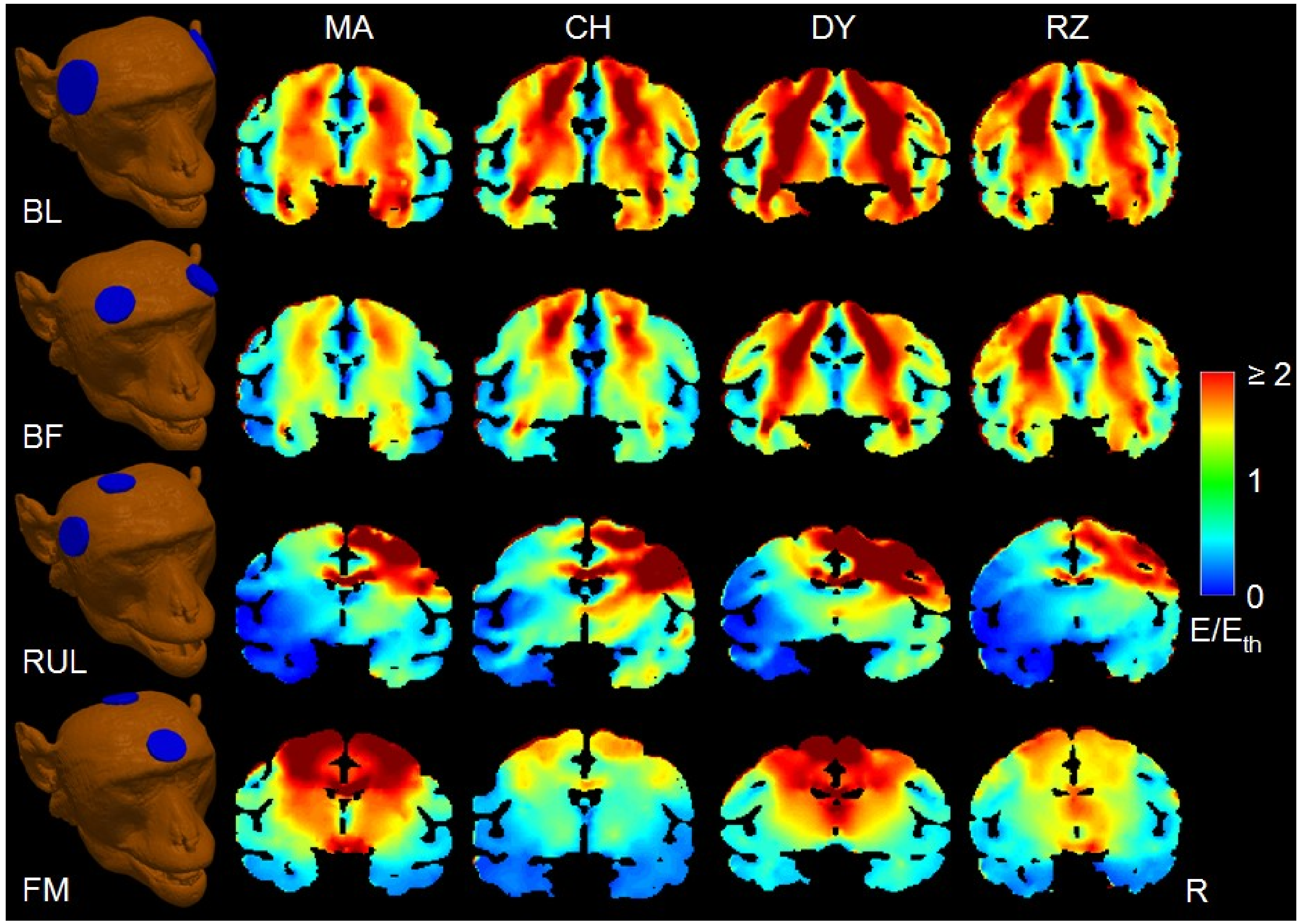
Electroconvulsive therapy (ECT) is the most effective treatment for severe depression due to its powerful and rapid therapeutic action in patients who are otherwise treatment resistant.[1] However, ECT can cause amnesia and other adverse effects, which impedes its broader application.[2,3] Various alterations of ECT technique have been introduced to achieve more focal stimulation, based on the theory that increased focality of the electrical stimulus and the resultant seizure may be a means of reducing adverse effects.[4]

