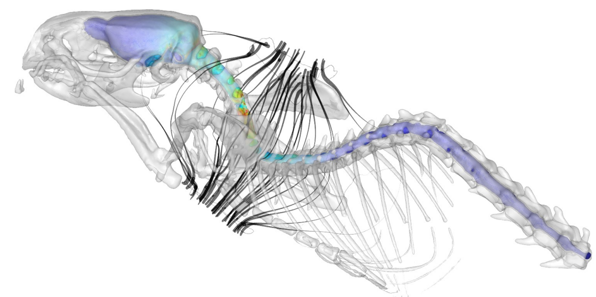
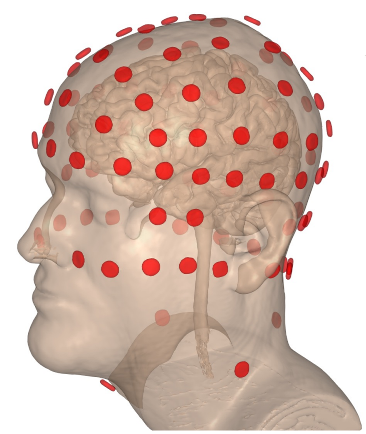
Developing tDCS as a therapeutic tool

Translational Neural Engineering: Hypothesis-based Devices Design



Marom Bikson
The City College of New York of CUNY



Disclosure
The City University of New York: Patents on brain stimulation.
Soterix Medical: Produces tDCS and High-Definition tDCS.
Grants, assigned inventions, and/or serves SAB for SafeToddles, Boston Scientific, GlaxoSmithKline, Biovisics, Mecta, Lumenis, Halo Neuroscience, Google-X, i-Lumen, Humm, Allergan (Abbvie), Apple

Support
NYS DOH, NIH (NIMH, NINDS) – *BRAIN Initiative*, NSF, Grove Foundation, Harold Shames, CCNY Fund, 21st Century Fund

Slides and References @MaromBikson

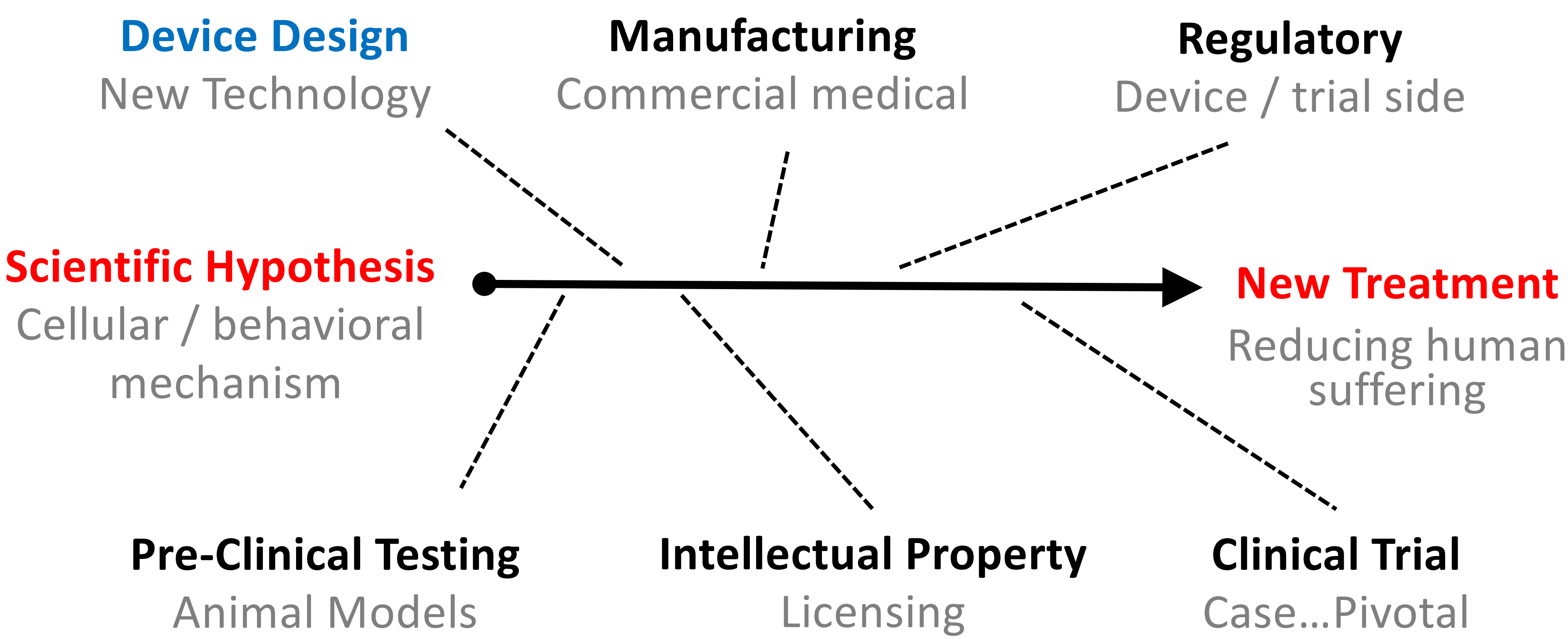
Translational Medical Device Design

Scientific Hypothesis
Cellular / behavioral mechanism

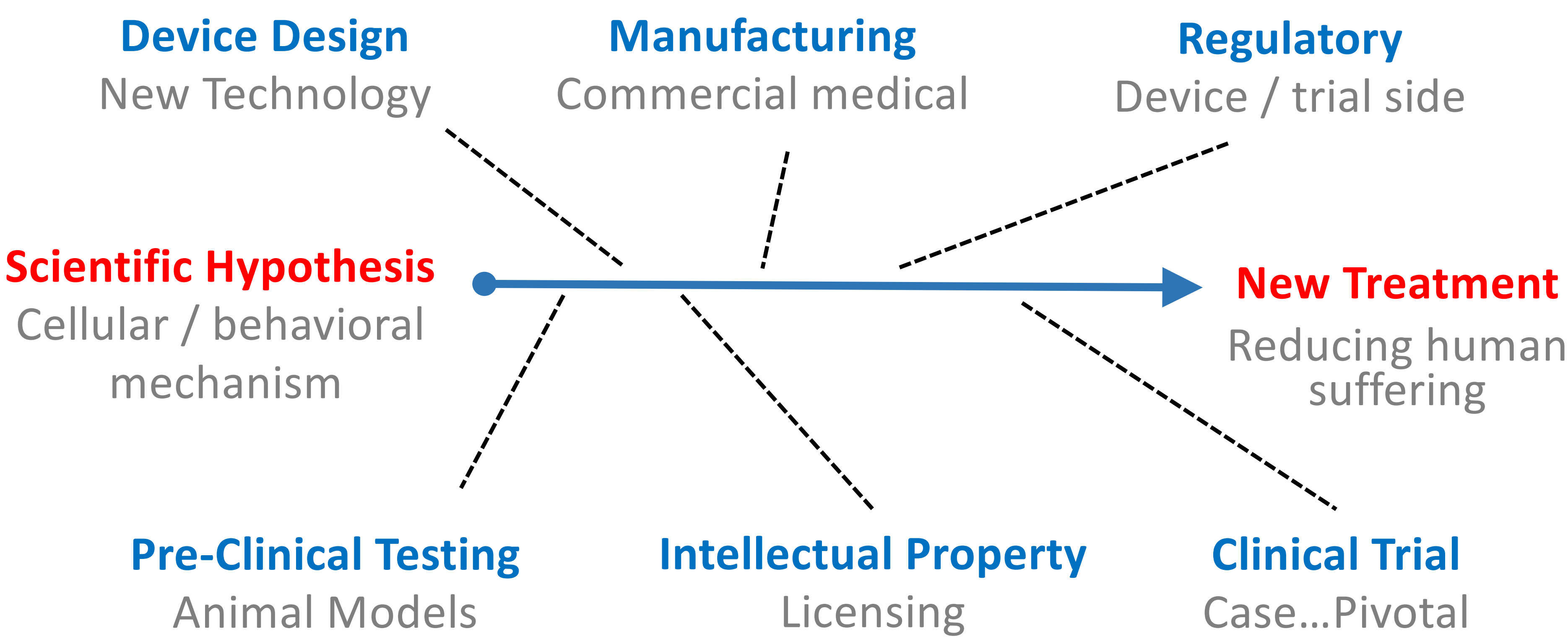
→

New Treatment
Reducing human suffering

Translational Medical Device Design



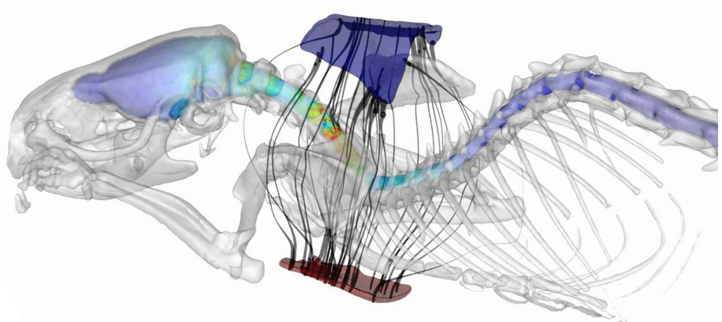
Translational Medical Device Design

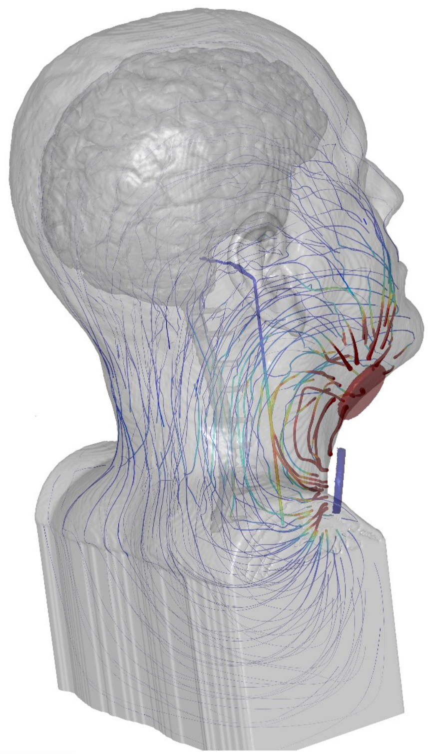


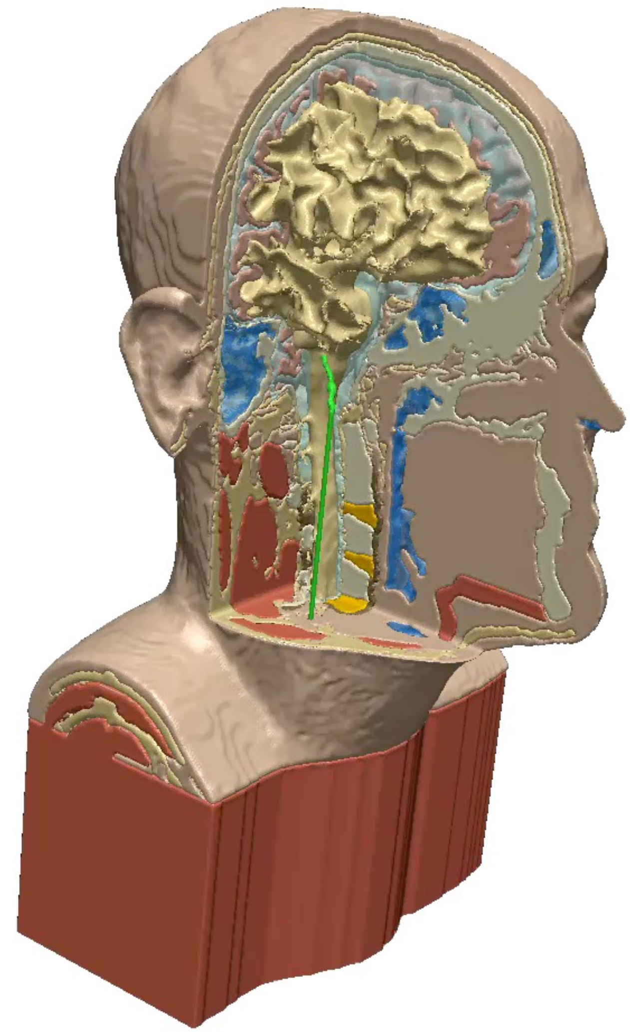
Design as a continuum. Multidisciplinary. Primary outcome is reduced suffering (commercialization is means to end).

