DBS and Beyond: Emerging Approaches to Neuromodulation

Michael S. Okun, M.D.

Adelaide Lackner Distinguished Professor of Neurology

Medical Advisor, Parkinson Foundation

Director, Norman Fixel Institute for Neurological Diseases

UFHealth
NORMAN FIXEL INSTITUTE FOR NEUROLOGICAL DISEASES

Parkinson's Foundation

Tourette Association of America
Awareness. Research. Support.

Tyler's Hope for a Dystonia Cure

NIH
National Institutes of Health

Disclosure

- Nothing to Disclose

Objective

- Compare the potential benefits and limitations of traditional DBS compared with new adaptive DBS (aDBS) devices and therapies

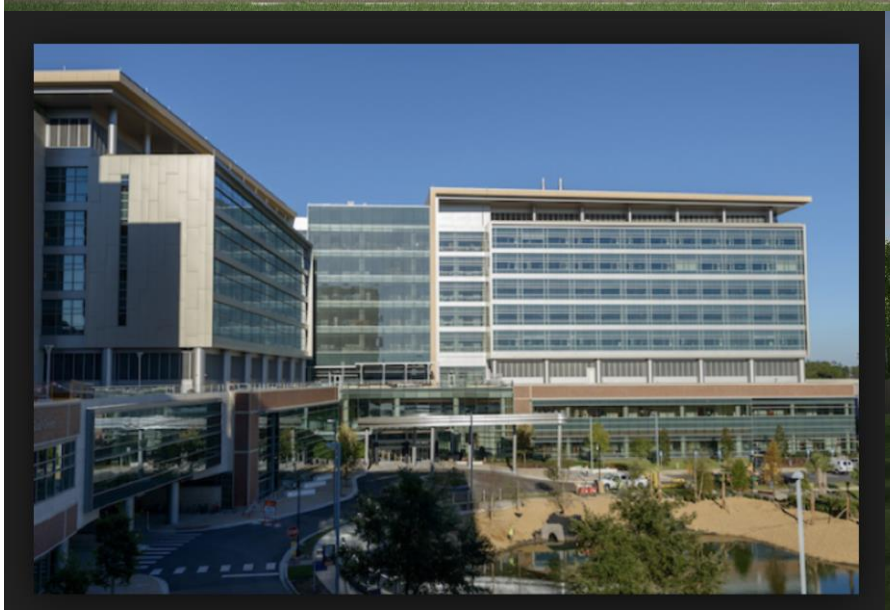
NIH Support

- UH3 NS18-023 Defining Targets for Tic Detection and Suppression in Tourette Syndrome Deep Brain Stimulation NS18-023
- U01 Automated Image Differentiation of Parkinson's
- R25NS108939 University of Florida R25 Early Research Program for Neurology and Neurosurgery Residents
- R01NS096008 The Human Thalamocortical Network in Tourette Syndrome
- R01NR014852 Mobile Decision Support System for Nurse Management of Neuromodulation Therapy
- R21NS072897 Neural Correlates of Tourette Syndrome
- R34MH080764 Scheduled and Responsive Brain Stimulation for the Treatment of Tourette Syndrome

Fixel Institute Campus for Neurological Diseases at UF

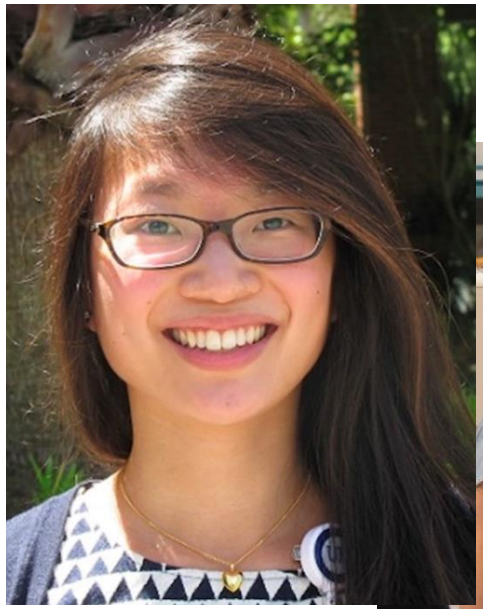
Twitter, Instagram, Threads: @MichaelOkun

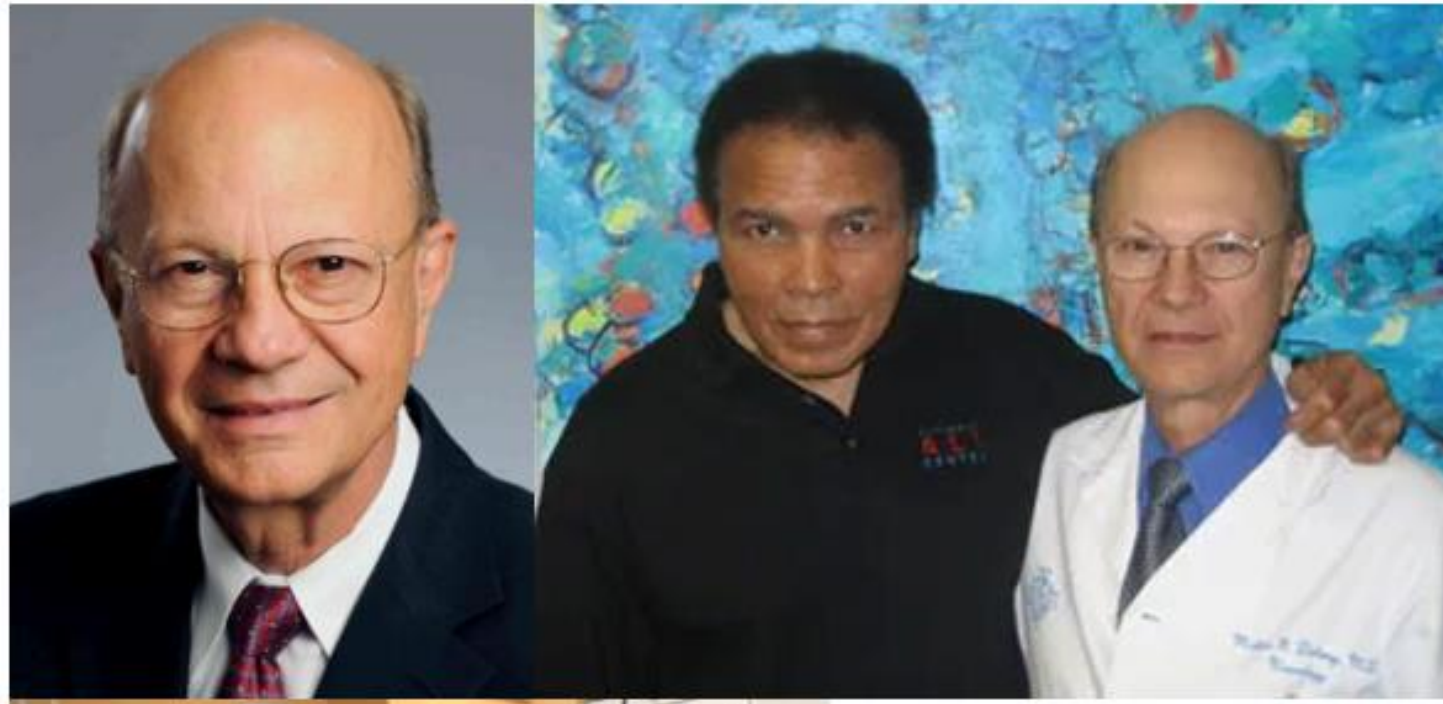
Blog: parkinsonsecrets.com



Acknowledgements

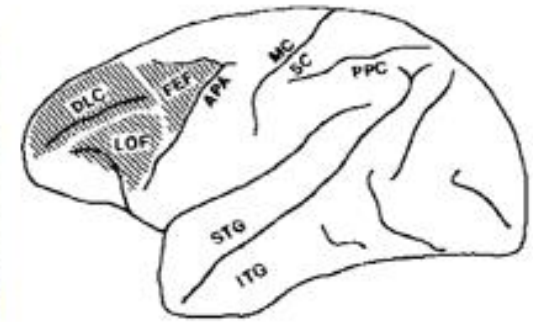
‘Shout out’ to the fellows





PARALLEL ORGANIZATION OF FUNCTIONALLY SEGREGATED CIRCUITS LINKING BASAL GANGLIA AND CORTEX*

BASAL GANGLIA CIRCUITS IN PRIMATES



American Neurologist-Neuroscientist and Pioneer (1938-2024)

Focused Ultrasound

Where are we going?

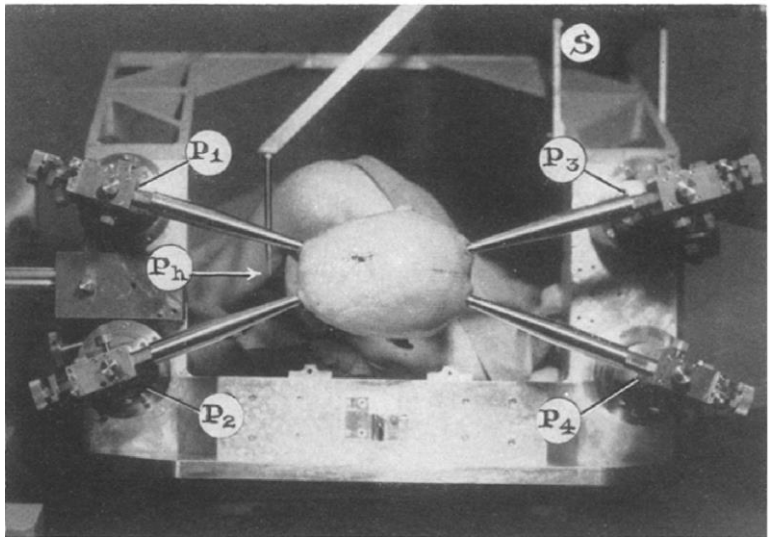
EARLY EXPERIENCES WITH ULTRASONIC IRRADIATION OF THE PALLIDOFUGAL AND NIGRAL COMPLEXES IN HYPERKINETIC AND HYPERTONIC DISORDERS*

RUSSELL MEYERS, M.D.,† WILLIAM J. FRY, Sc.M.,‡ FRANK J. FRY, Sc.M.,‡ LEROY L. DREYER, Sc.B.,‡ DONALD F. SCHULTZ, M.D.,† and ROBERT F. NOYES‡

Division of Neurosurgery, State University of Iowa, Iowa City, Iowa

(Received for publication April 25, 1958)

Journal of Neurosurgery 1958



Case #	Initials	Age	Sex	Duration of Disease (years)	Diagnosis				
					Classification	Pertinent Symptoms	Akinesia	Disparity	Etiology
1	R.H.	45	M	3½	P	Tremor and rigidity	Minimal	R>L	Undetermined
2	R.R.	49	M	33	P	Tremor and rigidity	Severe	R>L	Postencephalitic
3	F.L.	50	M	30	P	Tremor and rigidity	Moderate	L>R	Postencephalitic
4	C.M.	55	M	4–6*	P	Tremor and rigidity	Moderate	R>L	Arteriosclerosis (?)
5	E.B.	51	M	4–9*	P	Tremor and rigidity	Moderate	R>L	Undetermined
6	M.G.	15	F	15	A	Abnormal movement and rigidity	Severe	R=L	Birth trauma
7	E.F.	49	M	12	P	Tremor and rigidity	Moderate	R>L	Undetermined
8	S.G.	50	M	5–15*	P	Tremor and rigidity	Severe	R>L	Undetermined
9	R.M.	38	F	3–6*	P	Rigidity, minimal tremor	Severe	R>L	Undetermined
10	A.G.	44	F	3–4*	P	Rigidity, minimal tremor	Severe	R>L	Postencephalitic
11	M.S.	52	F	7–10*	P	Tremor and rigidity	Severe	L>R	Undetermined
12	A.N.	50	M	2–12*	P	Tremor and rigidity	Severe	L>R	Undetermined

A = Athetoid (tension and abnormal movement)
P = Parkinson's disease
L = Left
R = Right
> = Greater than
* Time required for progressive involvement of all limbs.

Slide provided by Jeff Elias

Acoustic Spatial Heterogeneity of the Skull

- Reflects
- Absorbs
- Scatters (acoustic beams)
- Contribute to “patient specific thermal responses”
- Occasional failures

Vyas, U. Med Phys 2016

Lesion or not? or sometimes? Does it matter?