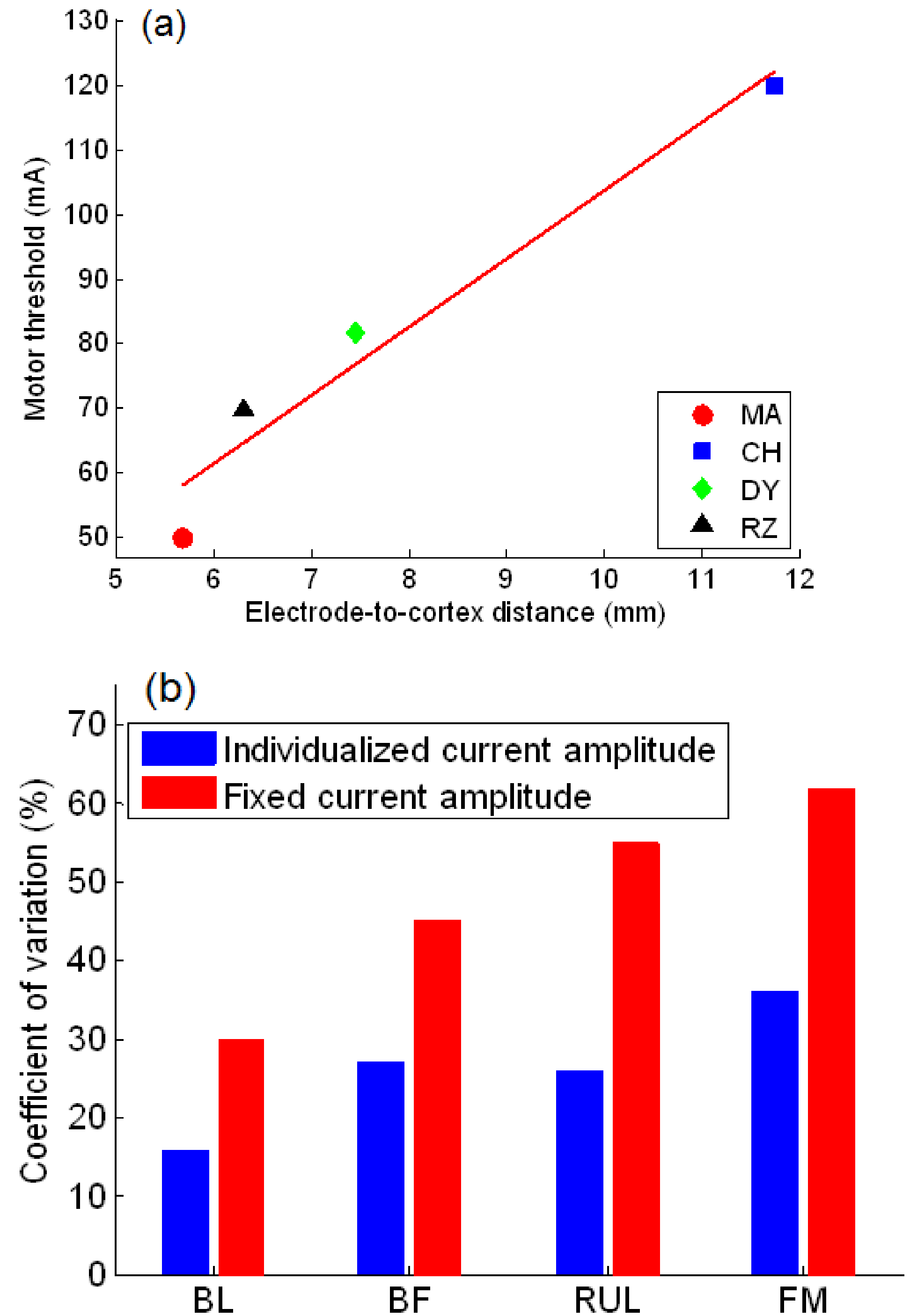
Among the approaches that make ECT more focal, electrode placement has been the subject of most intensive investigation. The shift from bilateral (BL) to right unilateral (RUL) electrode placement is representative of the move toward more focal electrical stimulus delivery, based on the assumption that by reducing the spacing between the electrodes and placing them over the right hemisphere, the direct stimulation and seizure intensity in the left hemisphere can be reduced, thereby sparing verbal and memory functions. Indeed, with appropriately dosed electrical stimulus,

"Current amplitude individualization

can compensate for inter-individual anatomical variability."