Model driven design

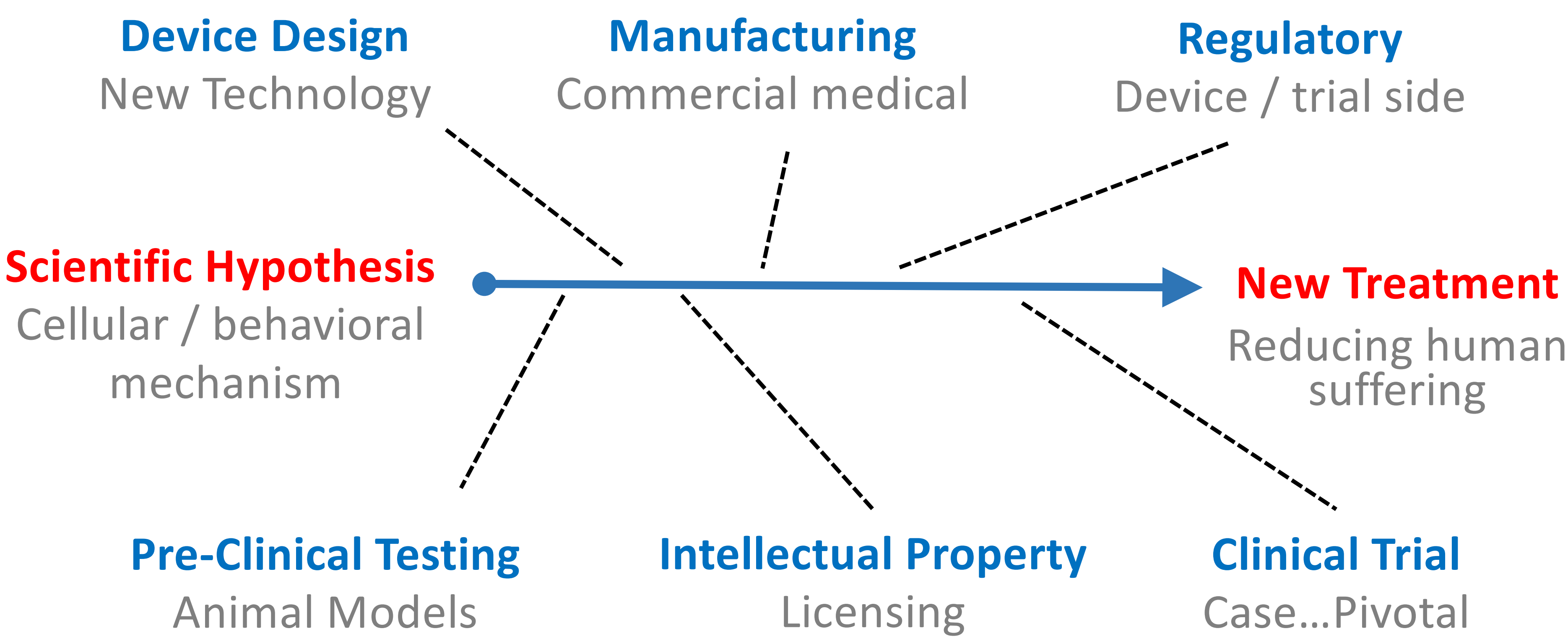
- Part of equipment design, personalized software
- Supports translation from pre-clinical models
- Supports trial design
- Supports regulatory



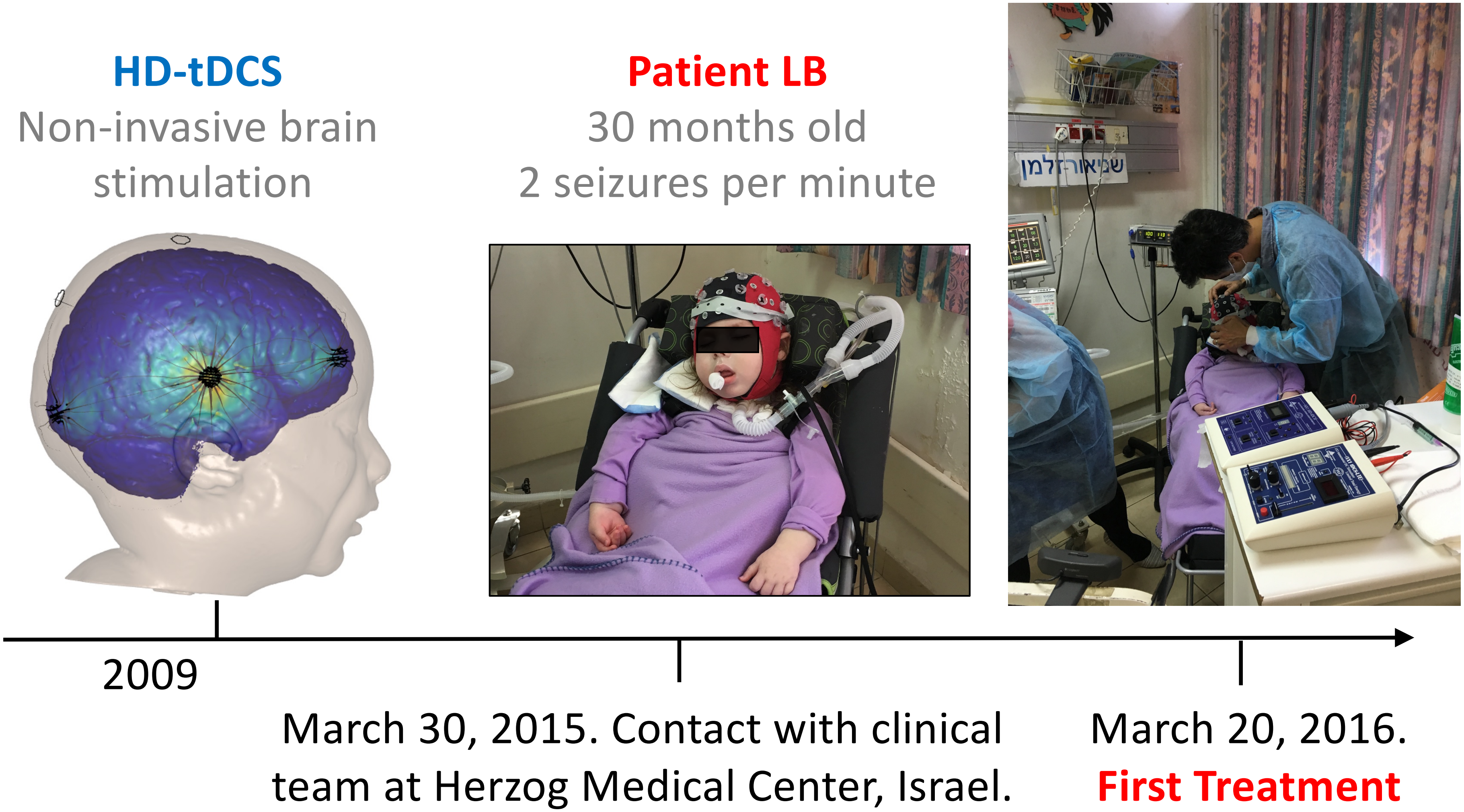


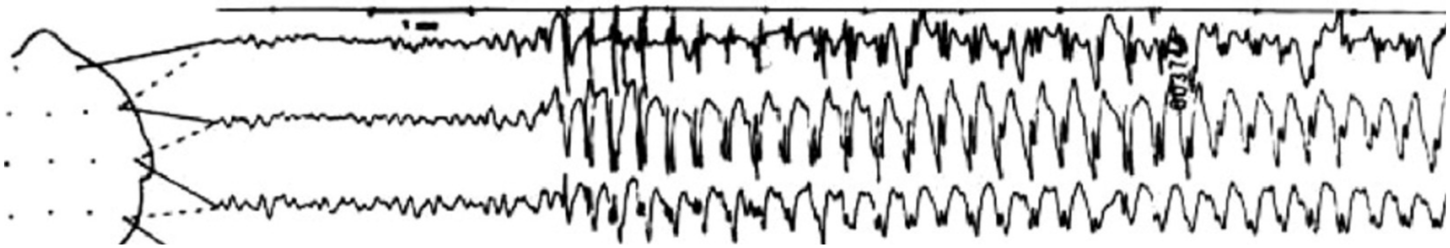


Translational Medical Device Design



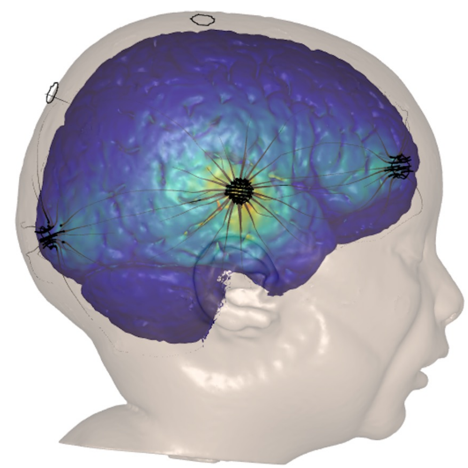
Case study of process


HD-tDCS
Non-invasive brain stimulation
Patient LB
30 months old
2 seizures per minute
2009
March 30, 2015. Contact with clinical team at Herzog Medical Center, Israel.
March 20, 2016.
First Treatment



