Quantification of Dose with Neuromodulation Device

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BRAIN
STIMULATION

www.brainstimjrnl.com

REVIEW ARTICLE

Fundamentals of transcranial electric and magnetic stimulation dose: Definition, selection, and reporting practices

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Neuromodulation dose is "defined by all parameters of the stimulation device that affect the electric and current density fields generated in the body"

1)Stimulation electrode / coil configuration parameters: shape, size, position, and electrical properties

2)Electrode / coil current or voltage waveform parameters: pulse amplitude, width, polarity, repetition frequency, train duration, interval and number of stimulation sessions

1) A box (battery or wall powered) that generates a electrical waveform

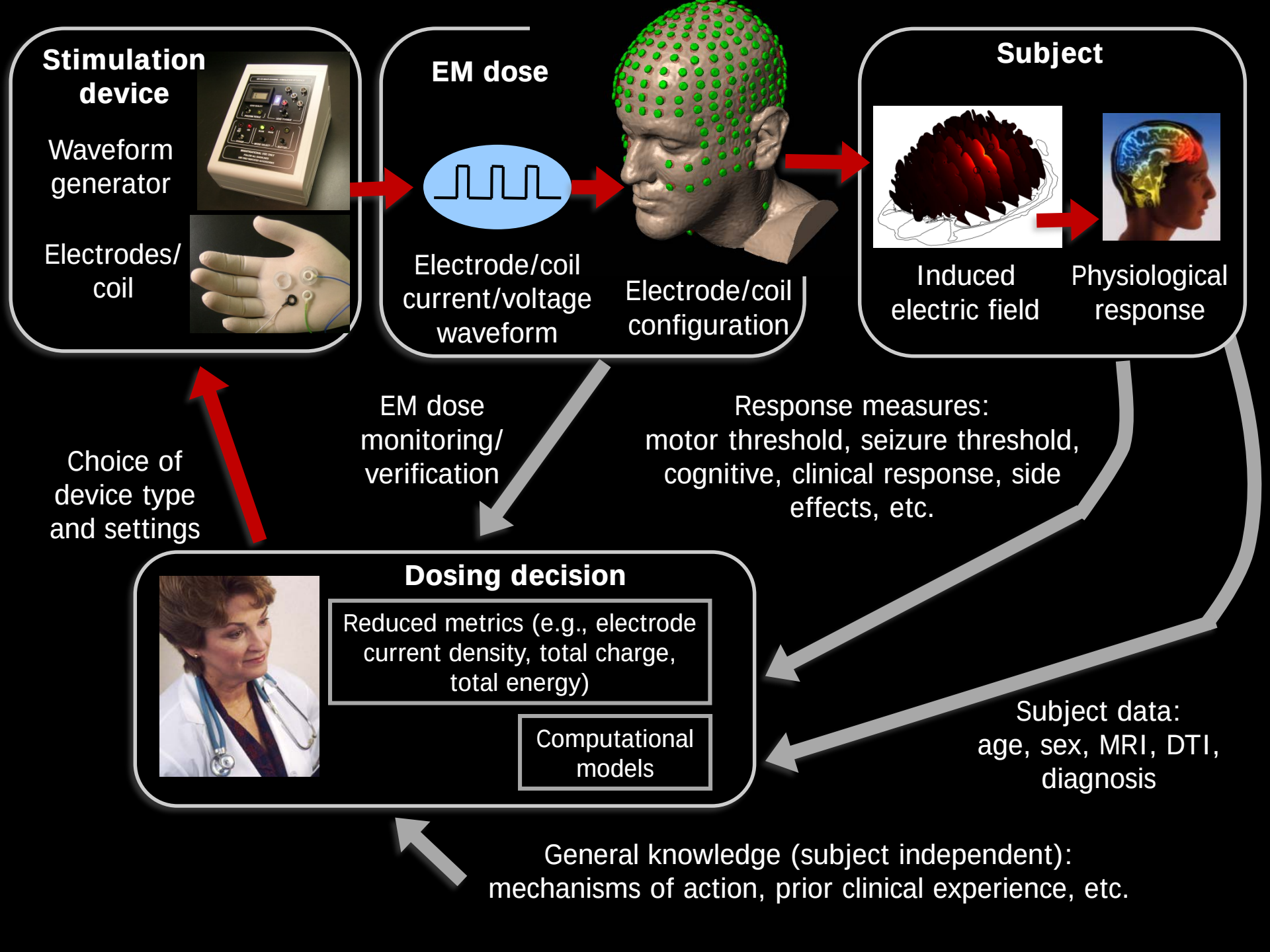
wire

2) Electrodes outside or inside body, or coil outside body

Dose of neuromodulation devices

Electrical current are generated inside the body leading to (govern) changes

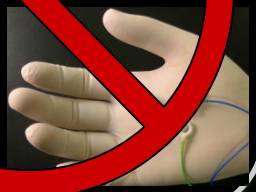
Only those parameters that influence currents in body