Application of current amplitude individualization

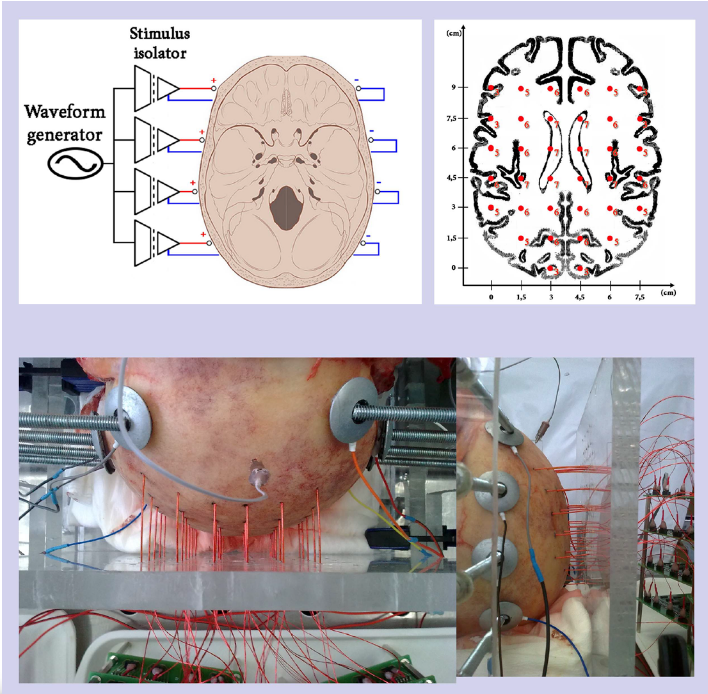




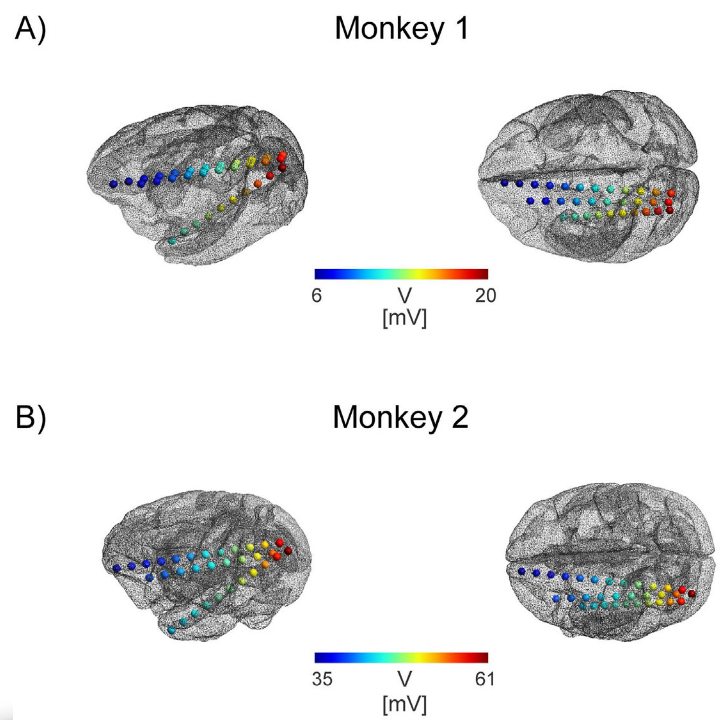
Lee et al., *Conf Proc IEEE Eng Med Biol Soc*, 2013; Peterchev et al., *Neuropsychopharmacology*, 2015

Zhi, what about uncertainties in tissue conductivity?

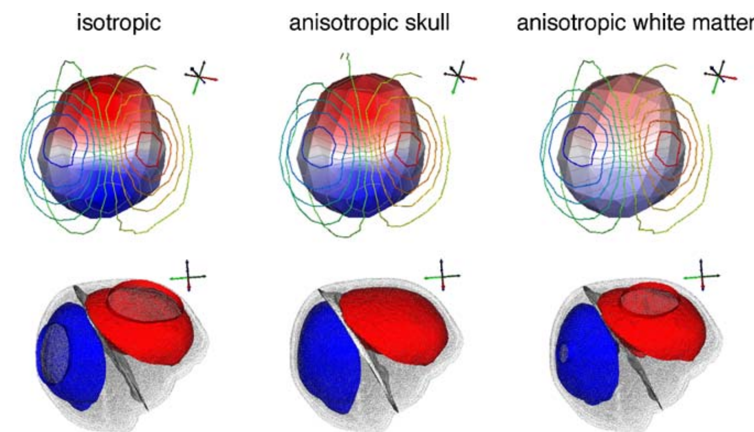
Model validation and parameter estimation



Vöröslakos et al., 2014
Measure E field in cadaver



Opitz et al., 2016
Measure induced voltage in NHP



Wolters et al., 2006
Tissue conductivity & anisotropy effects on EEG

Take home

- A major source of variability in clinical/behavioral outcome is inter-individual differences in head anatomy and tissue electric properties

- Some of this anatomical variability can be compensated with proper individualized dosing strategies

- Despite uncertainties in parameters, computational models are improving and becoming more ubiquitous

"Essentially, all models are wrong,
but some are useful."

~George E. P. Box