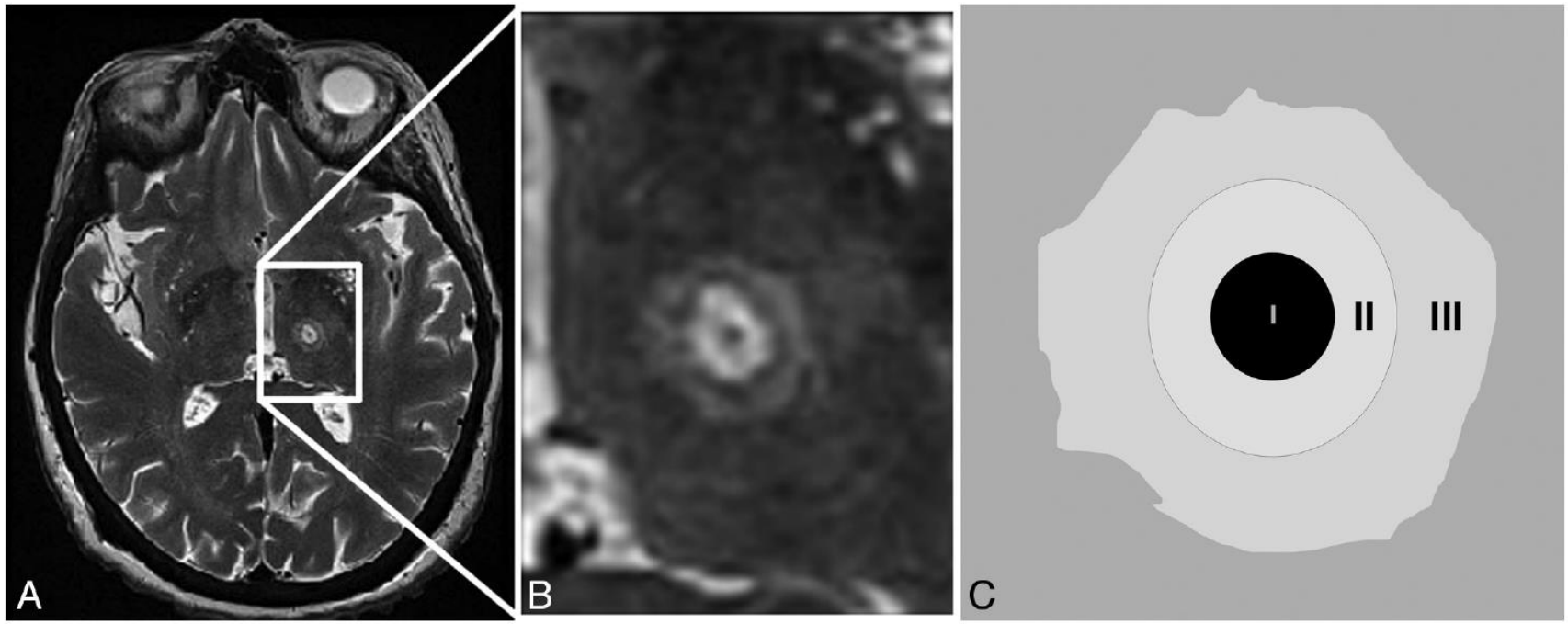


FIG 1. Schematic representation of zones I, II, and III visualized on T2-weighted imaging and the corresponding T2-weighted image of the lesion. On T2-weighted imaging, the patient developed 3 concentric zones at the site of lesioning: a hypointense zone I at the center; a strongly hyperintense zone II demarcated by a hypointense rim; and finally, a fuzzy, slightly hyperintense zone III at the periphery.

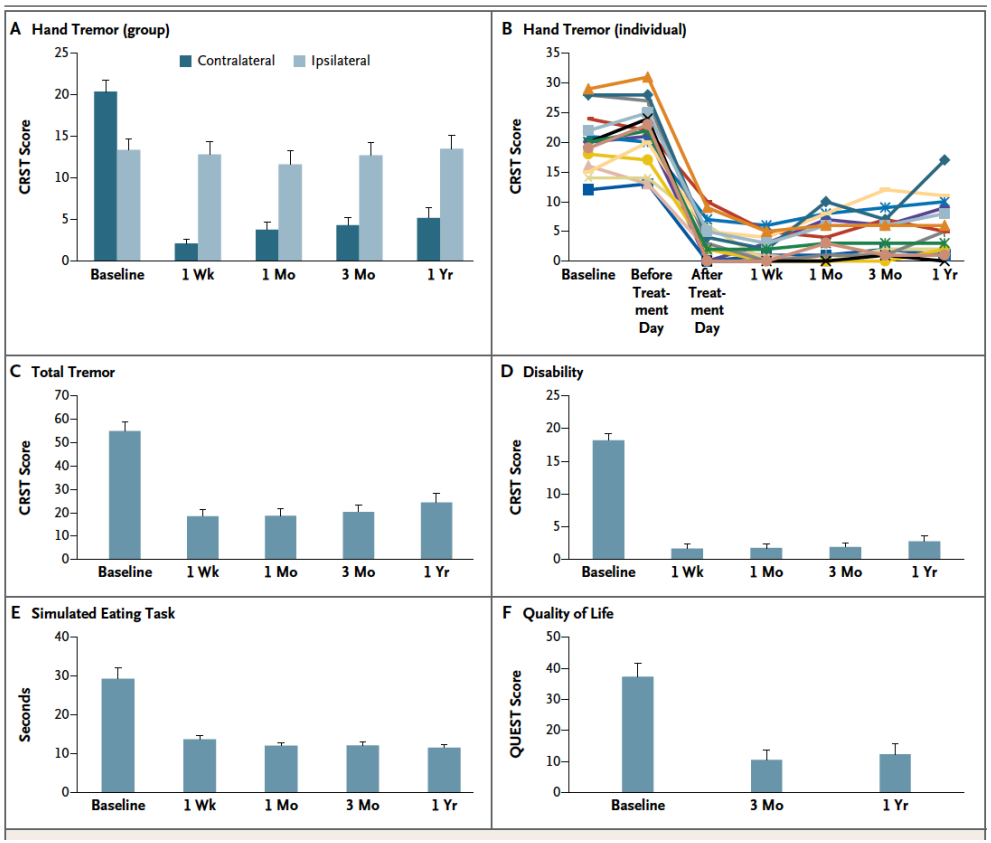
AJNR Am J Neuroradiol 35:891–96 May 2014 www.ajnr.org 893

Penumbra- edematous brain is dysfunctional
Permanent efficacy (can you make it large enough) vs. (hopefully) temporary adverse effects

ORIGINAL ARTICLE

A Pilot Study of Focused Ultrasound Thalamotomy for Essential Tremor

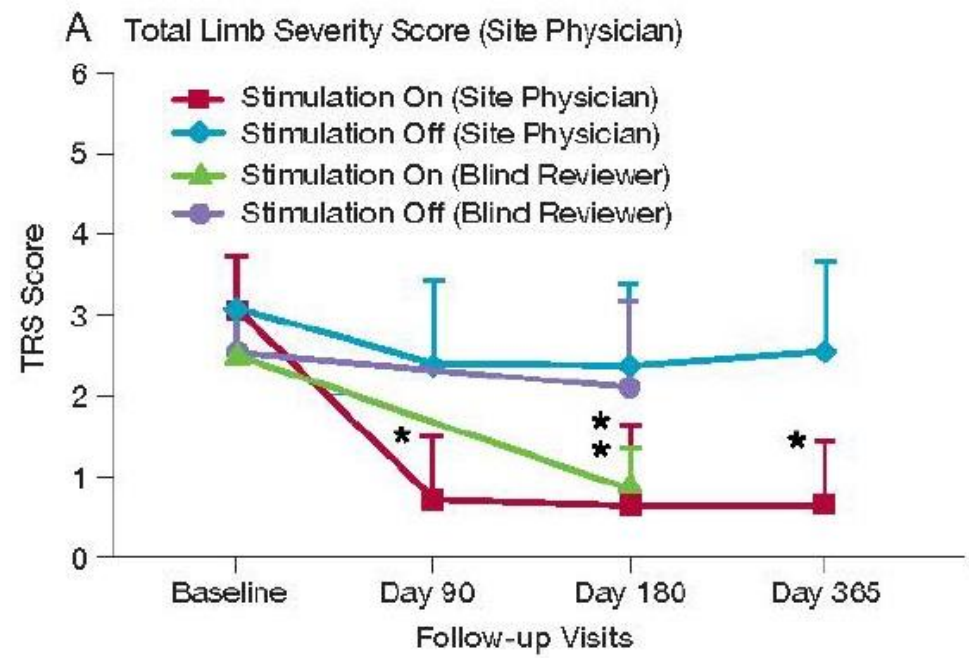
W. Jeffrey Elias, M.D., Diane Huss, P.T., D.P.T., N.C.S., Tiffini Voss, M.D., Johanna Loomba, B.S., Mohamad Khaled, M.D., Eyal Zadicario, M.Sc., Robert C. Frysinger, Ph.D., Scott A. Sperling, Psy.D., Scott Wylie, Ph.D., Stephen J. Monteith, M.D., Jason Druzgal, M.D., Ph.D., Binit B. Shah, M.D., Madaline Harrison, M.D., and Max Wintermark, M.D.



Contents lists available at ScienceDirect
Parkinsonism and Related Disorders
journal homepage: www.elsevier.com/locate/parkreldis

Thalamic DBS with a constant-current device in essential tremor: A controlled clinical trial*

DBS sustained improvement 1 year 127 patients



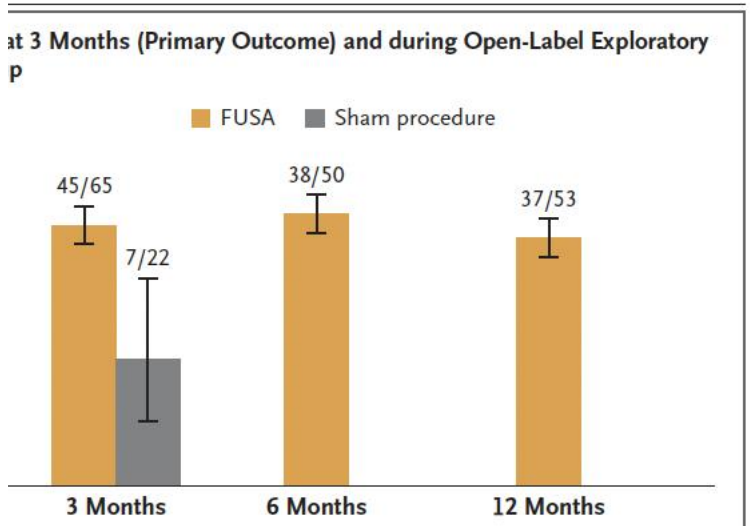
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 23, 2023 VOL. 388 NO. 8

Trial of Globus Pallidus Focused Ultrasound Ablation in Parkinson's Disease

Vibhor Krishna, M.D., Paul S. Fishman, M.D., Ph.D., Howard M. Eisenberg, M.D., Michael Kaplitt, M.D., Ph.D., Gordon Baltuch, M.D., Jin Woo Chang, M.D., Wei-Chieh Chang, M.D., Raul Martinez Fernandez, M.D., Marta del Alamo, M.D., Casey H. Halpern, M.D., Pejman Ghanouni, M.D., Ph.D., Roberto Eleopra, M.D., Ph.D., Rees Cosgrove, M.D., Jorge Guridi, M.D., Ryder Gwinn, M.D., Pravin Khemani, M.D., Andres M. Lozano, M.D., Ph.D., Nathan McDannold, Ph.D., Alfonso Fasano, M.D., Ph.D., Marius Constantinescu, M.D., Ilana Schlesinger, M.D., Arif Dalvi, M.D., and W. Jeff Elias, M.D.

- Positive Trial
- Outcome was not standard 'UPDRS' so hard to compare across studies
- 30%+ Non-responders
- Questions on shape, size lesions and longer term follow-up
- Did not address bilateral lesions
- Lesion shape for this target



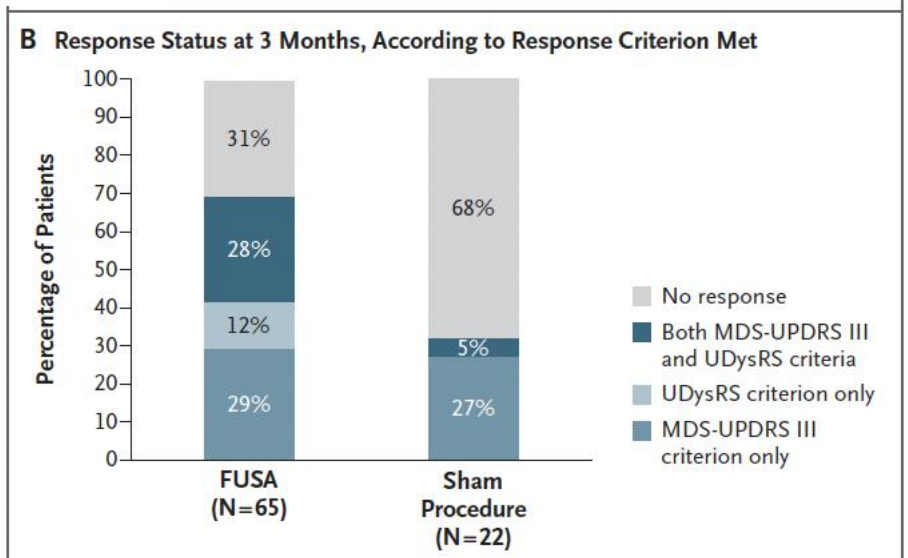


Figure 2. Response Status.