HD-tDCS

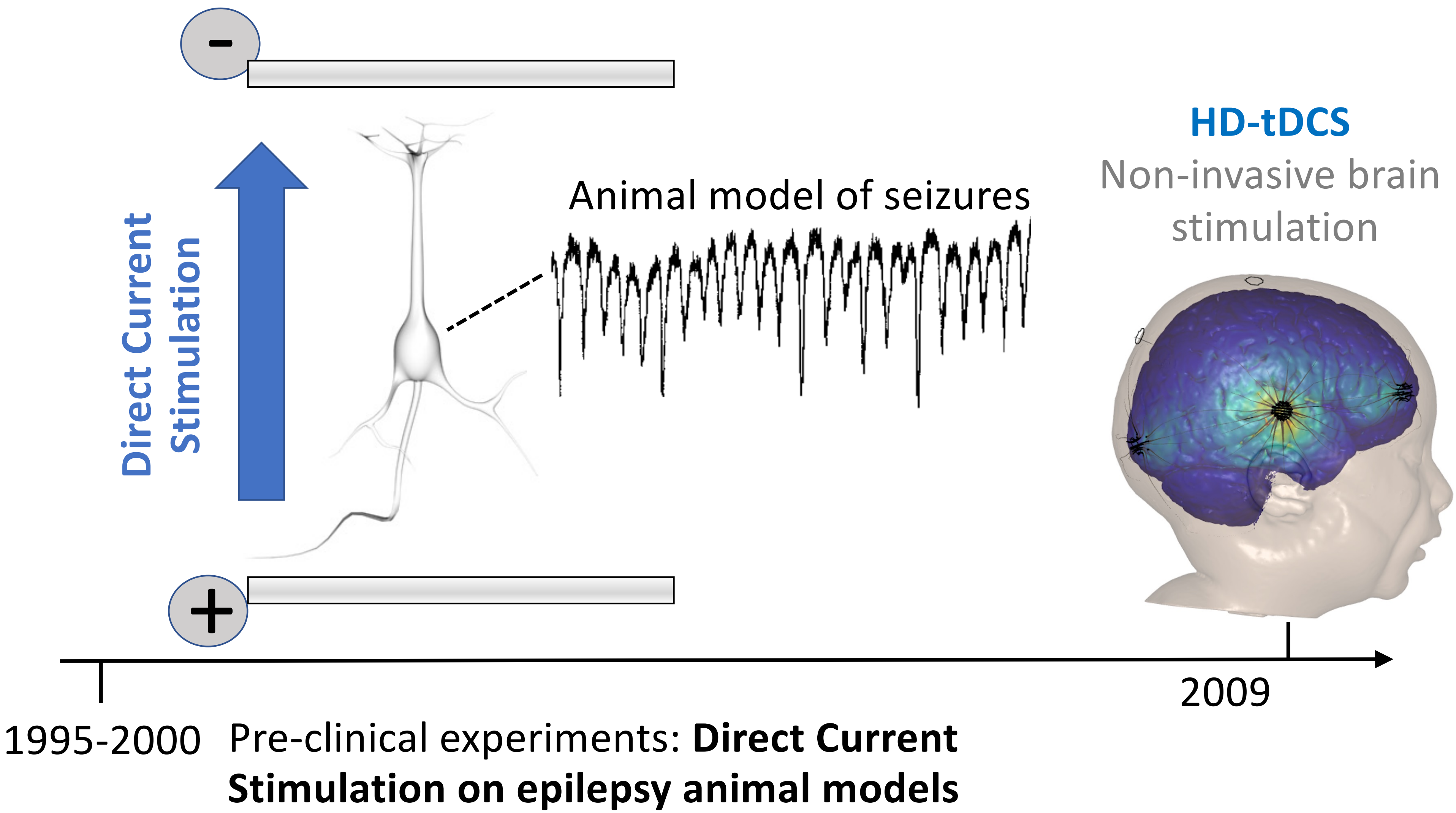
Non-invasive brain stimulation



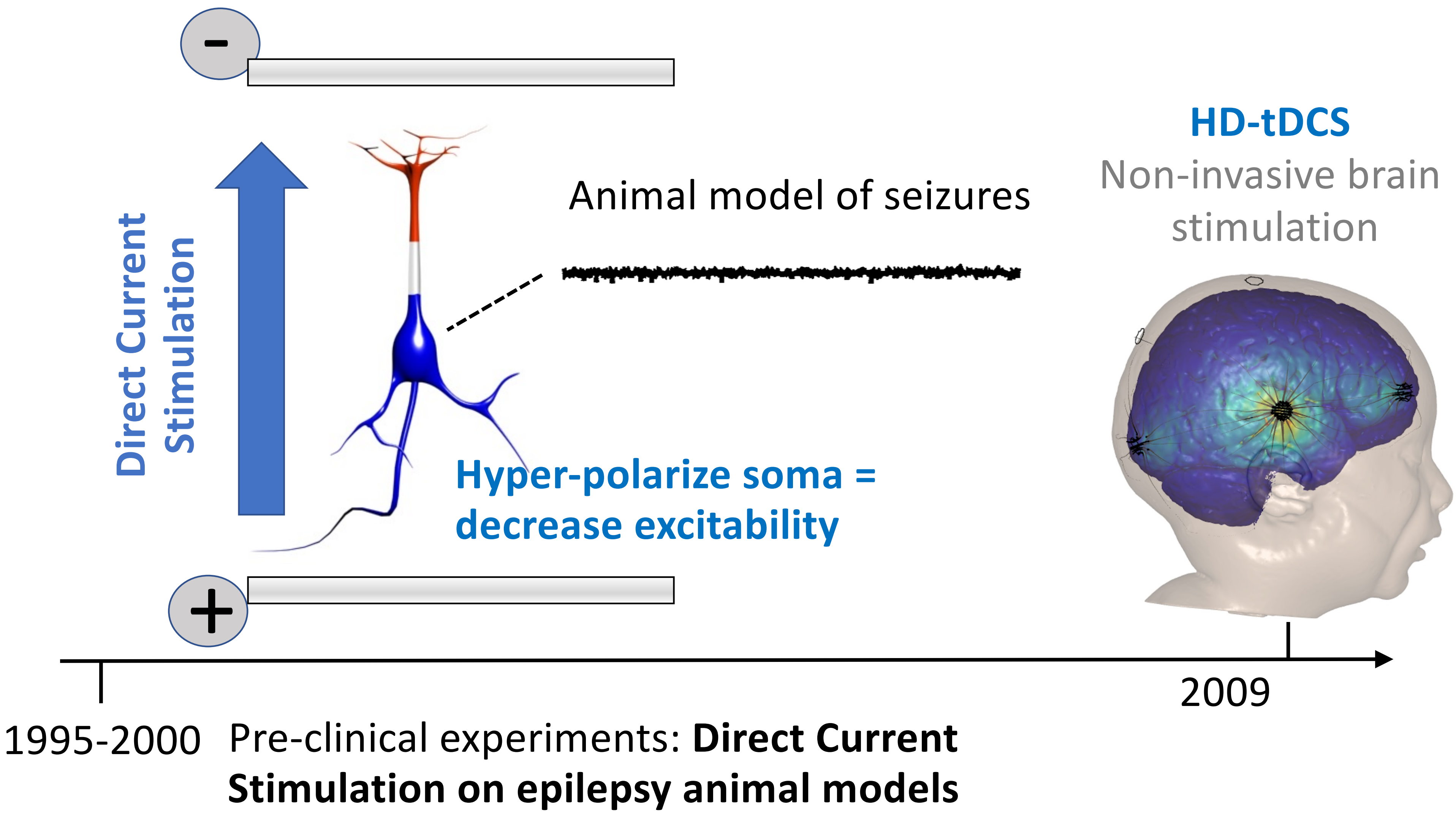
- Epilepsy: Seizures of hyper-active neurons
- Treatments decrease excitability
- More electrical stimulation increase activity
- **Direct Current Stimulation can decrease activity: control seizures**

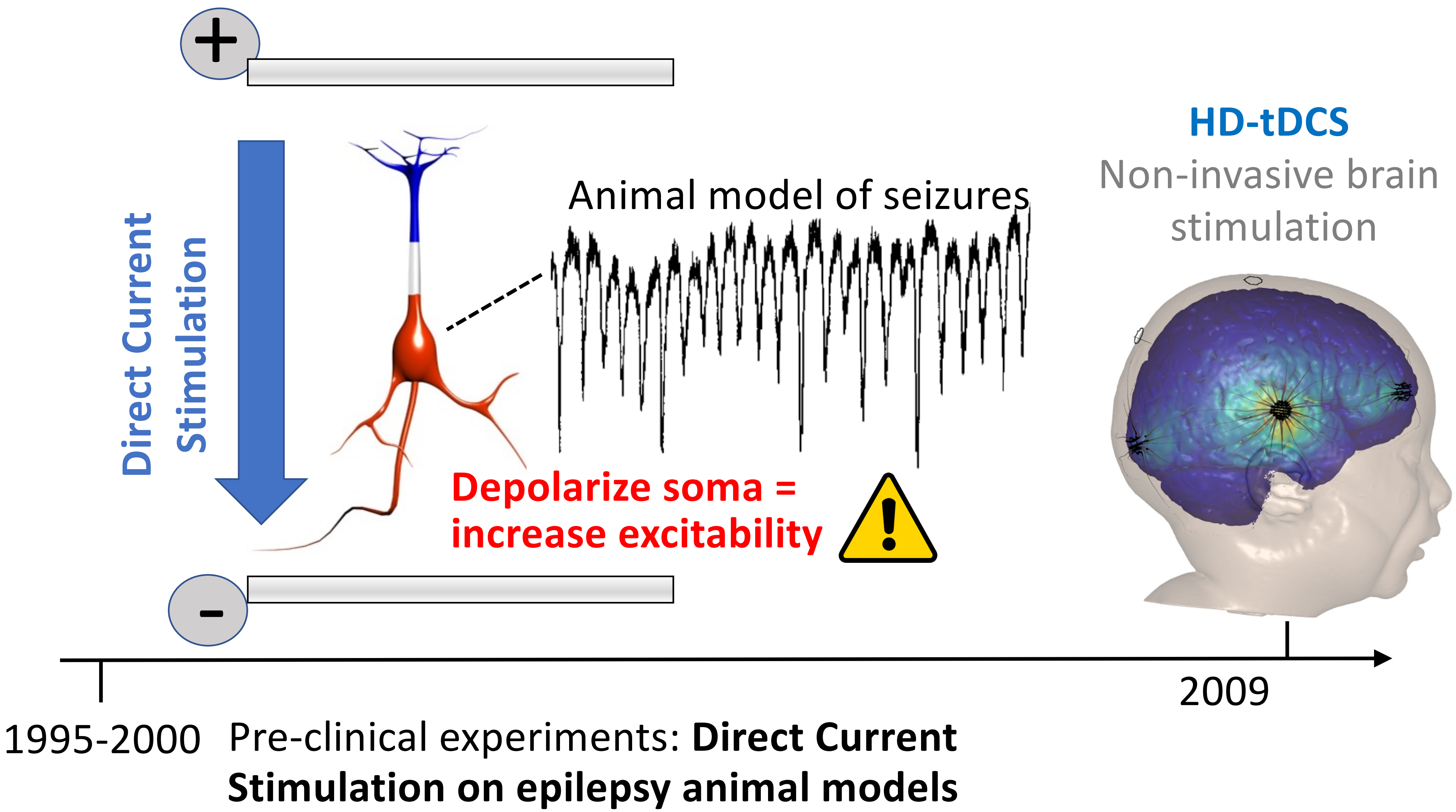
2009

1995-2000 Pre-clinical experiments: **Direct Current Stimulation on epilepsy animal models**



-
+
Direct Current Stimulation
Animal model of seizures
HD-tDCS
Non-invasive brain stimulation
2009
1995-2000
Pre-clinical experiments: **Direct Current Stimulation on epilepsy animal models**


Direct Current Stimulation
Animal model of seizures
Hyper-polarize soma = decrease excitability
HD-tDCS
Non-invasive brain stimulation
2009
1995-2000
Pre-clinical experiments: **Direct Current Stimulation on epilepsy animal models**



Direct Current Stimulation
Animal model of seizures
Depolarize soma = increase excitability
HD-tDCS
Non-invasive brain stimulation
2009
1995-2000
Pre-clinical experiments: **Direct Current Stimulation on epilepsy animal models**

PROCEEDINGS OF THE IEEE, VOL. 89, NO. 7, JULY 2001

Suppression and Control of Epileptiform Activity by Electrical Stimulation: A Review

DOMINIQUE M. DURAND, MEMBER, IEEE, AND MAROM BIKSON

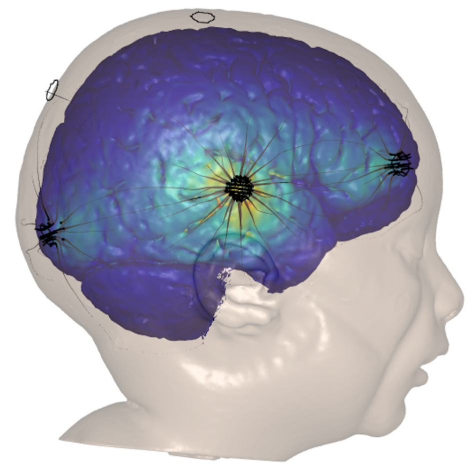
Dominique M. Durand (Member, IEEE) was born in Monbazillac, France, in 1951. He received the Eng. degree from Ecole Nationale Superieure d'Electronique, Hydrolique, Informatique et Automatique de Toulouse, France, in 1973, the M.S. degree in Biomedical Engineering from Case Reserve University, Cleveland, OH, in 1974, and the Ph.D. degree in electrical engineering from the Institute of Biomedical Engineering, University of Toronto, Canada, in 1982.

Marom Bikson was born in Tel-Aviv, Israel, in 1975. He received the B.S. degree in biomedical engineering from Johns Hopkins University, and the Ph.D. in biomedical engineering from Case Western Reserve University in 2001.