Stimulation device
Waveform generator
Electrodes/ coil
EM dose
Electrode/coil current/voltage waveform
Electrode/coil configuration
Subject
Induced electric field
Physiological response
Choice of device type and settings
EM dose monitoring/ verification
Response measures: motor threshold, seizure threshold, cognitive, clinical response, side effects, etc.
Dosing decision
Reduced metrics (e.g., electrode current density, total charge, total energy)
Computational models
Subject data: age, sex, MRI, DTI, diagnosis
General knowledge (subject independent): mechanisms of action, prior clinical experience, etc.

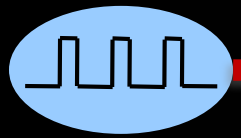
Stimulation device

Waveform generator

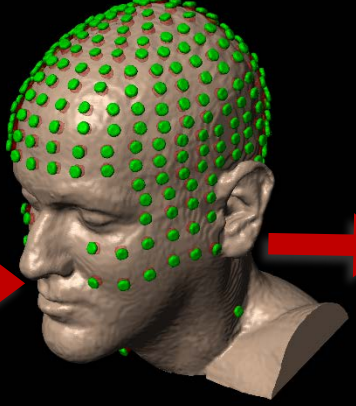
Electrodes/ coil



EM dose

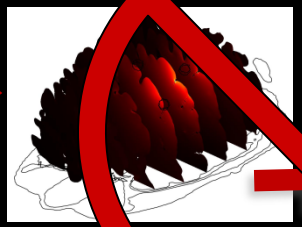


Electrode/coil current/voltage waveform



Electrode/coil configuration

Subject



Induced electric field

Physiological response

Choice of device type and settings

EM dose monitoring/ verification

Response measures: motor threshold, seizure threshold, cognitive, clinical response, side effects, etc.

Dosing decision

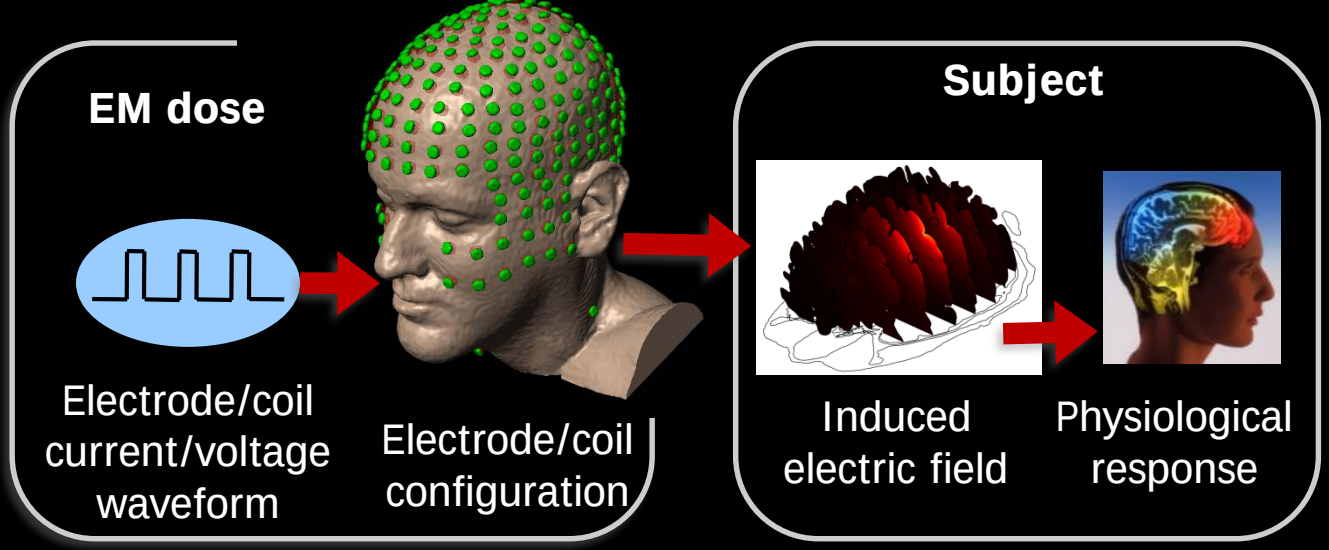
Reduced metrics (e.g., electrode current density, total charge, total energy)