A response was defined as a decrease (improvement) of at least 3 points from baseline either in the score on part III of the Movement Disorders Society–Unified Parkinson's Disease Rating Scale (MDS-UPDRS III) for the treated side in the off-medication state (range, 0 to 44, with higher scores indicating worse motor impairment) or in the score on the Unified Dyskinesia Rating Scale (UDysRS) in the on-medication state (range, 0 to 104, with higher scores indicating worse dyskinesia). I bars indicate 95% confidence intervals.

Movement Disorders CLINICAL PRACTICE
Official Journal of the International Parkinson and Movement Disorder Society

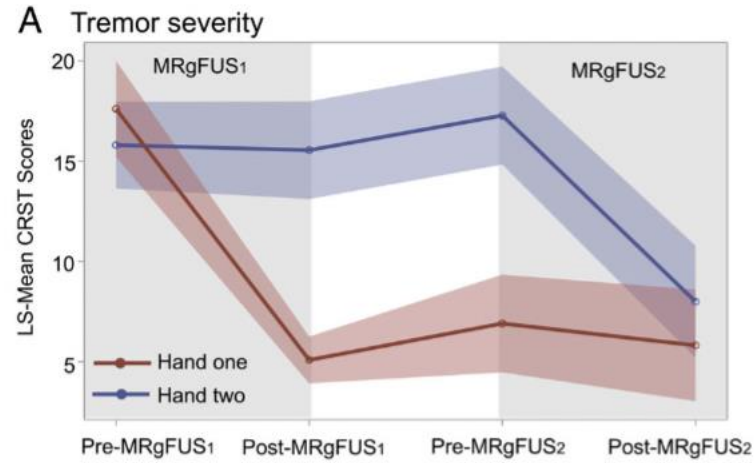
LETTER: NEUROMODULATION | Open Access

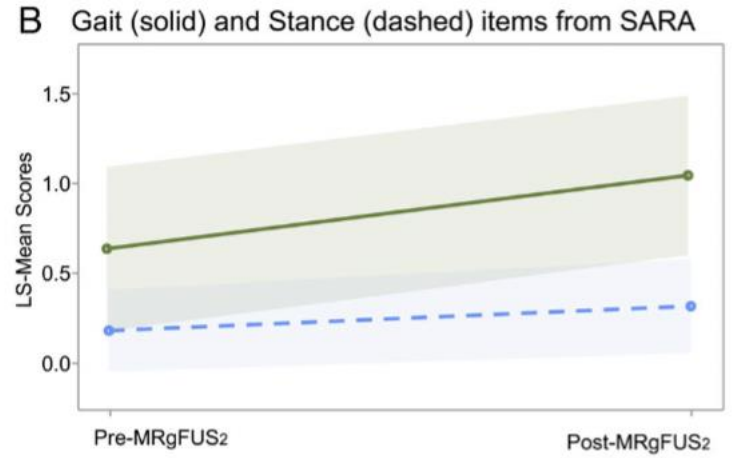
Safety of Bilateral Staged Magnetic Resonance-Guided Focused Ultrasound Thalamotomy for Essential Tremor

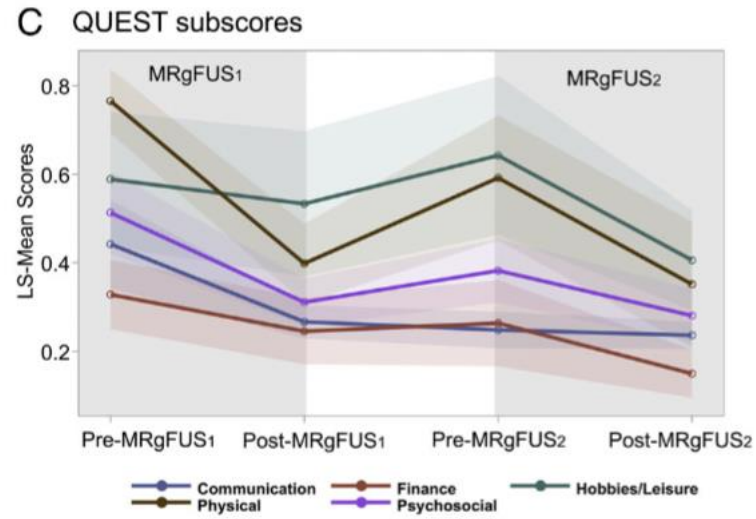
Nadia Scantlebury PhD, Camryn R. Rohringer BSc, Jennifer S. Rabin PhD, Yana Yunusova PhD, Yuexi Huang PhD, Ryan M. Jones PhD, Ying Meng MD, PhD ... See all authors

First published: 12 September 2023 | https://doi.org/10.1002/mdc3.13882 | Citations: 2

- n=16 subjects
- Increased risk of disequilibrium
- Speech dysfunction not detected (was tool sensitive enough?)
- 25% increase in dysgeusia incidence relative to unilateral



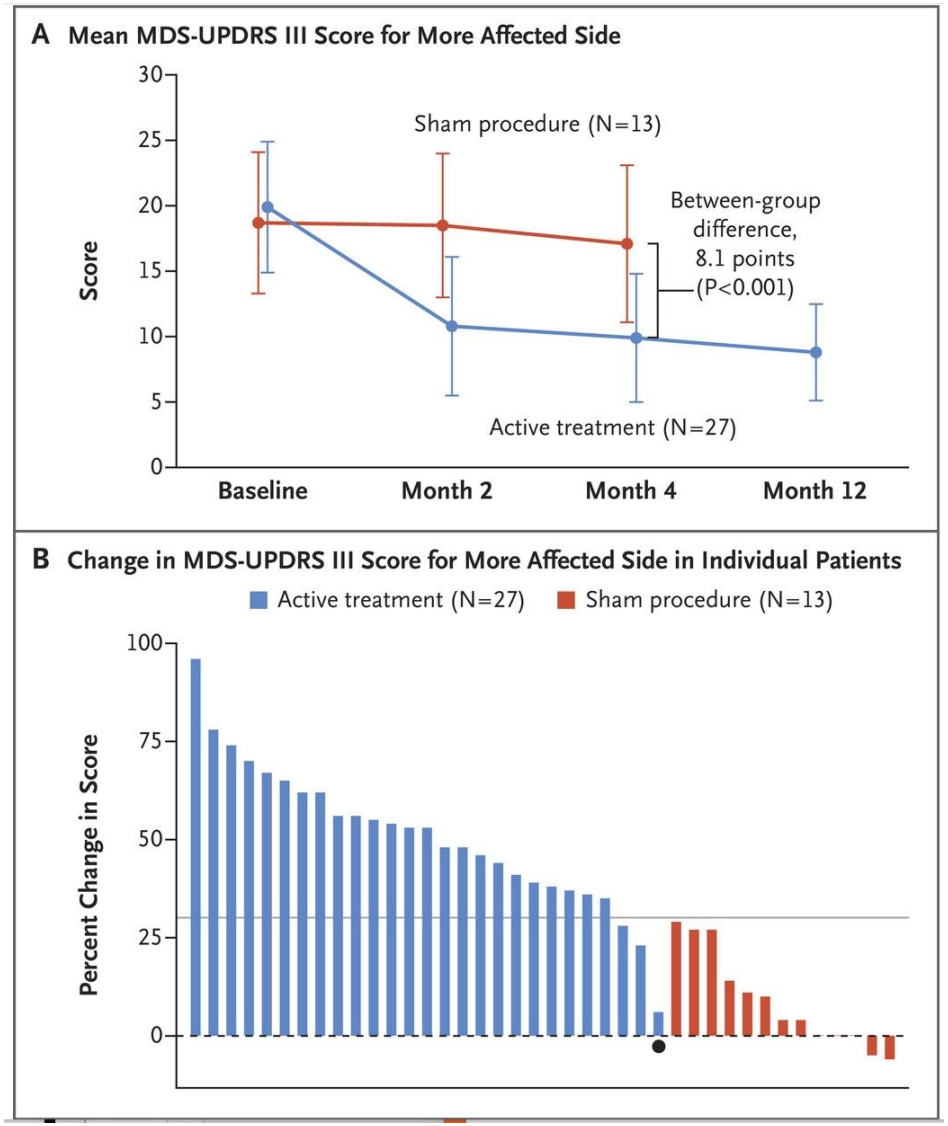




ORIGINAL ARTICLE

Randomized Trial of Focused Ultrasound Subthalamotomy for Parkinson's Disease

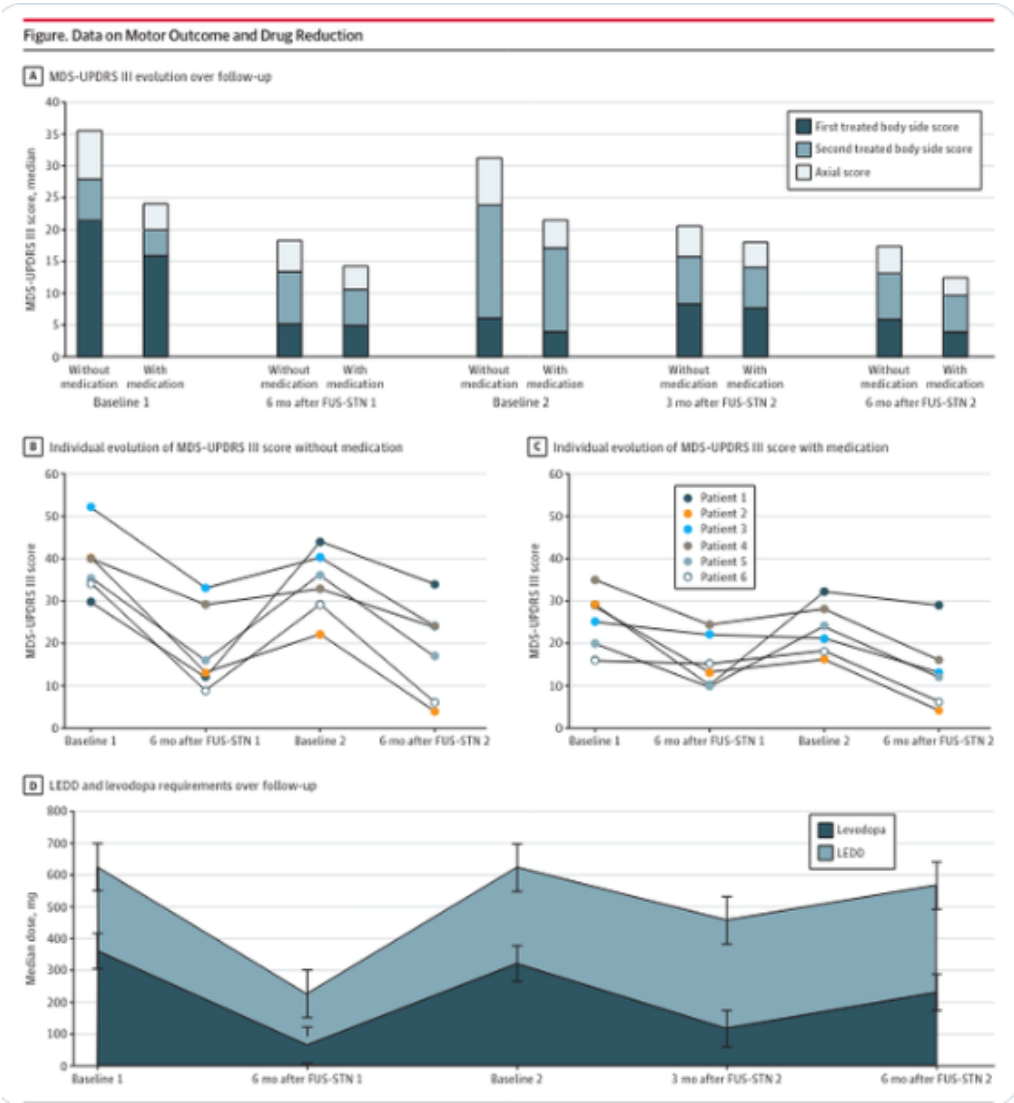
Raúl Martínez-Fernández, M.D., Ph.D., Jorge U. Máñez-Miró, M.D., Rafael Rodríguez-Rojas, Ph.D., Marta del Álamo, M.D., Binit B. Shah, M.D., Frida Hernández-Fernández, M.Sc., José A. Pineda-Pardo, Ph.D., Mariana H.G. Monje, M.D., Ph.D., Beatriz Fernández-Rodríguez, M.D., Scott A. Sperling, Psy.D., David Mata-Marín, M.Sc., Pasqualina Guida, M.Sc., et al.