He worked at Sontra Medical, Cambridge, MA. He is currently a post-doctoral fellow in the Department of Neurophysiology, Division of Neuroscience, University of Birmingham, U.K. His research interests include nonsynaptic interactions in the CNS and the effects of

HD-tDCS

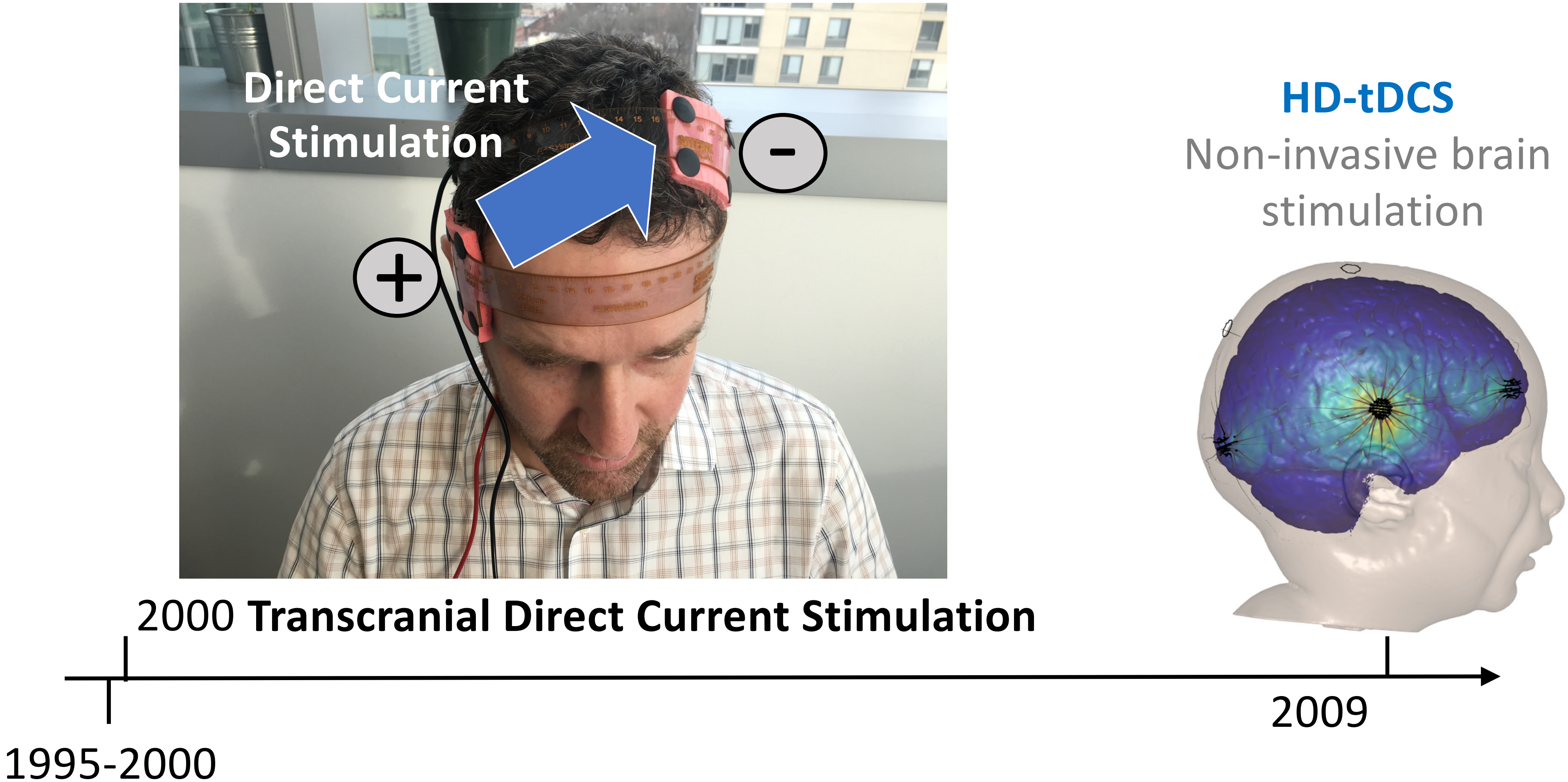
Non-invasive brain stimulation

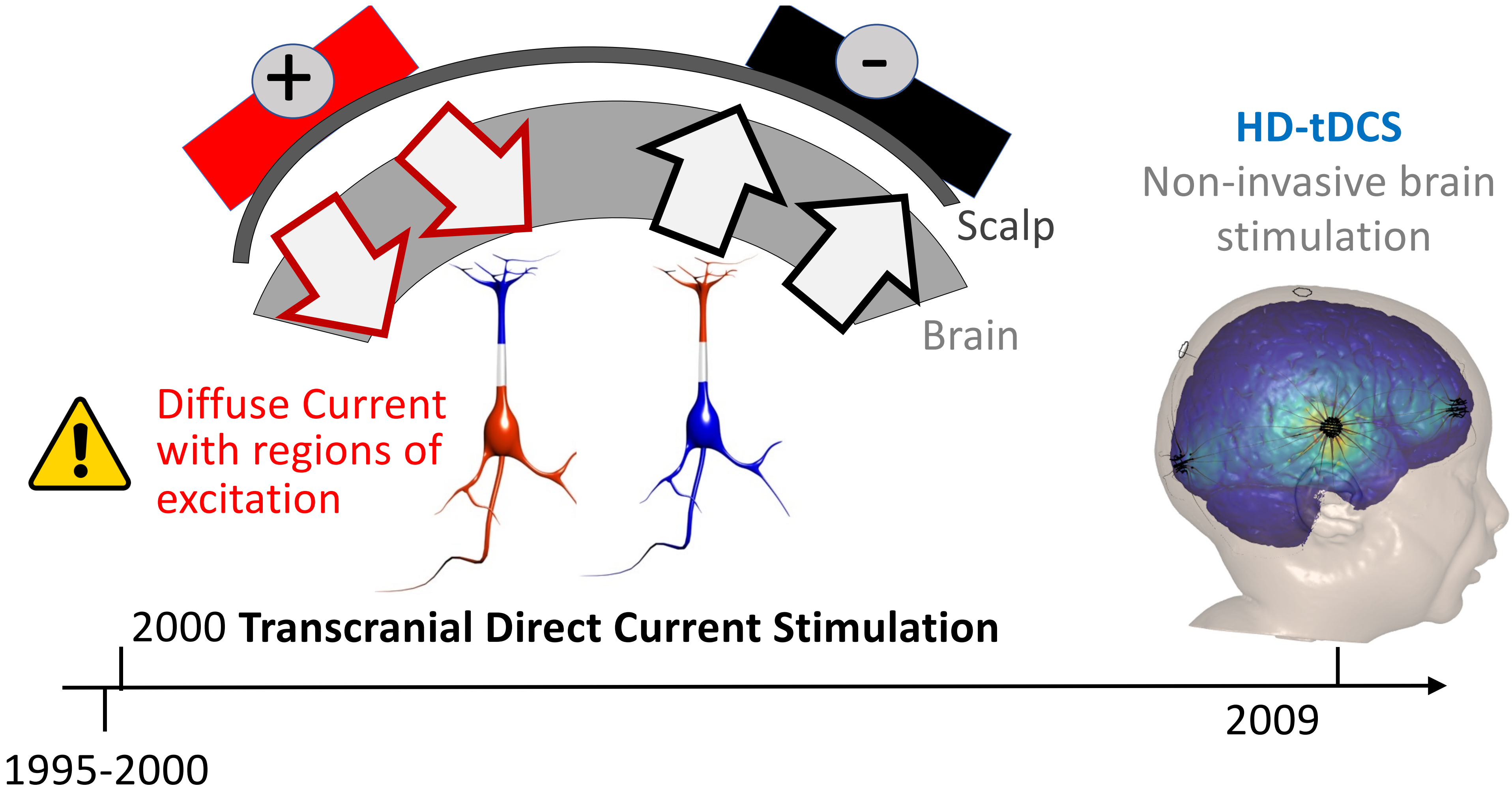


Solid biomedical science + engineering. No translation.

2009

1995-2000 Pre-clinical experiments: **Direct Current Stimulation on epilepsy animal models**


Direct Current
Stimulation
+
-
HD-tDCS
Non-invasive brain
stimulation
2000 **Transcranial Direct Current Stimulation**
1995-2000
2009



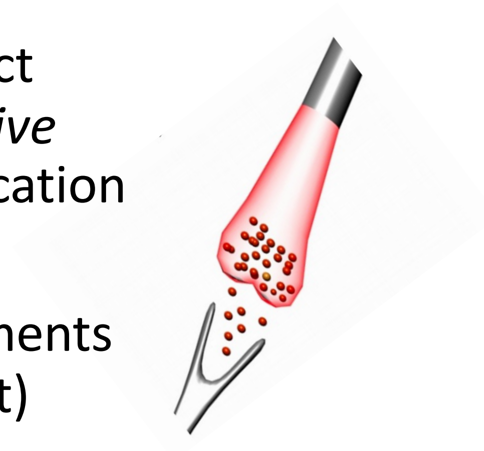
HD-tDCS
Non-invasive brain stimulation
Scalp
Brain
Diffuse Current with regions of excitation
2000 Transcranial Direct Current Stimulation
2009
1995-2000

J Physiol 557.1 (2004) pp 175–190

Effects of uniform extracellular DC electric fields on excitability in rat hippocampal slices *in vitro*

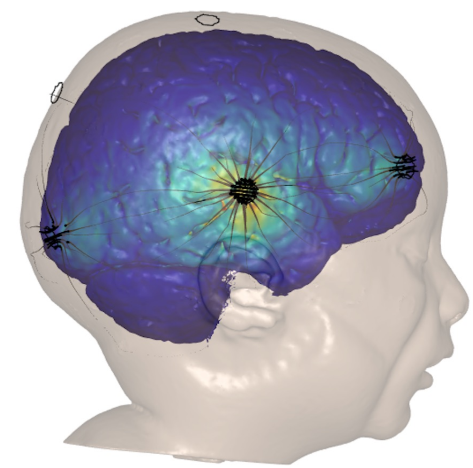
Marom Bikson[1], Masashi Inoue[2], Hiroki Akiyama[2], Jackie K. Deans[1], John E. Fox[1], Hiroyoshi Miyakawa[2] and John G. R. Jefferys[1]

- Established that low-intensity direct current modulate only already *active* synaptic processing (human application use "functional targeting")
- Soma, dendrite, or axon compartments targeted (all field directions potent)



HD-tDCS

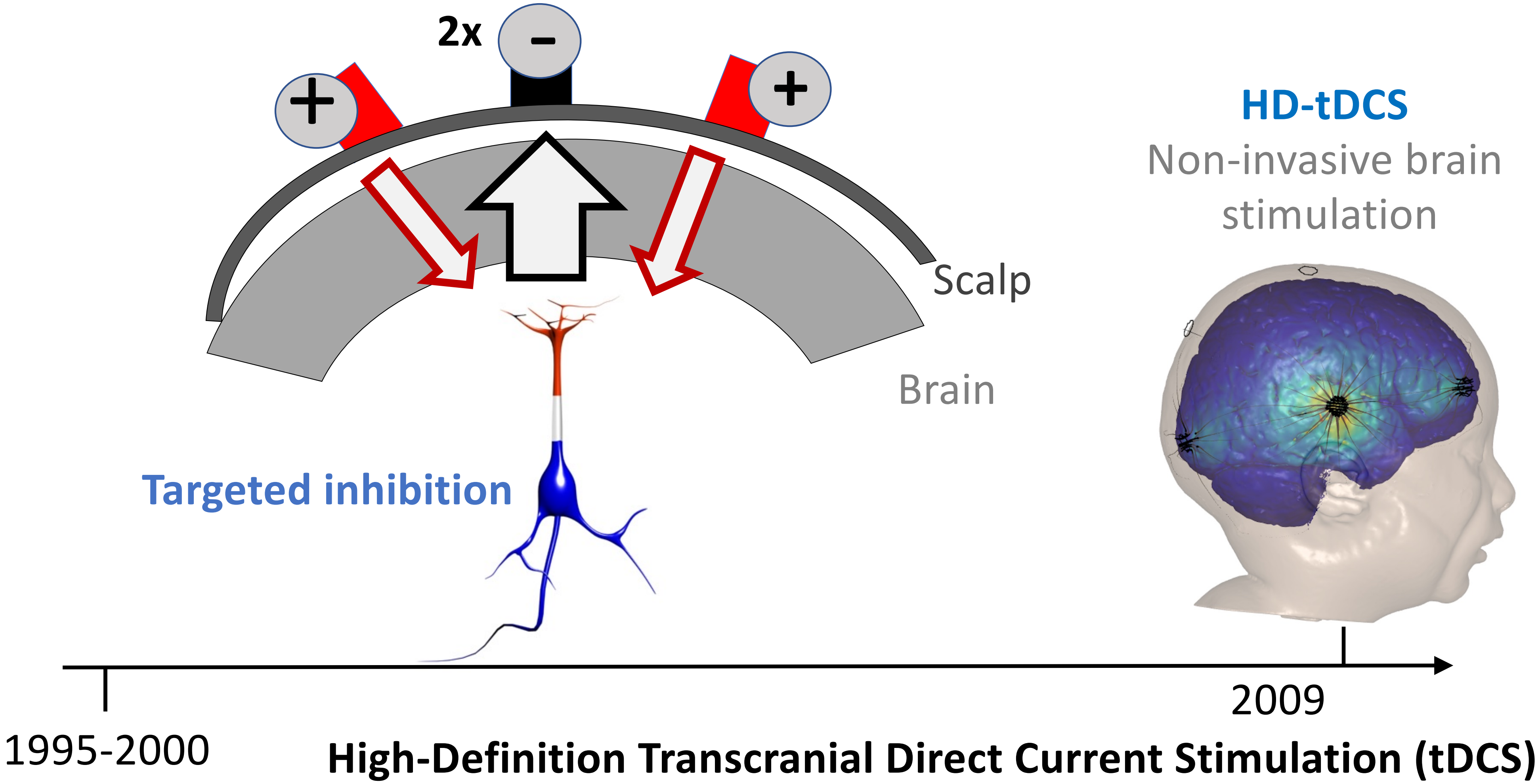
Non-invasive brain stimulation



1995-2000

2004 + **Mechanisms of Direct Current Stimulation**

2009


2x
Scalp
Brain
Targeted inhibition
HD-tDCS
Non-invasive brain stimulation
1995-2000
2009
High-Definition Transcranial Direct Current Stimulation (tDCS)