Computational models

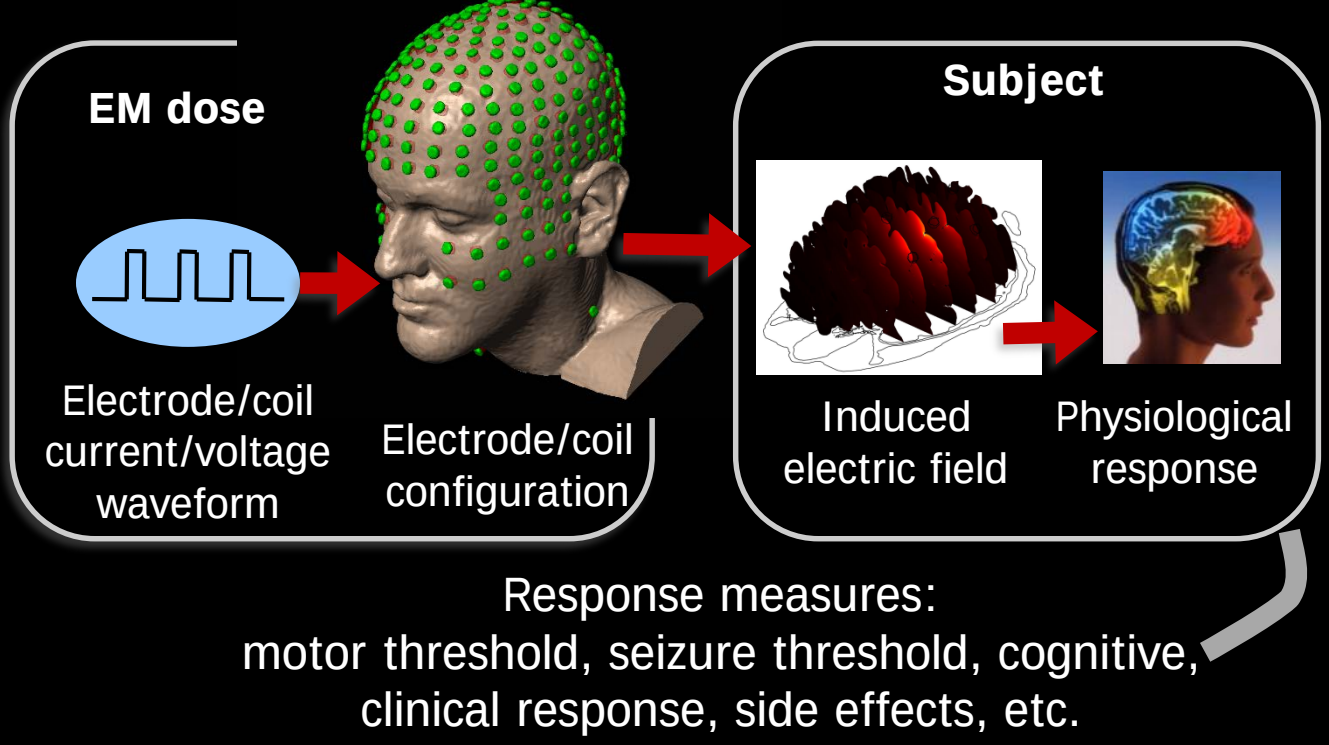
Subject data: age, sex, MRI, DTI, diagnosis

General knowledge (subject independent): mechanisms of action, prior clinical experience, etc.