JAMA Neurology | Original Investigation

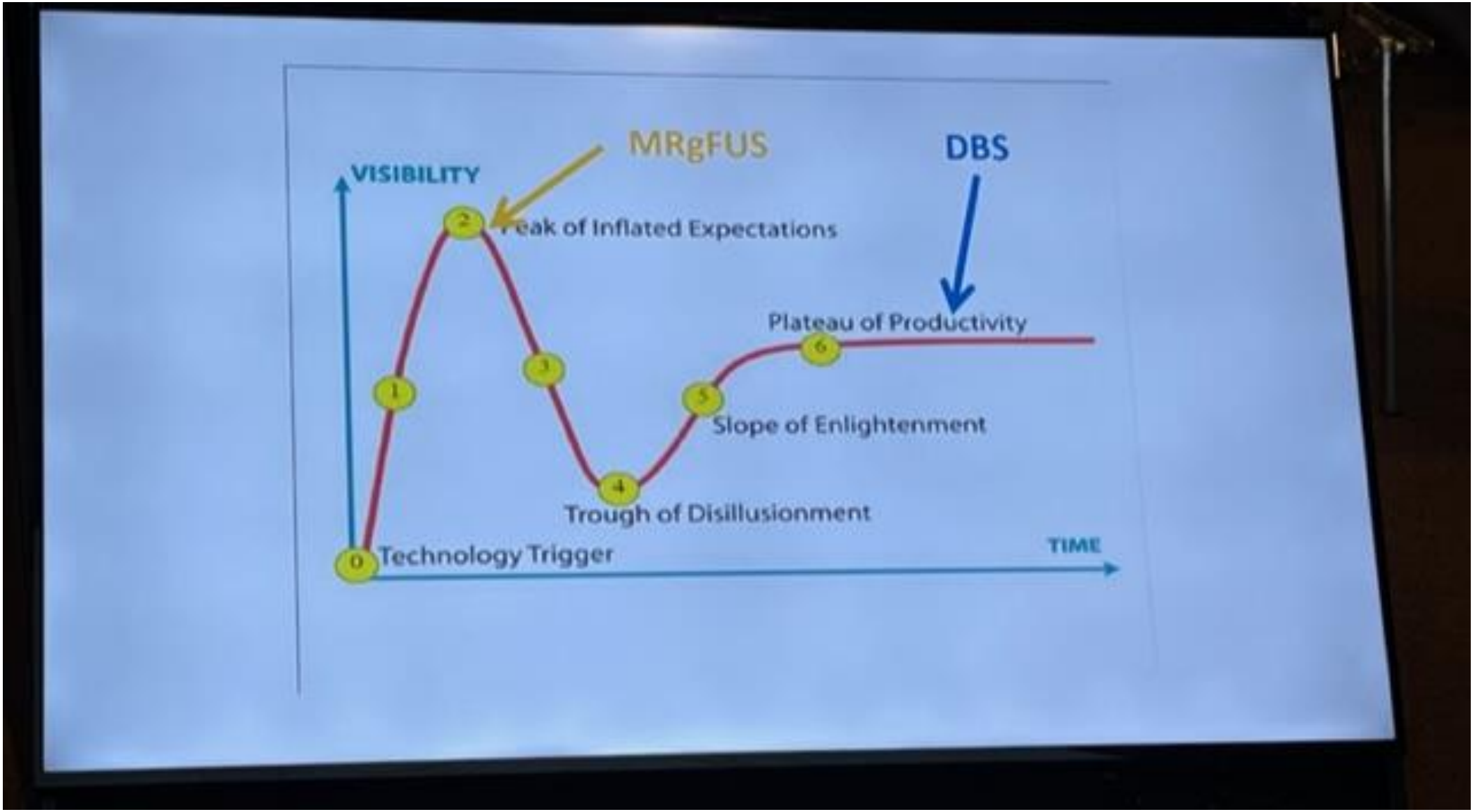
Staged Bilateral MRI-Guided Focused Ultrasound Subthalamotomy for Parkinson Disease

Raúl Martínez-Fernández, MD, PhD; Elena Natera-Villalba, MD; Rafael Rodríguez-Rojas, PhD; Marta del Álamo, MD; Jose A. Pineda-Pardo, PhD; Ignacio Obeso, PhD; Pasqualina Guida, MsC; Tamara Jiménez-Castellanos, MsC; Diana Pérez-Bueno, MD; Alicia Duque, MD, PhD; Jorge U. Mañez-Miró, MD, PhD; Carmen Gasca-Salas, MD, PhD; Michele Matarazzo, MD; Fernando Alonso-Frech, MD, PhD; Jose A. Obeso, MD, PhD

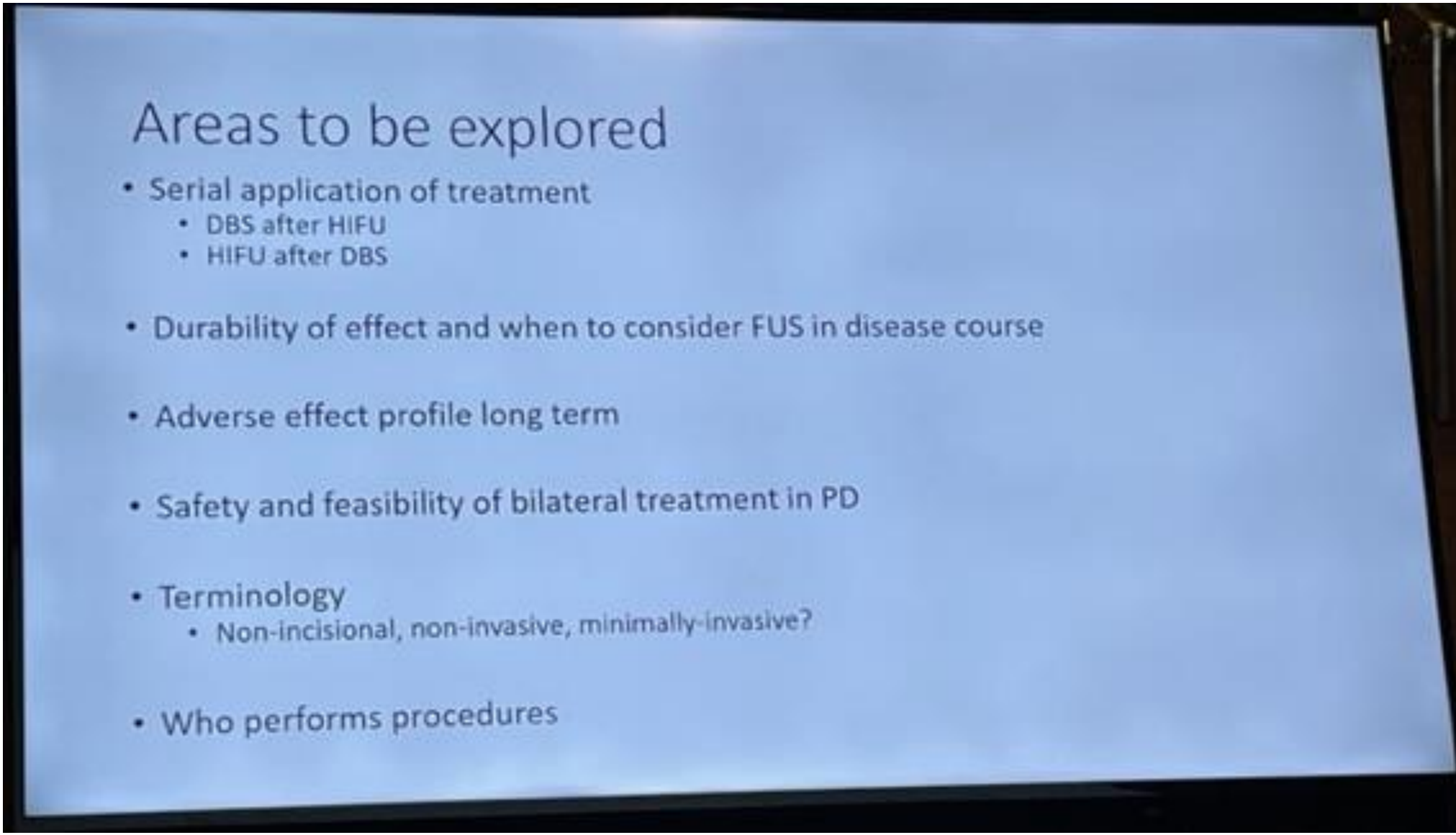


- **Original cohort** n= 45
- Remaining 34; **6 experienced progression**
- 4/6: new **'contralateral choreic dyskinesia**, which resolved by 3 months.'
- 4 **speech disturbances** described as gradually improving, but persisted in 2.
- 1 person had **mild imbalance** and **dysphagia** during the first week after treatment
- No **behavioral or cognitive** disturbances.

2024

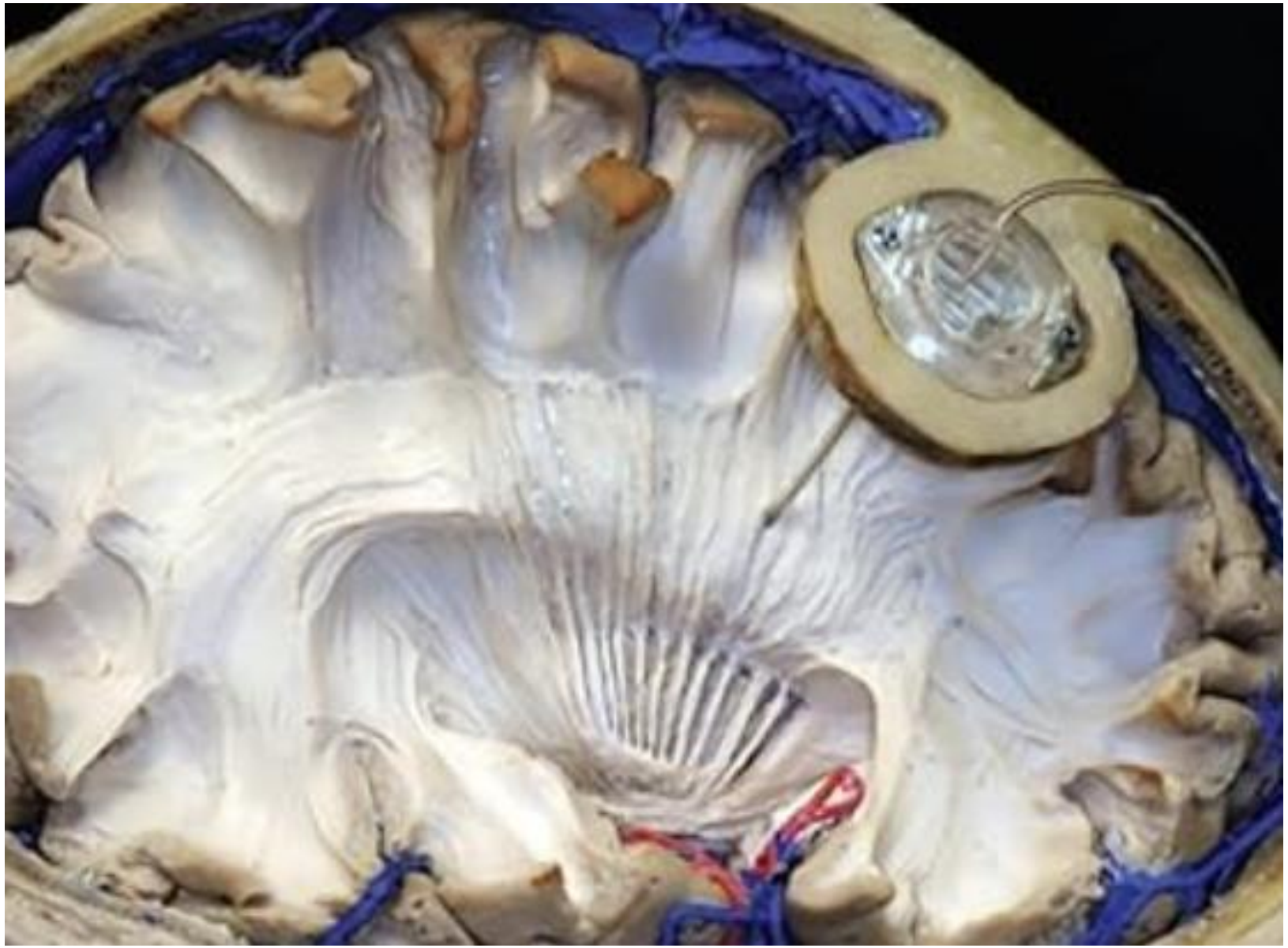


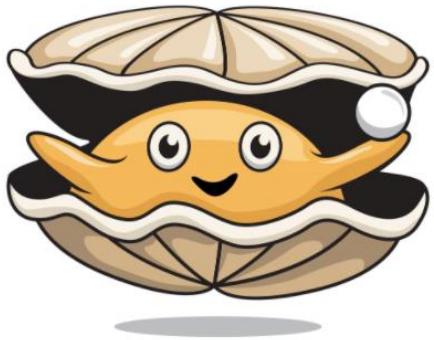
Binit Shah 2023 World Parkinson Congress