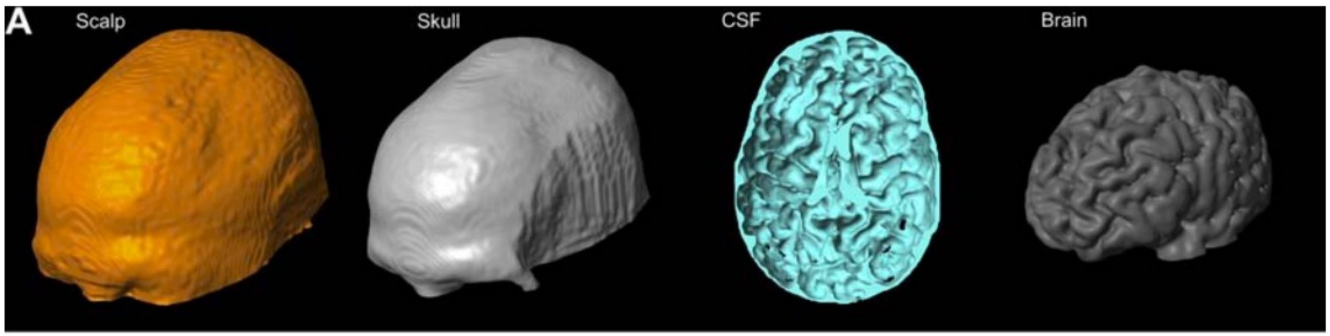
Brain Stimulation (2009) 2, 201 7

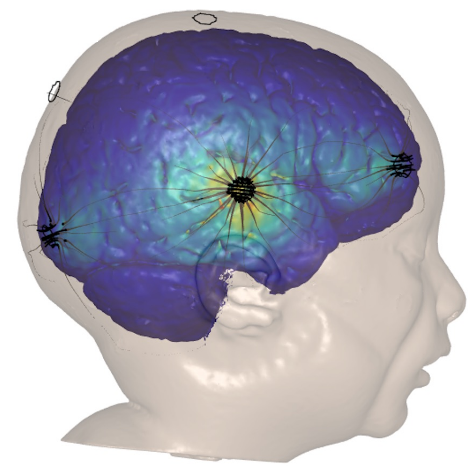
Gyri-precise head model of transcranial direct current stimulation: Improved spatial focality using a ring electrode versus conventional rectangular pad

HD-tDCS

Non-invasive brain stimulation

Model workflow preserves anatomy precision of MRI

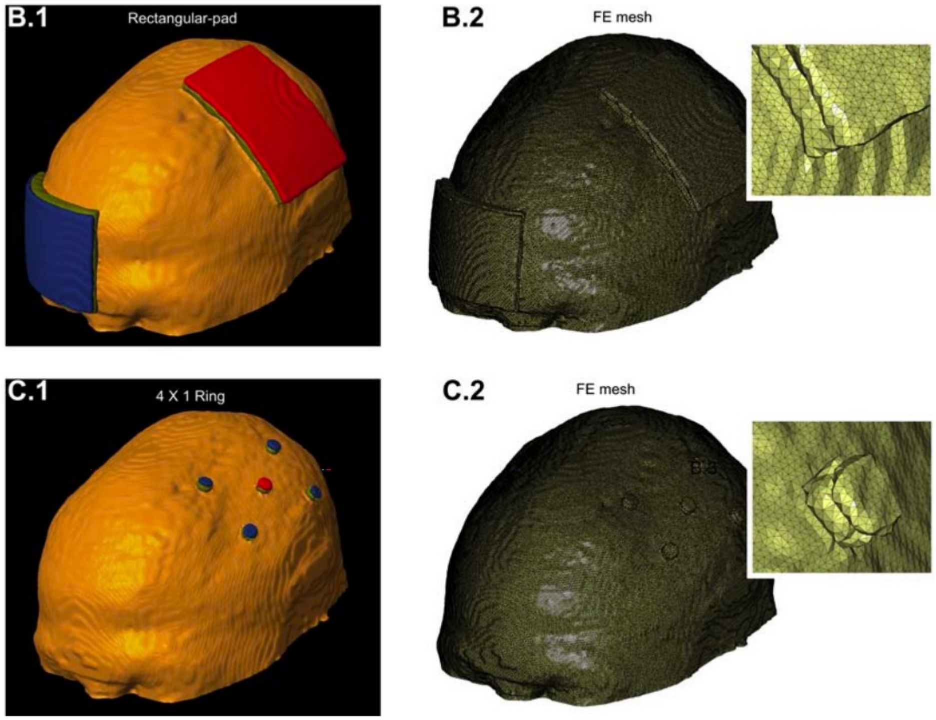




2009

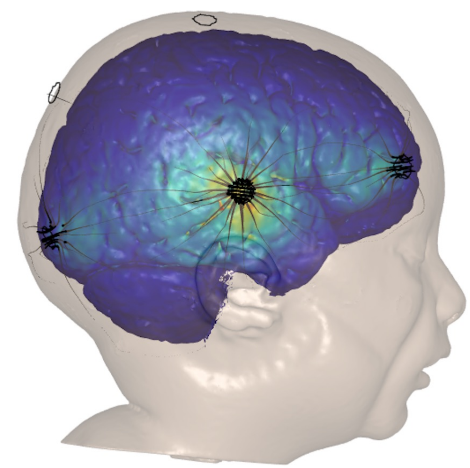
1995-2000

High-Definition Transcranial Direct Current Stimulation (tDCS)



HD-tDCS

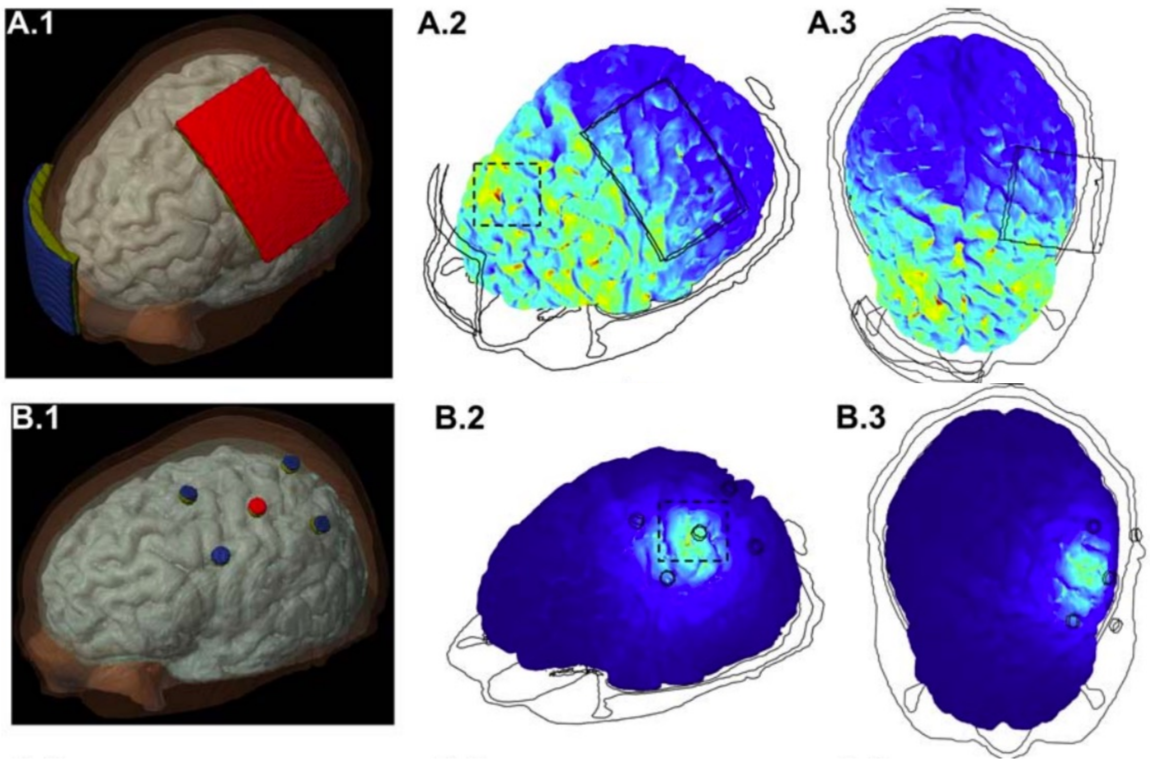
Non-invasive brain stimulation



2009

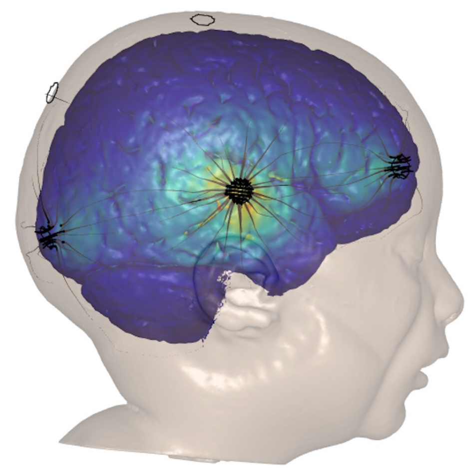
1995-2000

High-Definition Transcranial Direct Current Stimulation (tDCS)



HD-tDCS

Non-invasive brain stimulation



2009

1995-2000

High-Definition Transcranial Direct Current Stimulation (tDCS)

Brain Stimulation (2009) 2, 201 7

Gyri-precise head model of transcranial direct current stimulation: Improved spatial focality using a ring electrode versus conventional rectangular pad

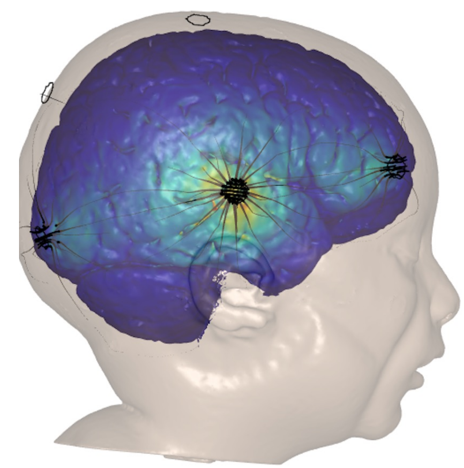
Abhishek Datta, MS, Varun Bansal, BS, Julian Diaz, BS, Jinal Patel, MS, Davide Reato, MS, Marom Bikson, PhD

Since 2009 cited >1100 times. At time was criticized.

1. Seems to refute common understanding of tDCS
2. No possible to pass DC through small electrodes
3. Just a model.

HD-tDCS

Non-invasive brain stimulation



2009

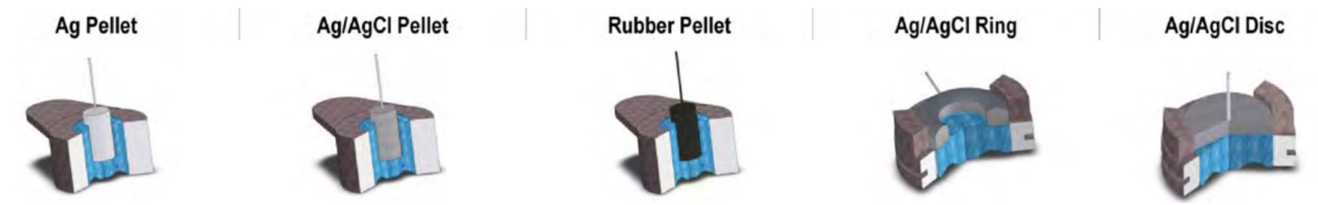
1995-2000

High-Definition Transcranial Direct Current Stimulation (tDCS)

Journal of Neuroscience Methods 190 (2010) 188–197

Electrodes for high-definition transcutaneous DC stimulation for applications in drug delivery and electrotherapy, including tDCS

Preet Minhas[1], Varun Bansal[1], Jinal Patel[1], Johnson S. Ho, Julian Diaz, Abhishek Datta, Marom Bikson*