Not Dose



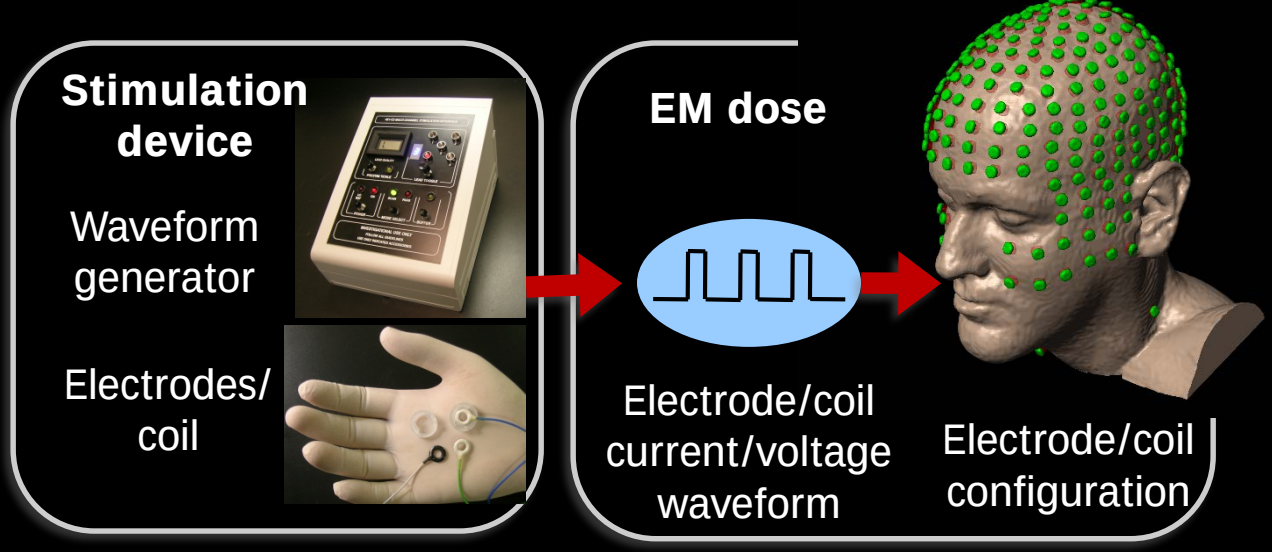
- **Current generated in the body is NOT dose**
- But critically defines outcomes of stimulation
- Current in body determined by dose and tissue properties
- And so is subject specific
- Can be predicted using models or measured (dosimetry)



- **Response to stimulation is NOT dose**
- But represent outcomes of stimulation
- Can be used to adjust dose

  (rTMS for Depression uses TMS MEP, closed-loop for epilepsy uses EEG, Seizure for ECT)
- Essentially all FDA cleared technologies measure responses to adjust stimulation* (biomarker, sensation, behavior..)

  *And studies / protocols do not report individual dose



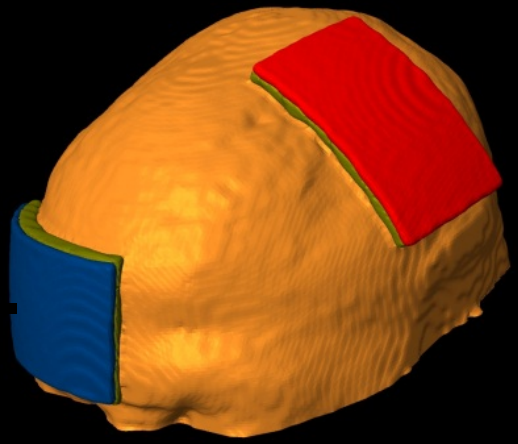
- **Device name (brand) is NOT dose**
- Names end with “s” (Stimulation) that typically refer to how current is delivered to body and “intended” target.

  “Transcranial”, “deep”, “nerve X”

Dose is controlled (prescribed)

Drug dose is set by systemic application (tablets...)

Pharmacologic activity (efficacy and safety) is determined by drug concentration at tissue



“Electroceutical” dose is set by stimulation parameters (coil/electrode and waveform)

“Electrical activity” (efficacy and safety) is determined by electric fields at tissue

1) A box (battery or wall powered) that generates a electrical waveform

wire

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Electrical current are generated inside the body leading to (govern) changes