Binit Shah 2023 World Parkinson Congress

Deep Brain Stimulation





“The idea that such a small amount of electricity could have such a profound effect on a Parkinson’s disease patient surprised and delighted even the wisest of neuroscientists”

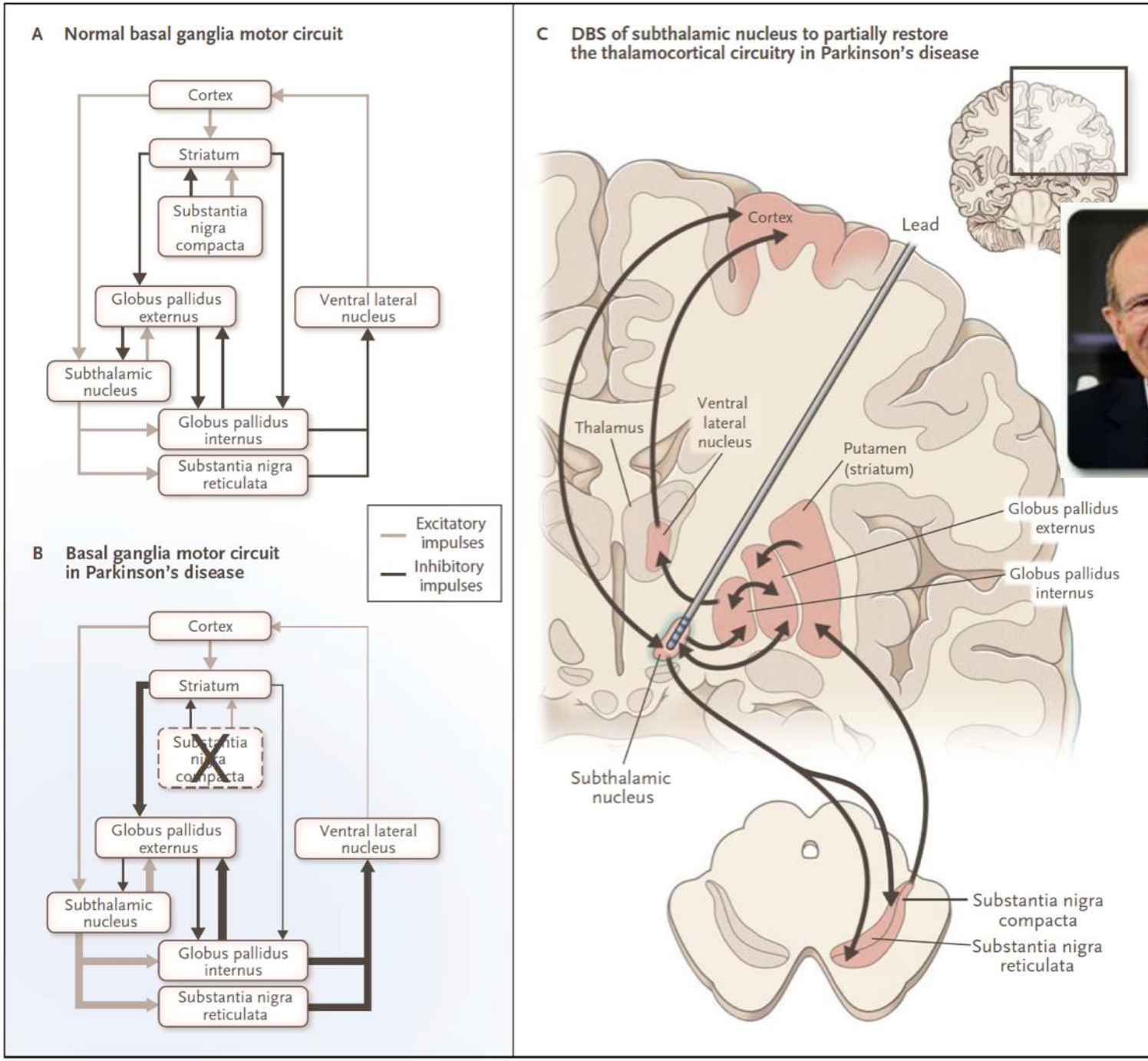


Figure 1. The DeLong "Box" Models of Basal Ganglia Circuitry and Their Use in Guiding Deep-Brain Stimulation (DBS).

Pre-op

Post-op

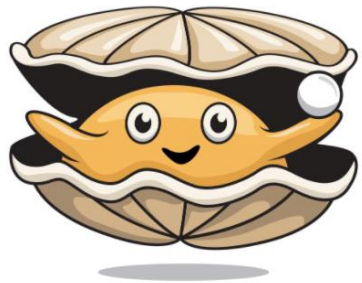
Parkinson's Disease

Tremor

Dyskinesia

On-off fluctuations

Levodopa responsive symptoms



Shortcomings

Gait

Freezing

Balance

Speech

Cognition

The NEW ENGLAND JOURNAL of MEDICINE

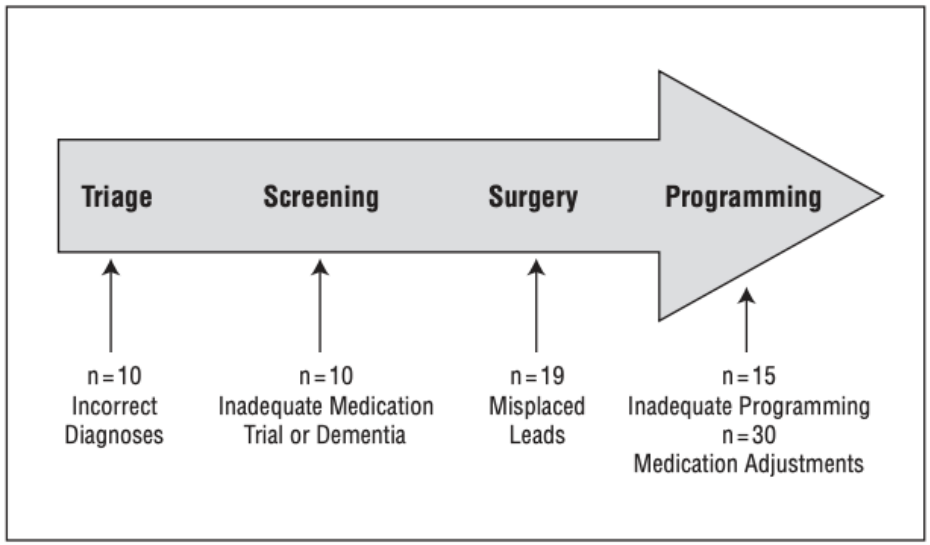
ORIGINAL CONTRIBUTION

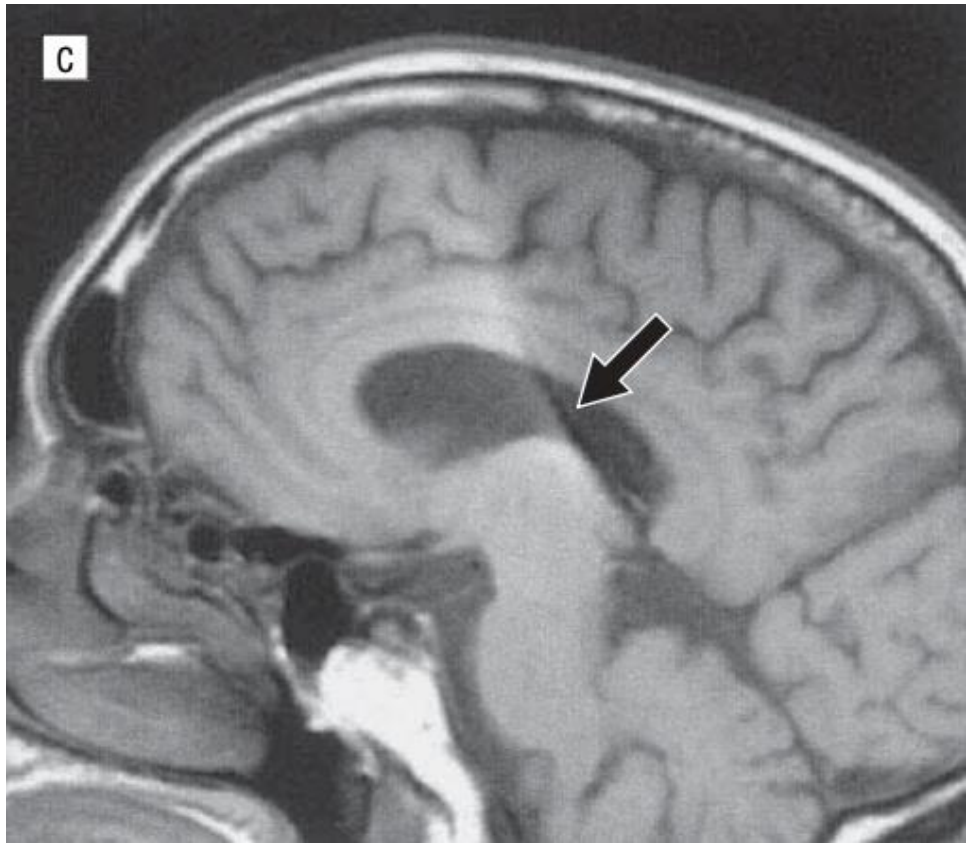
Management of Referred Deep Brain Stimulation Failures

A Retrospective Analysis From 2 Movement Disorders Centers

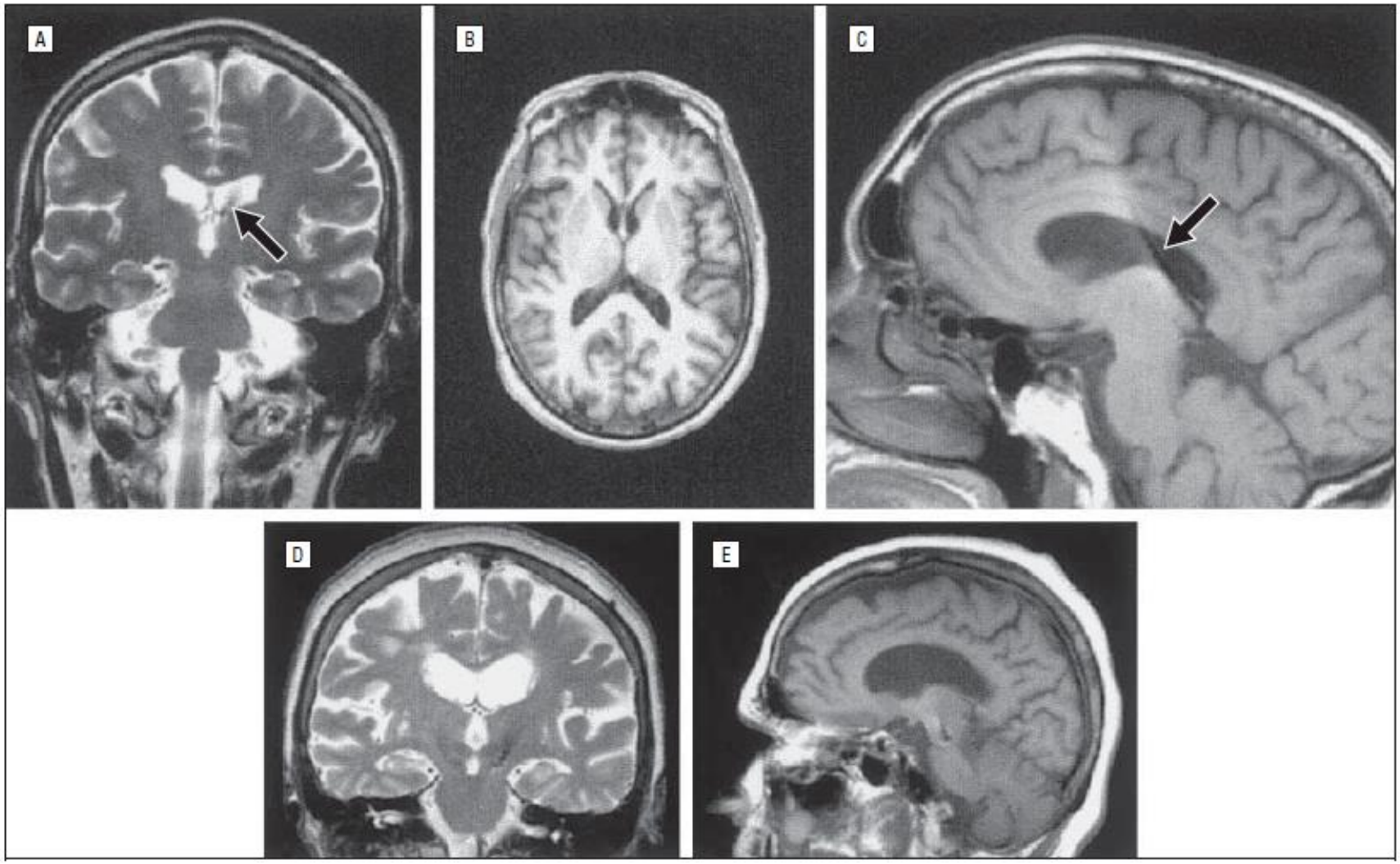
Michael S. Okun, MD; Michele Tagliati, MD; Michael Pourfar, MD; Hubert H. Fernandez, MD; Ramon L. Rodriguez, MD; Ron L. Alterman, MD; Kelly D. Foote, MD