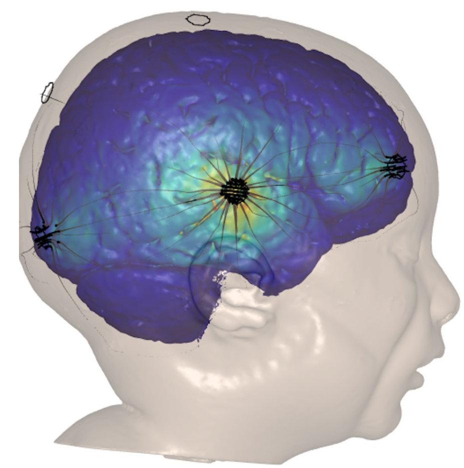


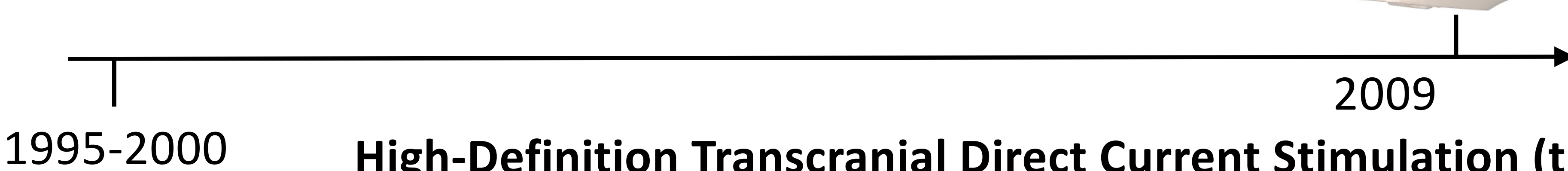
"**High Definition**" electrodes that pass 3 criteria for 'good' electrode

2. No possible to pass DC through small electrodes

HD-tDCS

Non-invasive brain stimulation

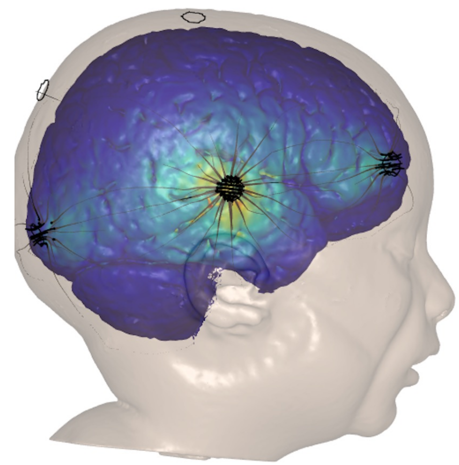




High-Definition Transcranial Direct Current Stimulation (tDCS)

HD-tDCS

Non-invasive brain stimulation



3. Just a model.

1995-2000

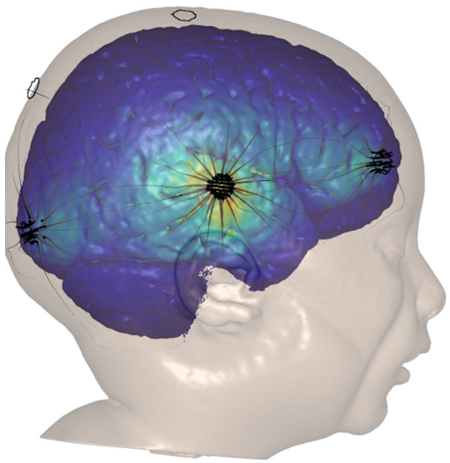
2009

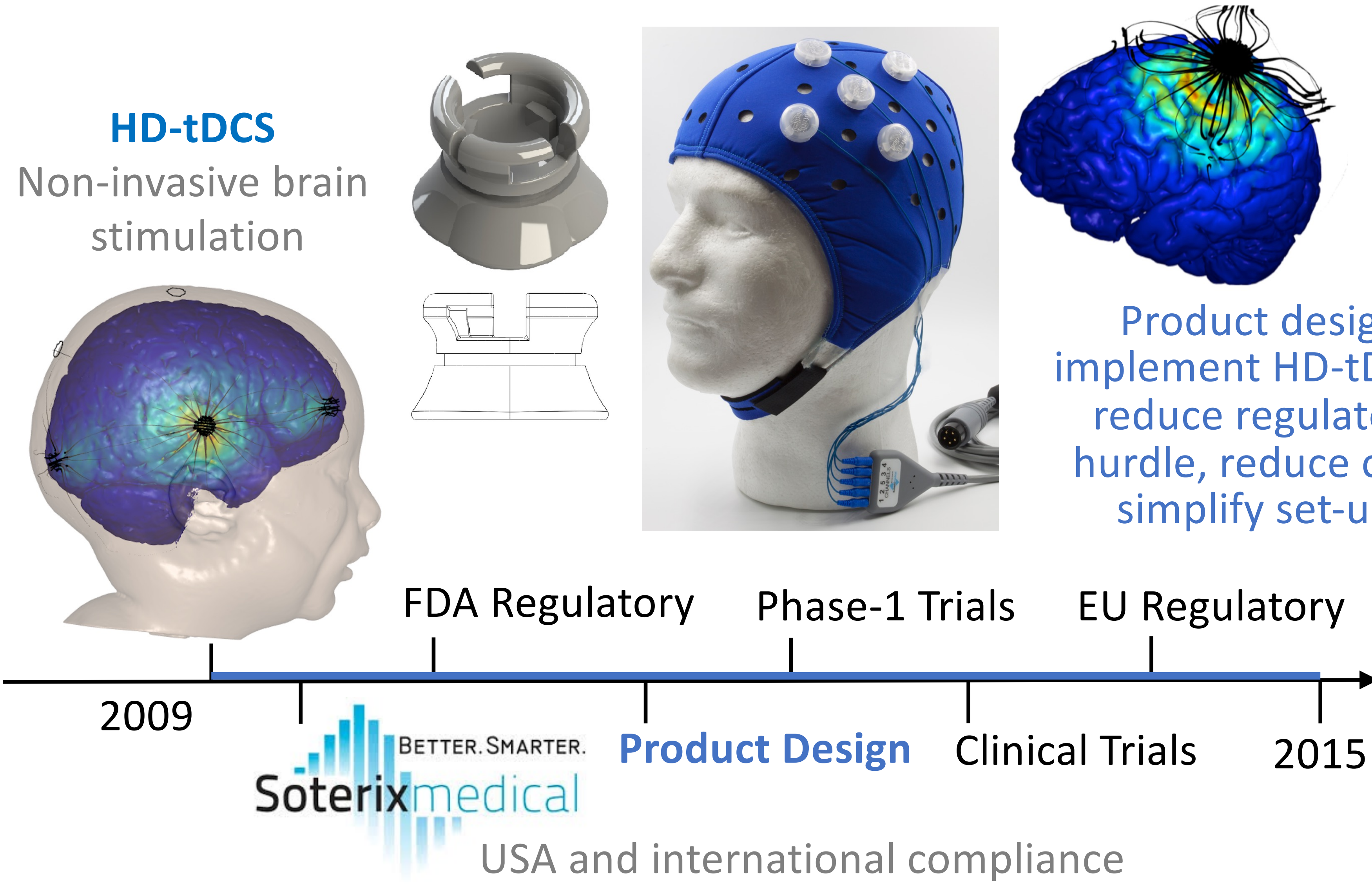
High-Definition Transcranial Direct Current Stimulation (tDCS)

3. Just a model.

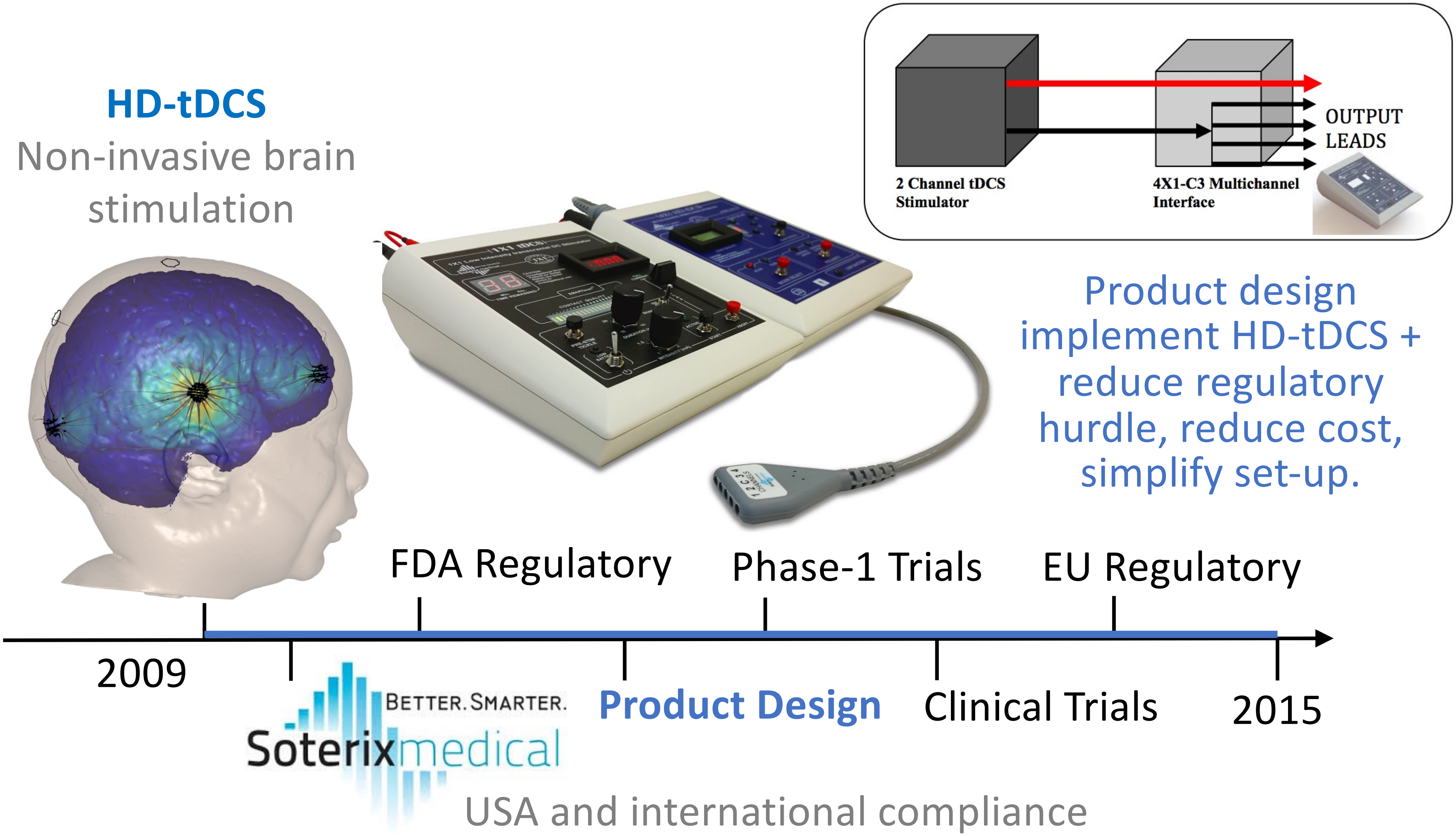
HD-tDCS

Non-invasive brain stimulation



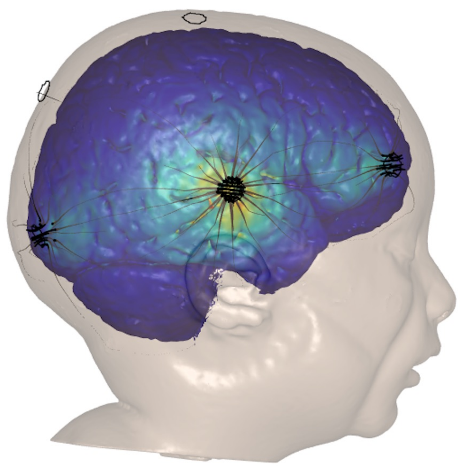


HD-tDCS
Non-invasive brain stimulation
Product design implement HD-tDCS + reduce regulatory hurdle, reduce cost, simplify set-up.
FDA Regulatory
Phase-1 Trials
EU Regulatory
2009
BETTER. SMARTER.
Soterix medical
Product Design
Clinical Trials
2015
USA and international compliance


HD-tDCS
Non-invasive brain stimulation
2 Channel tDCS Stimulator
4X1-C3 Multichannel Interface
OUTPUT LEADS
Product design implement HD-tDCS + reduce regulatory hurdle, reduce cost, simplify set-up.
FDA Regulatory
Phase-1 Trials
EU Regulatory
2009
BETTER.SMARTER.
Soterix medical
Product Design
Clinical Trials
2015
USA and international compliance

HD-tDCS

Non-invasive brain stimulation



American Pain Society — RESEARCH EDUCATION TREATMENT ADVOCACY
The Journal of Pain, Vol 13, No 2 (February), 2012: pp 112-120
Available online at www.sciencedirect.com

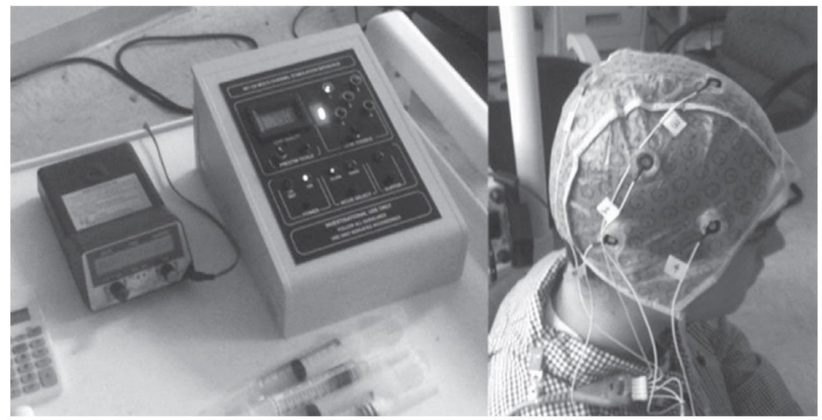


Figure 1. Photos of the HD-tDCS device and interface, and example of the electrode configuration used in the present study.