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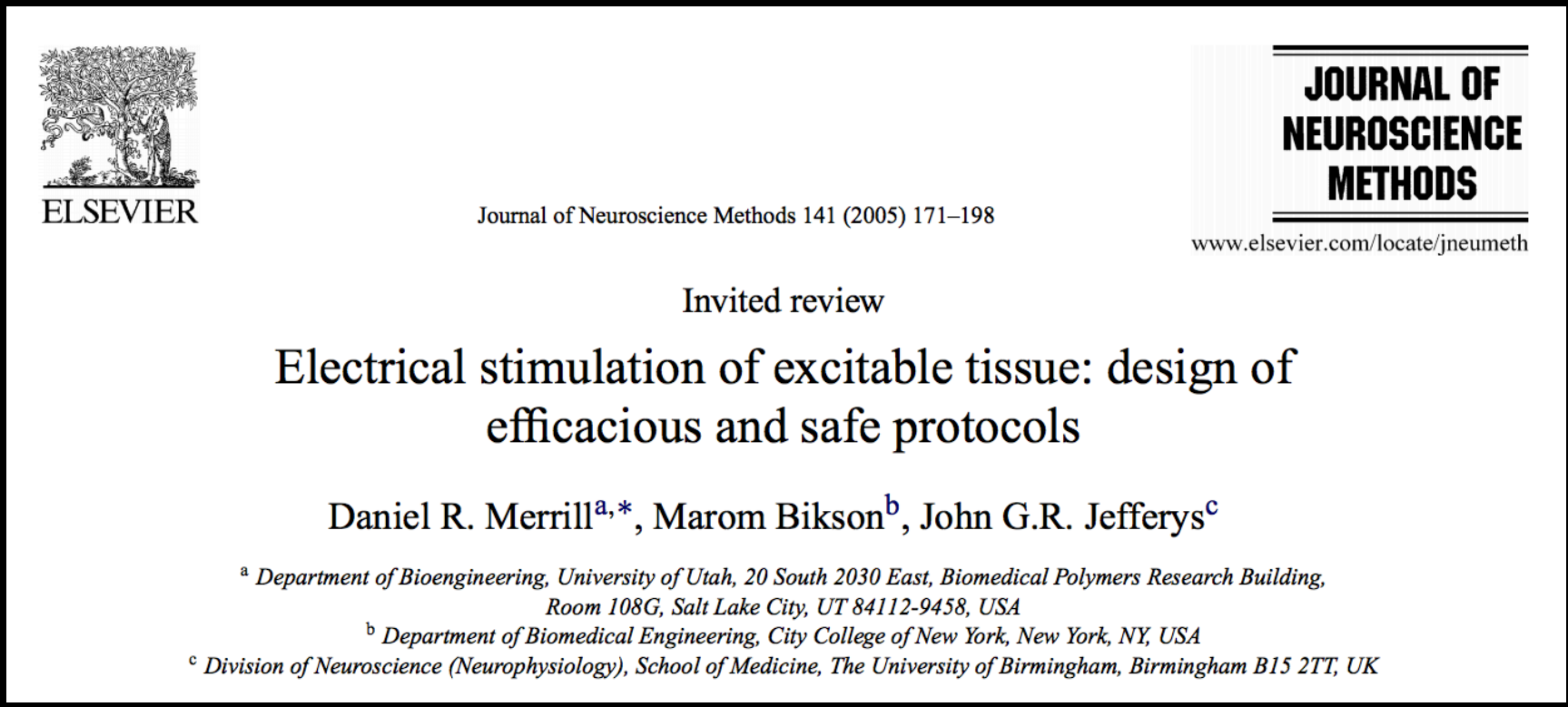
Things other than DOSE matter

- Efficacy: Subject state (concurrent interventions).
  "Functional Targeting" vs. "Anatomical Targeting"

- Safety: Device physical features (electrode materials)



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Journal of Neuroscience Methods 141 (2005) 171–198

JOURNAL OF NEUROSCIENCE METHODS

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Invited review

Electrical stimulation of excitable tissue: design of efficacious and safe protocols

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Neuromodulation technologies with “Super-Synergy” such as **transcranial Direct Current Stimulation***

- Mechanisms suggest limited functional outcomes when applied alone, but strong change in brain ‘responsiveness’
- Boosts effects of concurrent therapy
- Also sensitive to other neuromodulators (drugs)

tDCS known to enhance ongoing neuro-plasticity + **Behavioral / cognitive interventions produce lasting benefit through neuro-plasticity**

* As of 2016 the most studied neuromodulation technology
* Not proprietary (owned by one company)
* Safe enough to be widely used on healthy subjects

Recommendations

- Testing and application of neuromodulation devices should be driven by principle of REPRODUCABILITY.

  When can dose be unreported / uncontrolled?

- Use of biomarkers to adjust neuromodulation dose in a successful intervention should not be confused with verification the biomarker is useful. A name is not the same as verification of an anatomical target.
  - If assumptions are wrong, so are reasons to not report/control dose.

- Create path to clinic (patients) for technologies that are not proprietary and not specific to one indication. Yet are very tolerated/safe and independently tested.

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