ARCHIVES OF NEUROLOGY





Take a Picture After the Operation



Movement Disorders CLINICAL PRACTICE
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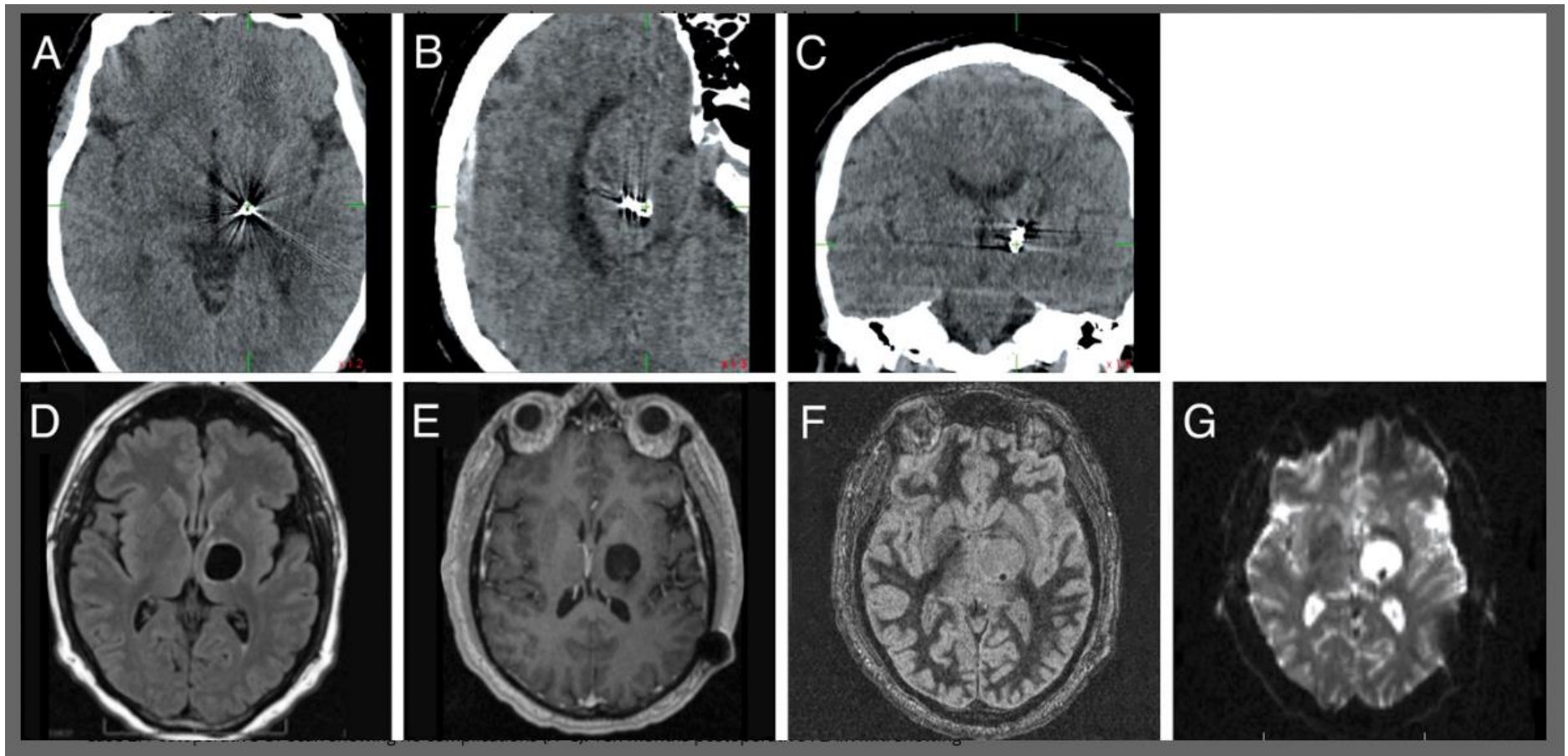
Case Series | Free Access

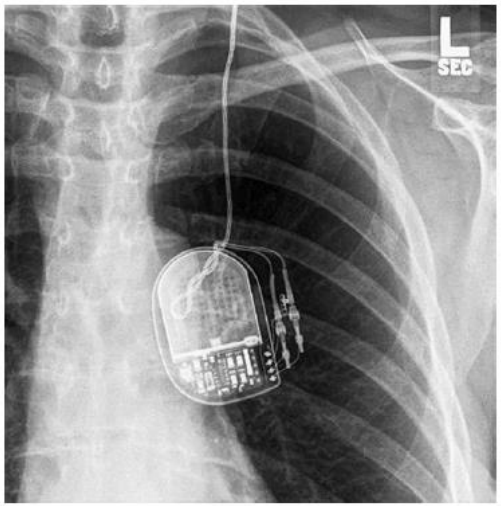
Cystic Lesions as a Rare Complication of Deep Brain Stimulation

Vibhash D. Sharma MD, Alberto R. Bona MD, Alessandra Mantovani MD, Svjetlana Miocinovic MD, PhD, Pravin Khemani MD, Mark P. Goldberg MD, Kelly D. Foote MD ... See all authors

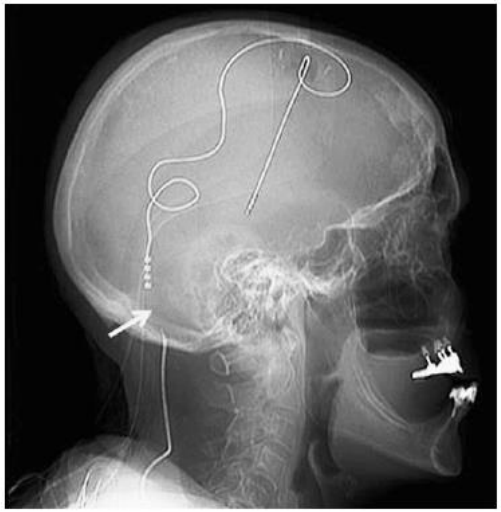
First published: 16 September 2015 | https://doi.org/10.1002/mdc3.12230 | Citations: 7

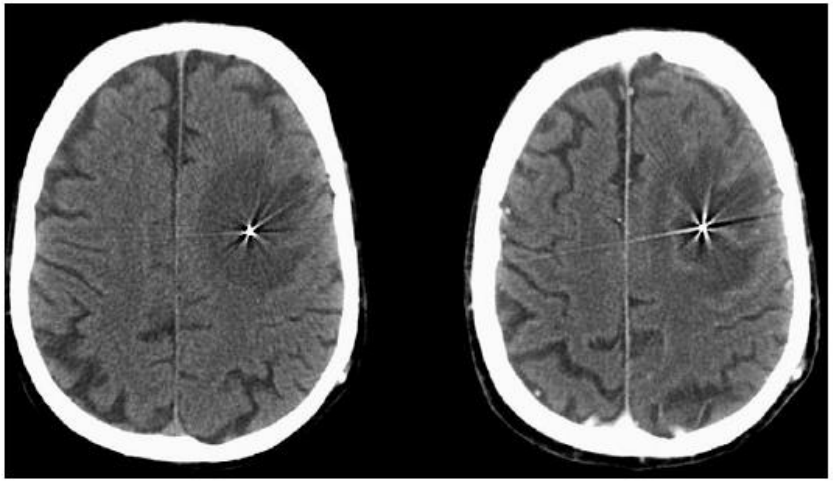


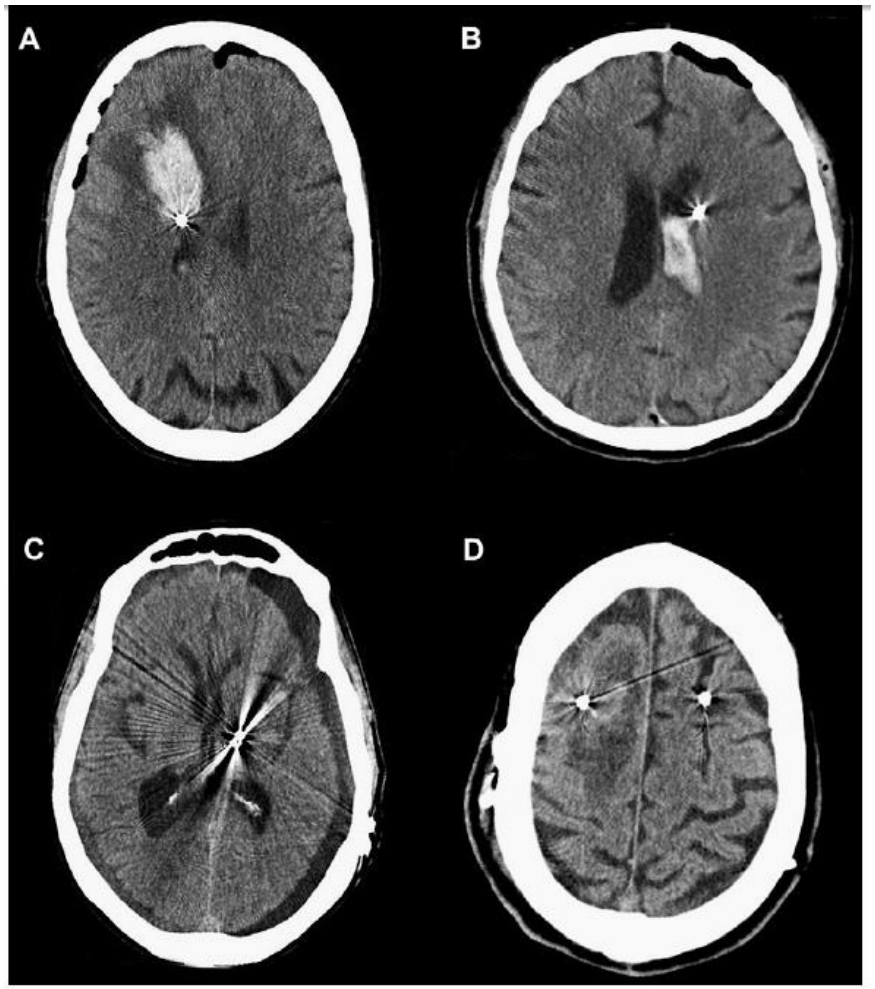
There are complications even at the expert centers