2009

FDA Regulatory

Phase-1 Trials

EU Regulatory

BETTER. SMARTER. Soterixmedical

Product Design

Clinical Trials

2015

USA and international compliance

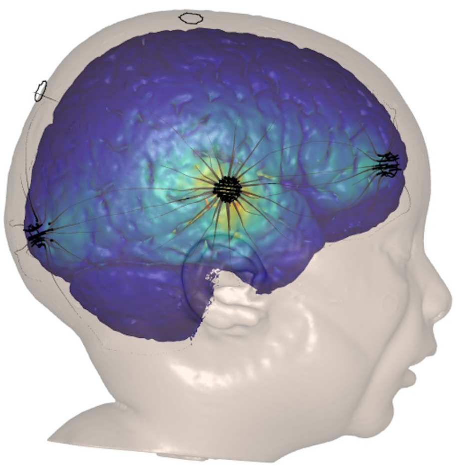
HD-tDCS

Non-invasive brain stimulation

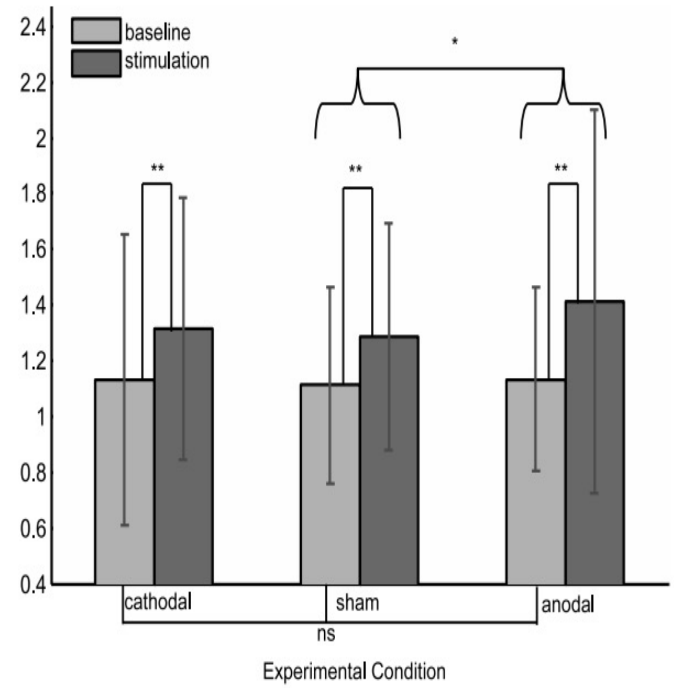
34th Annual International Conference of the IEEE EMBS
San Diego, California USA, 28 August - 1 September, 2012

A Pilot Study on Effects of 4x1 High-Definition tDCS on Motor Cortex Excitability

Egas M. Caparelli-Daquer[1], Trelawny J. Zimmermann[2], Eric Mooshagian[2], Lucas C. Parra[3], Justin K. Rice[3], Abhishek Datta[3], Marom Bikson[3], and Eric M. Wassermann[2]



4x1 HD-tDCS modulates cortical excitability



FDA Regulatory

Phase-1

2009

Soterix medical — BETTER. SMARTER.

Product Design

USA and international compliance

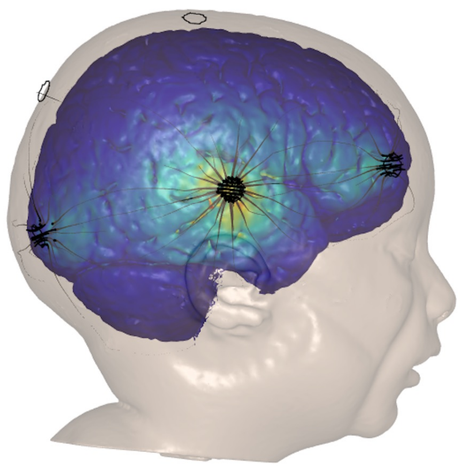
HD-tDCS

Non-invasive brain stimulation

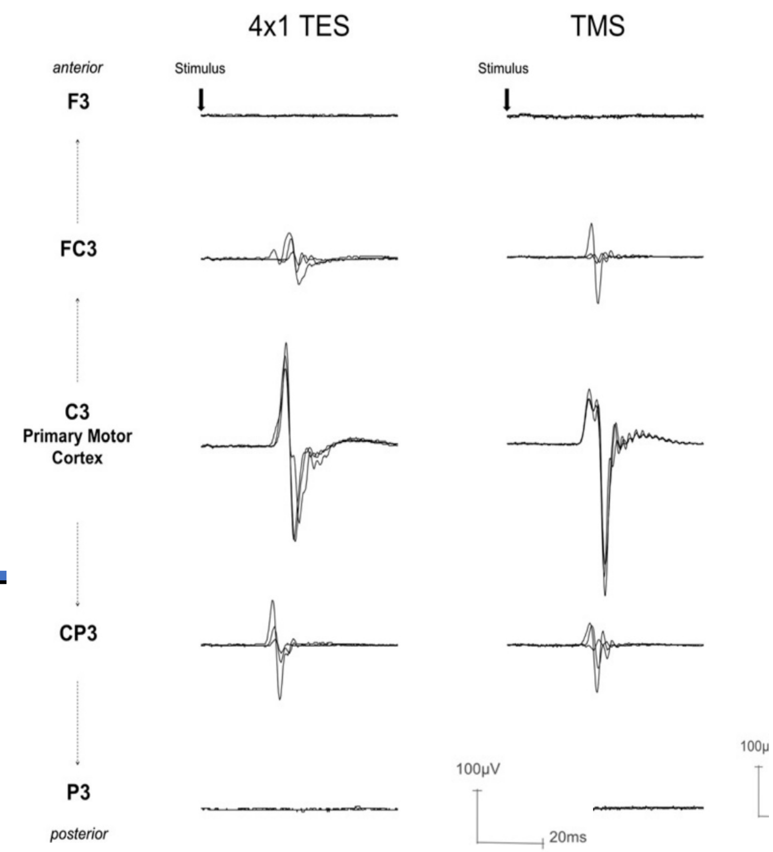
NeuroImage 74 (2013) 266–275

Physiological and modeling evidence for focal transcranial electrical brain stimulation in humans: A basis for high-definition tDCS

Dylan Edwards [a,b,c,d,*], Mar Cortes [a,b], Abhishek Datta [e], Preet Minhas [e], Eric M. Wassermann [f], Marom Bikson [e]



4x1 High-Definition with high intensity pulses, as focal as TMS in producing MEPs



2009

FDA Regulatory

Phase-1

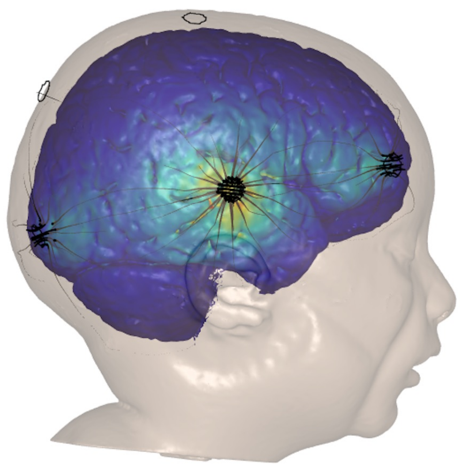
Product Design

BETTER. SMARTER.

Soterix medical

HD-tDCS

Non-invasive brain stimulation



ant neuro

ElMindA

Combining HD-tDCS with EEG mapping of brain

"Read and write the brain"

2009

BETTER. SMARTER.
Soterix medical

FDA Regulatory

Product Design

USA and international compliance

Phase-1 Trials

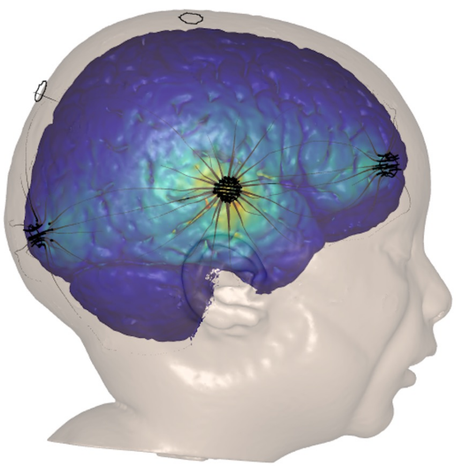
Clinical Trials

EU Regulatory

2015

HD-tDCS

Non-invasive brain stimulation



American Pain Society
RESEARCH EDUCATION TREATMENT ADVOCACY
PUBLISHED BY ELSEVIER

The Journal of Pain, Vol 17, No 1 (January), 2016: pp 14-26
Available online at www.jpain.org and www.sciencedirect.com

Clinically Effective Treatment of Fibromyalgia Pain With High-Definition Transcranial Direct Current Stimulation: Phase II Open-Label Dose Optimization

Laura Castillo-Saavedra,[*,1] Nigel Gebodh,[*,†,1] Marom Bikson,[†] Camilo Diaz-Cruz,[*] Rivail Brandao,[*,‡] Livia Coutinho,[*] Dennis Truong,[†] Abhishek Datta,[†,§] Revital Shani-Hershkovich,[¶] Michal Weiss,[¶] Ilan Laufer,[¶] Amit Reches,[¶] Ziv Peremen,[¶,||] Amir Geva,[¶,**] Lucas C. Parra,[†] and Felipe Fregni[*]

*Laboratory of Neuromodulation, Department of Physical Medicine and Rehabilitation, Spaulding Rehabilitation Hospital and Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts.
†Department of Biomedical Engineering, The City College of the City University of New York, New York, New York.
‡Postgraduate Program in Interactive Processes of Organs and Systems, Federal University of Bahia, Salvador, Bahia, Brazil.
§Soterix Medical, Inc, New York, New York.
¶ElMindA Ltd, Herzliya, Israel.
||Tel Aviv University, Tel Aviv, Israel.
**Ben Gurion University, Beersheba, Israel.

FDA Regulatory

Phase-1 Trials

EU Regulatory

2009

BETTER. SMARTER.
Soterix medical

Product Design

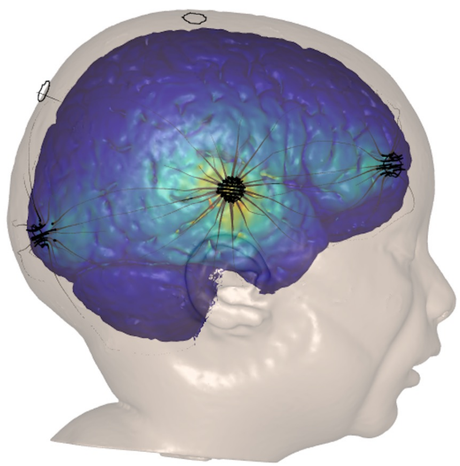
Clinical Trials

2015

USA and international compliance

HD-tDCS

Non-invasive brain stimulation



FDA Regulatory

Phase-1 Trials

EU Regulatory

2009

BETTER. SMARTER.