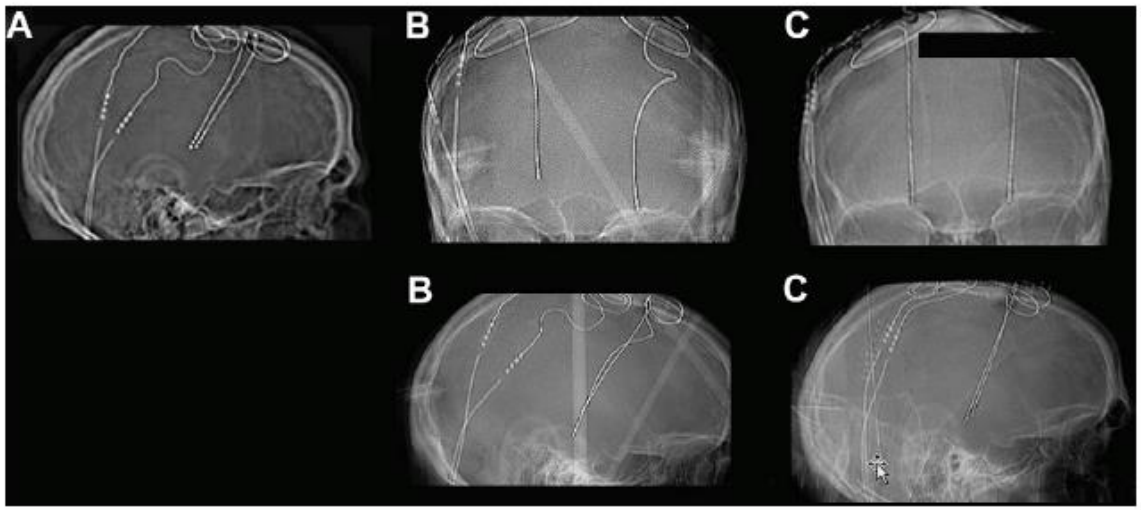


4. A chest x-ray revealed a twisted extension cable and flipped IPG following









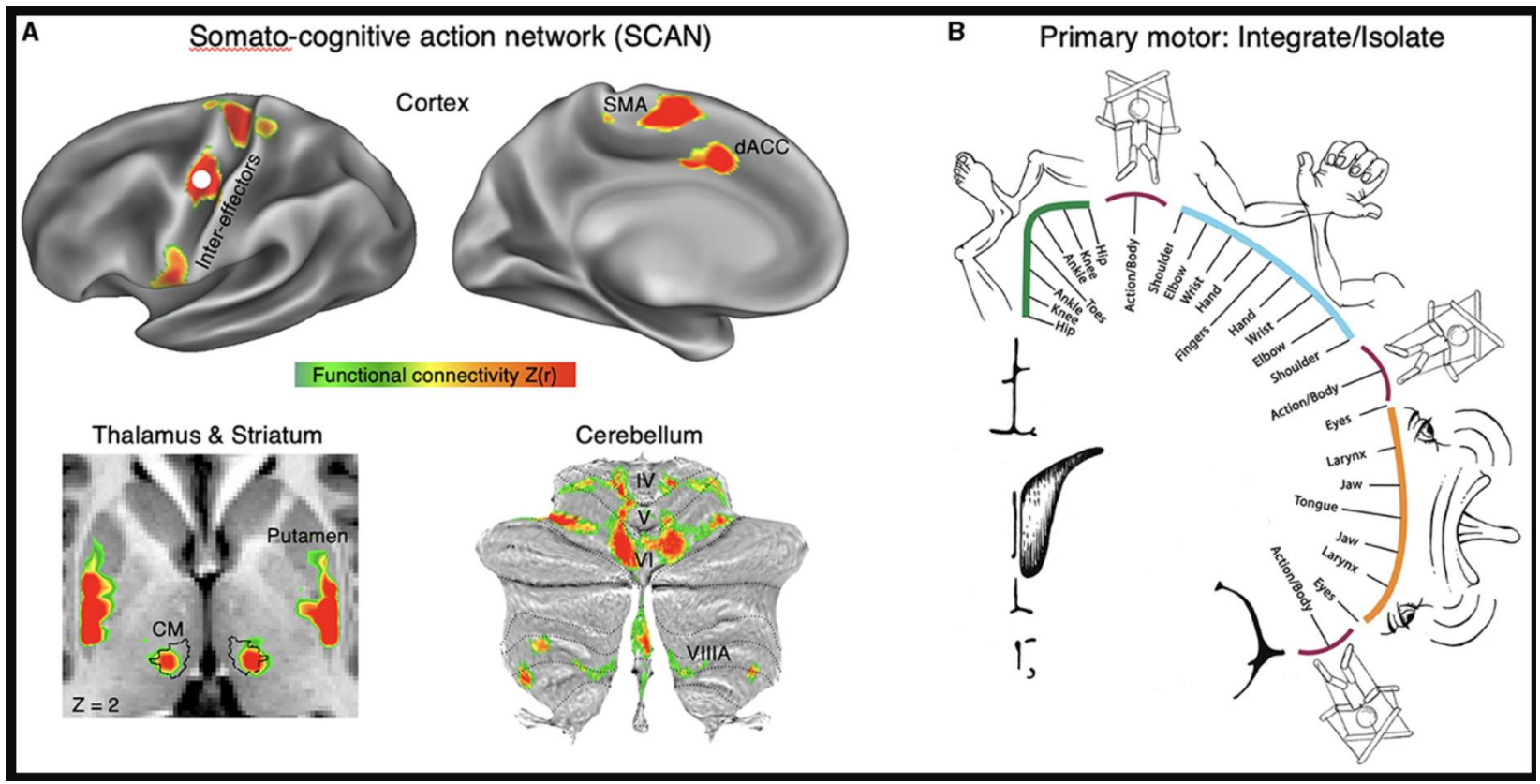
What will define the ‘beyond’ of next generation?

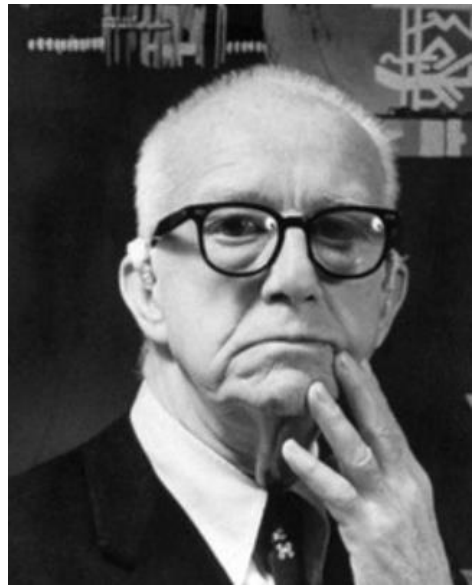
PERSPECTIVE article

Front. Hum. Neurosci., 21 February 2024
Sec. Brain Imaging and Stimulation
Volume 18 - 2024 | https://doi.org/10.3389/fnhum.2024.1320806

This article is part of the Research Topic
Deep Brain Stimulation Think Tank: Updates in Neurotechnology and Neuromodulation, Volume IV
View all 16 Articles >

Proceedings of the 11th Annual Deep Brain Stimulation Think Tank: pushing the forefront of neuromodulation with functional network mapping, biomarkers for adaptive DBS, bioethical dilemmas, AI-guided neuromodulation, and translational advancements





‘A fool with a tool is still a fool.’

- R Buckminster Fuller
-Ron Weinstein
-Grady Booch

‘Your brain controls everything and we can control your brain.’

– Foote, Okun (2012)

Plastic means ’reshape’
Greek πλαστική(τέχνη)
plastikē (*tekhnē*)

Joseph Constantine Carpue (1814)
Operated on a British officer

Nose damage from treatment with mercury

Technique applied WWI soldiers

David Noonan asks in 2014…

Why won’t people use neuromodulation to enhance mood, memory and neurologically based skills (in the future)?

SECTIONS

Smithsonian MAGAZINE

The most futuristic medical treatment ever imagined is now a reality

David Noonan

May 2014

Surgeon
Provides informed consent for the elective procedure which is intended to have therapeutic benefit.

Researcher
Provides information about the research study, the size of the biopsy, the risks of the biopsy, and how the biopsy tissue may or may not be used in the future.

Study Independent 'Consenter'
Reviews the procedure and consent form and addresses items which require clarification from the surgeon or researcher, before proceeding with consent. Obtains consent from subjects interested in proceeding with a non-therapeutic biopsy.

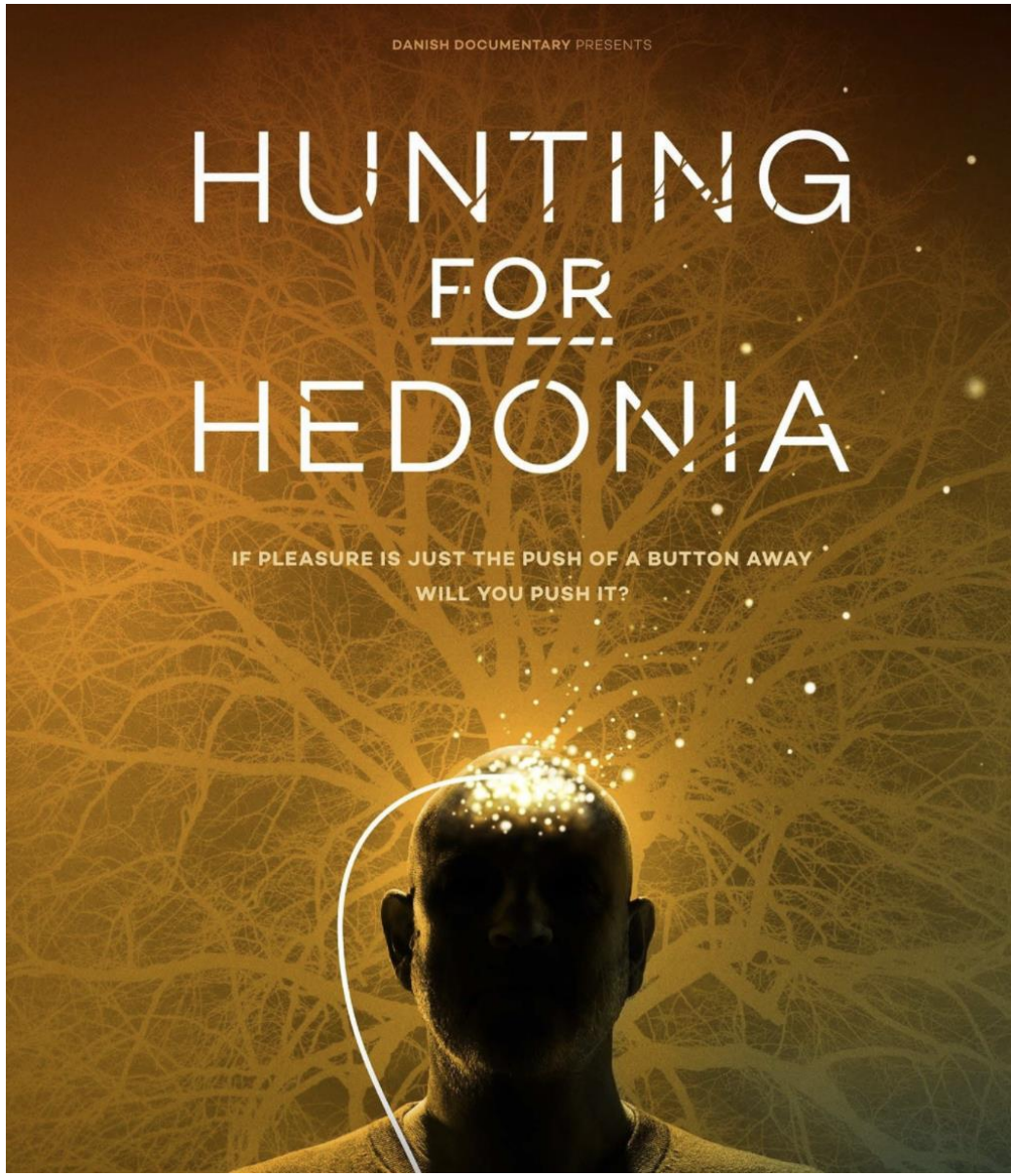
We need an ethical guiding principle.

‘Apply DBS to alleviate human suffering.’

‘The best preparation for tomorrow is to do today's work superbly well.’

-William Osler

‘The pleasure is just a push of the button away. Will you press it?’



Where ‘the field’ could go…

or where the field has already gone?

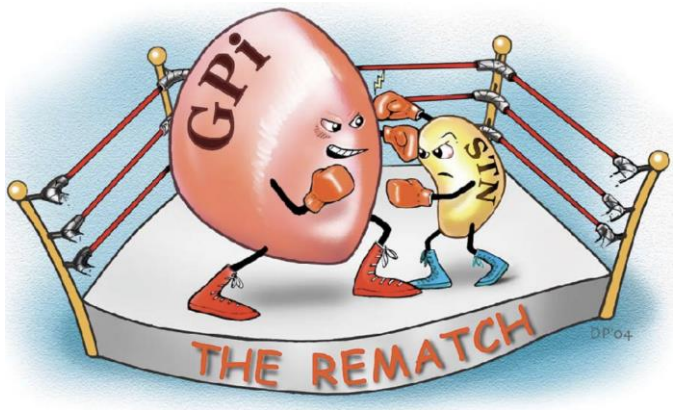
Hyper and hypokinetic movement disorders (mixed)

Depression, bipolar disorder, schizophrenia, thought disorders

Tourette, OCD, Autism

Addictions (alcohol, recreational drugs, eating, impulse control disorders)

Will technology bail you out?