Soterix medical

Product Design

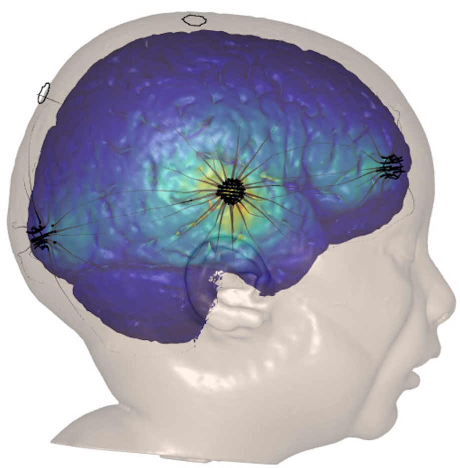
Clinical Trials

2015

USA and international compliance

HD-tDCS

Non-invasive brain stimulation



Patient LB

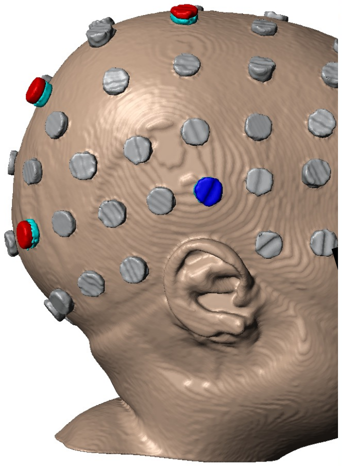
30 months old

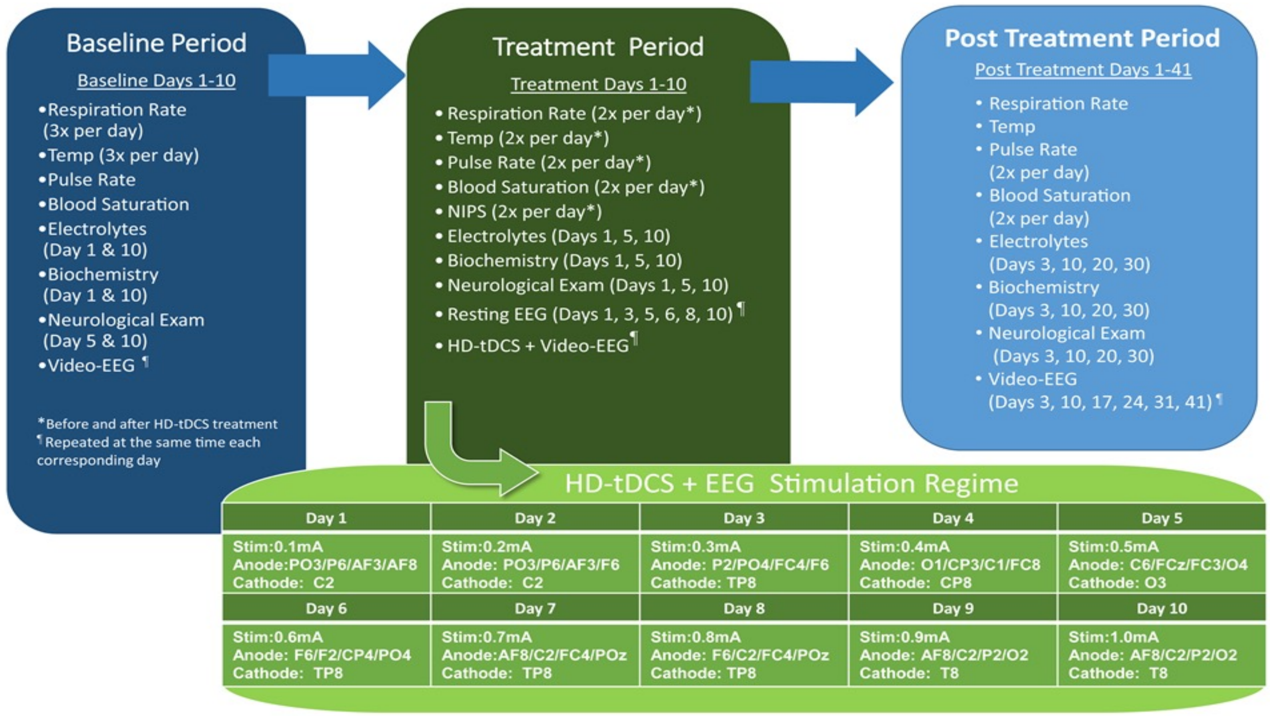
2 seizures per minute

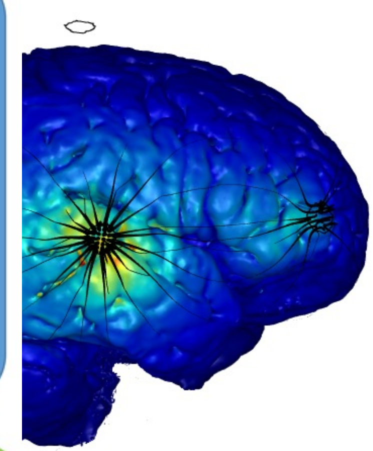
2009

March 30, 2015. Contact with clinical team at Herzog Medical Center, Israel.

March 20, 2016. **First Treatment**







HD-tDCS ir ... **fied by EEG.**

Tran ... **esign.**

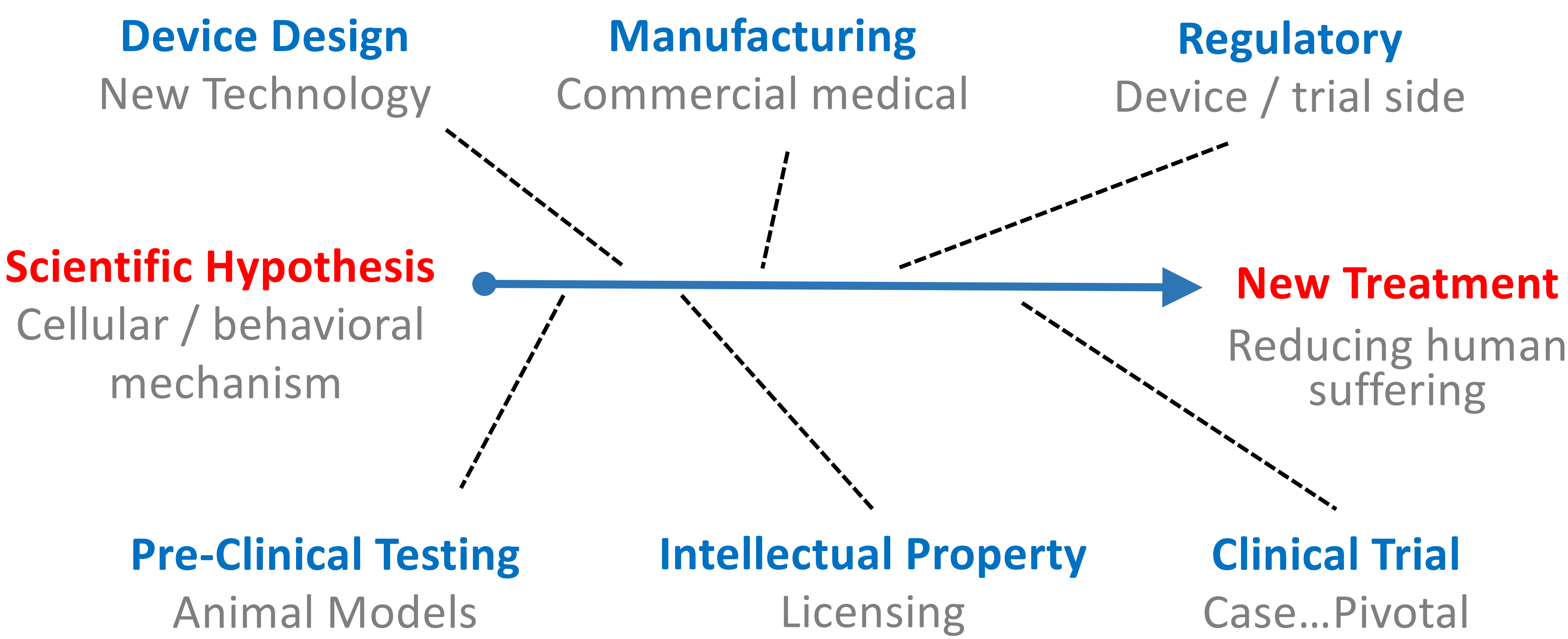
Trial design | Dose design | Device customization

March 30, 2015
Patient LB

Regulatory: Israel Ministry of Health

March 20, 2016.
First Treatment

Translational Medical Device Design



Design as a continuum. Multidisciplinary. Primary outcome is reduced suffering (commercialization is means to end).

Medical Device Design

Scientific Hypothesis → **New Treatment**

Cellular / behavioral mechanism → Reducing human suffering

Home-based tDCS

Remote-supervised tDCS

WiPOX: Wireless hand-help intraoperative sensor

(non-commercial)

Toddler-Cane

Wearable white cane

Non-profit (Safe Toddles)

Scientific Hypothesis

Safe mobility = health development of visually impaired toddlers

New Treatment

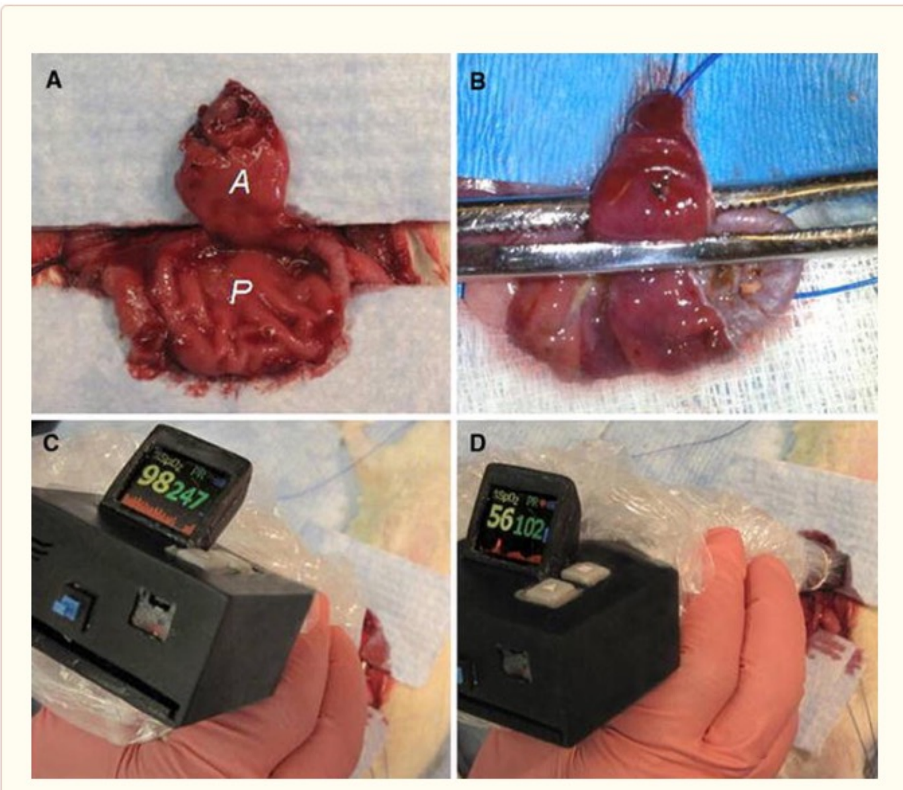
Toddler Cane: Hands-free, wearable, 2-step warning

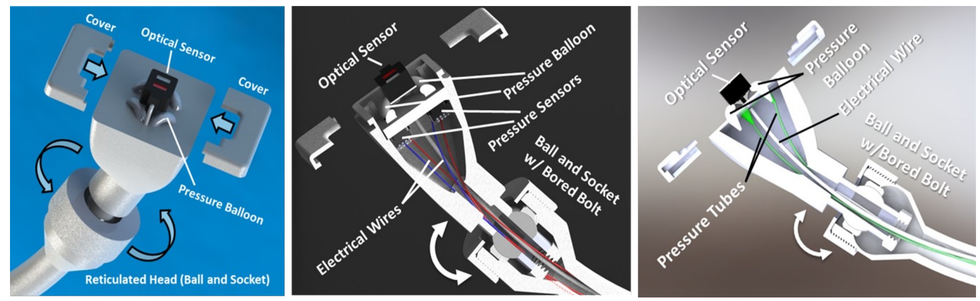
Scientific Hypothesis

Local tissue oxygen saturation determines viability after surgery

New Treatment

Intraoperative rapid-response pen-tip sensor of tissue viability





- **Surgical “tool”**
- **Rapid-prototype solution sterility**
- **Positive clinical trial.**

Developing tDCS as a therapeutic tool

Translational Neural Engineering: Hypothesis-based Devices Design

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