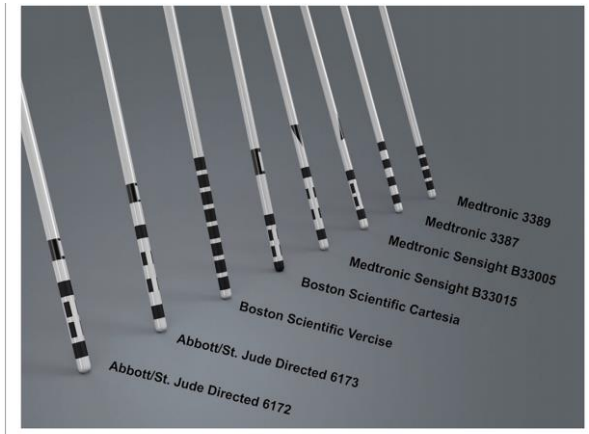
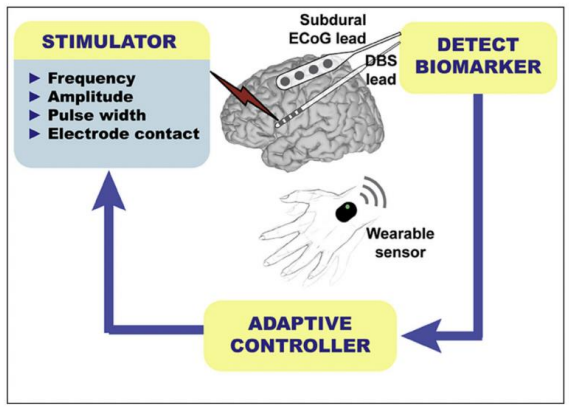
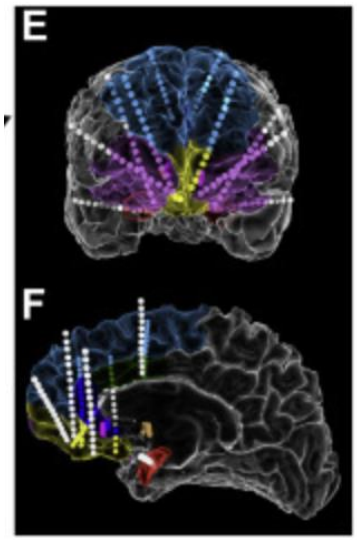


FIGURE 1 | Lead design currently commercially available from various DBS manufacturers. Contacts are either full rings, allowing for omnidirectional stimulation, or have segmented electrodes on the middle two levels, allowing for directional stimulation. Many manufacturers include stereotactic markers above the DBS contacts for post-operative directional lead orientation.





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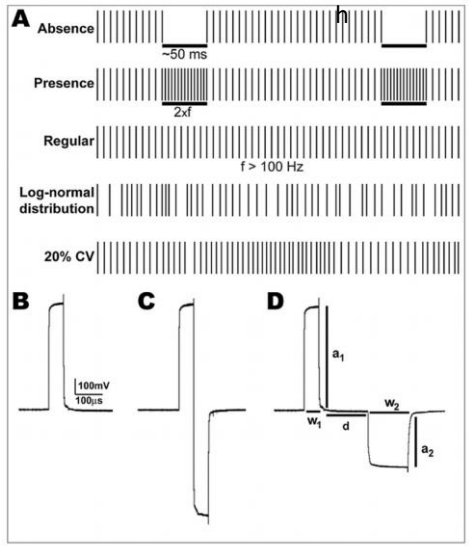
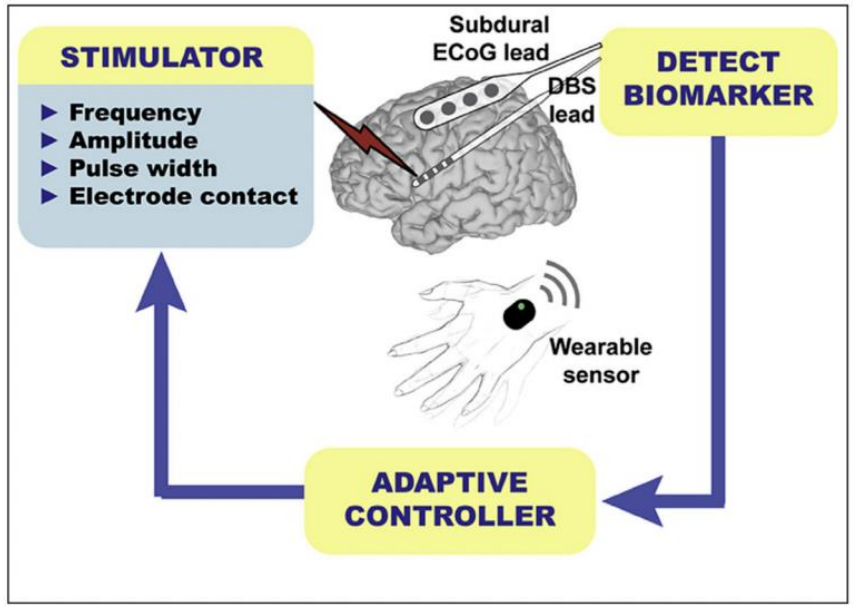
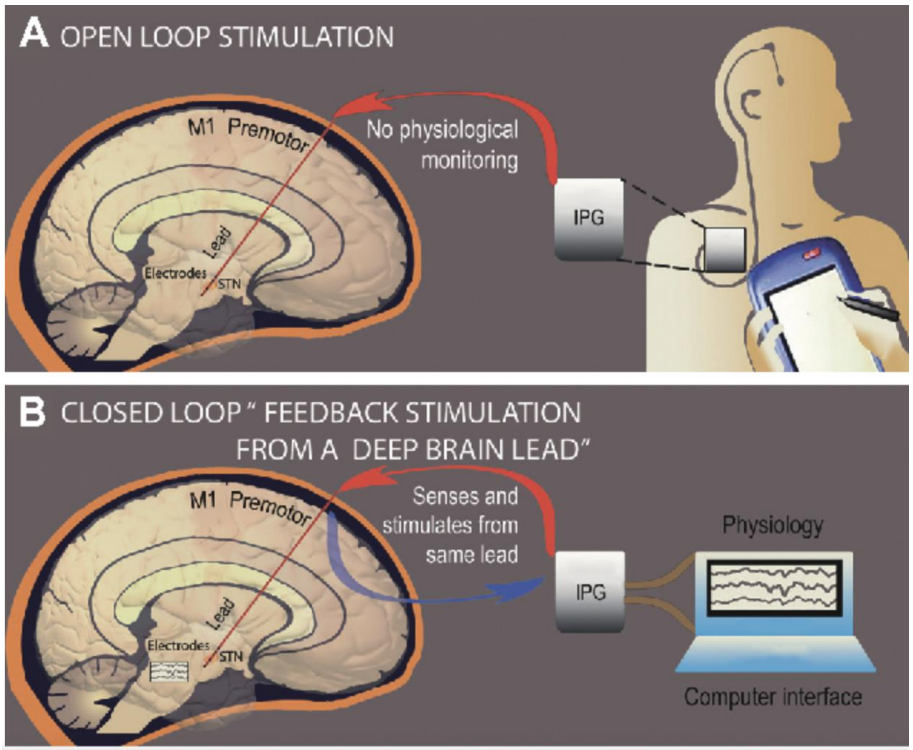
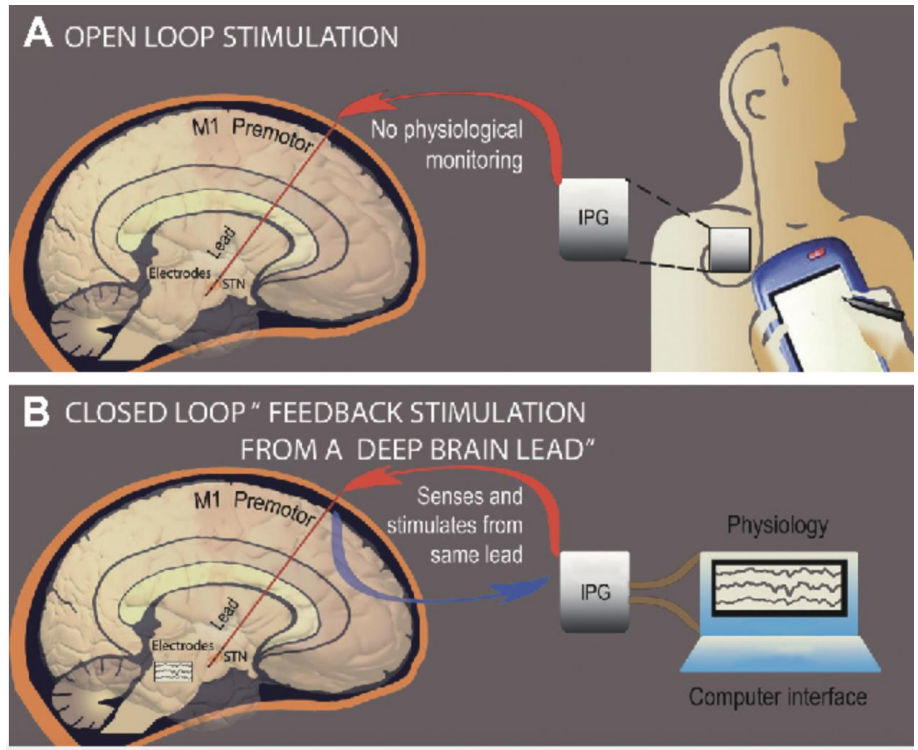


Should we apply ‘closed loop’ or adaptive deep brain stimulation for movement and neuropsychiatric symptoms?



Gunduz, Foote, Okun 2017

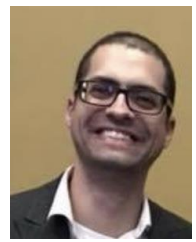




Almeida, Martinez-Ramirez…Okun, 2015

Even if we choose a 'closed loop' approach…

Which one? Which markers/(bio)markers?
Will it be completely adaptive or 'build on the baseline?'



“There are two great days in a person's life - the day we are born and the day we discover why.”

-William Barclay

Tourette Syndrome

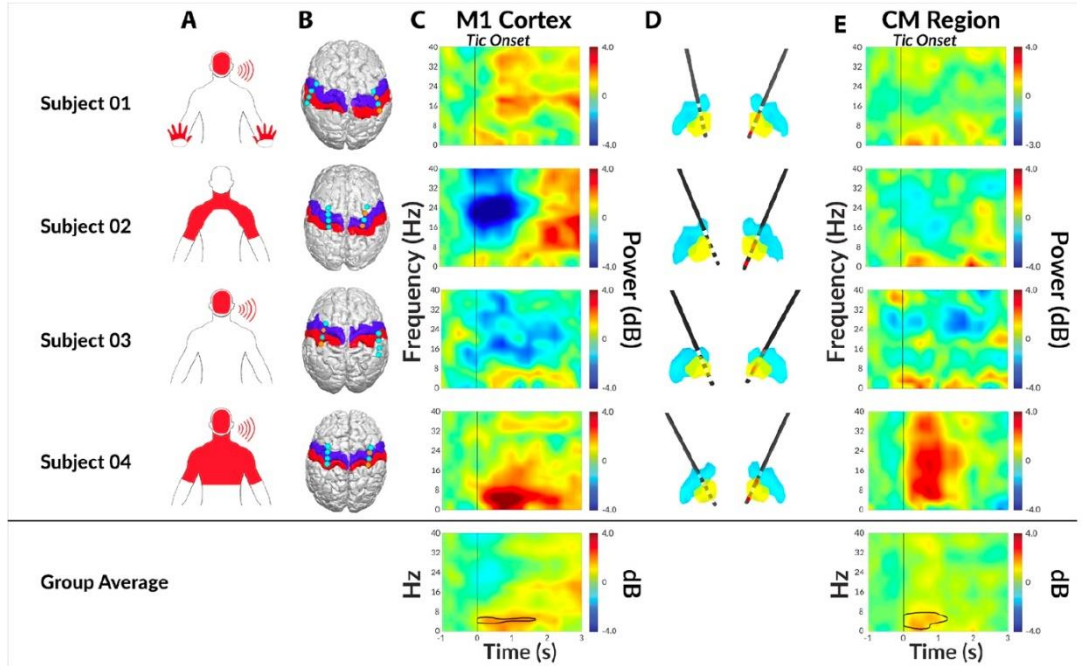
"Do I have the right circuit"

Neuropsychiatry

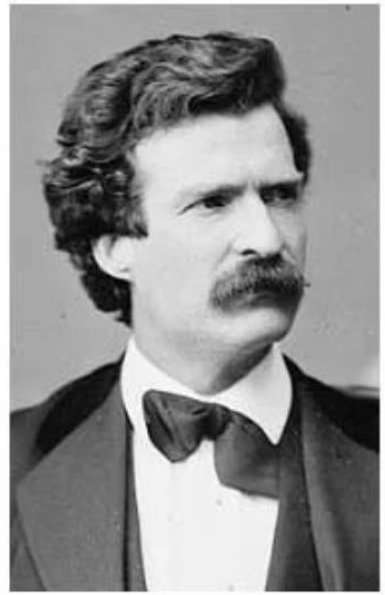
ORIGINAL RESEARCH

Differentiating tic electrophysiology from voluntary movement in the human thalamocortical circuit

Neuropsychiatry



It is likely that for some/many disorders/symptoms that as an alternative to ‘closed loop DBS,’ we will choose ‘scheduled’, ‘continuous’ or another mode/waveform.



“An open mind leaves a chance for someone to drop a worthwhile thought in it.”

--Mark Twain

Closed Loop (adaptive) DBS: Hope/Hype or Both?

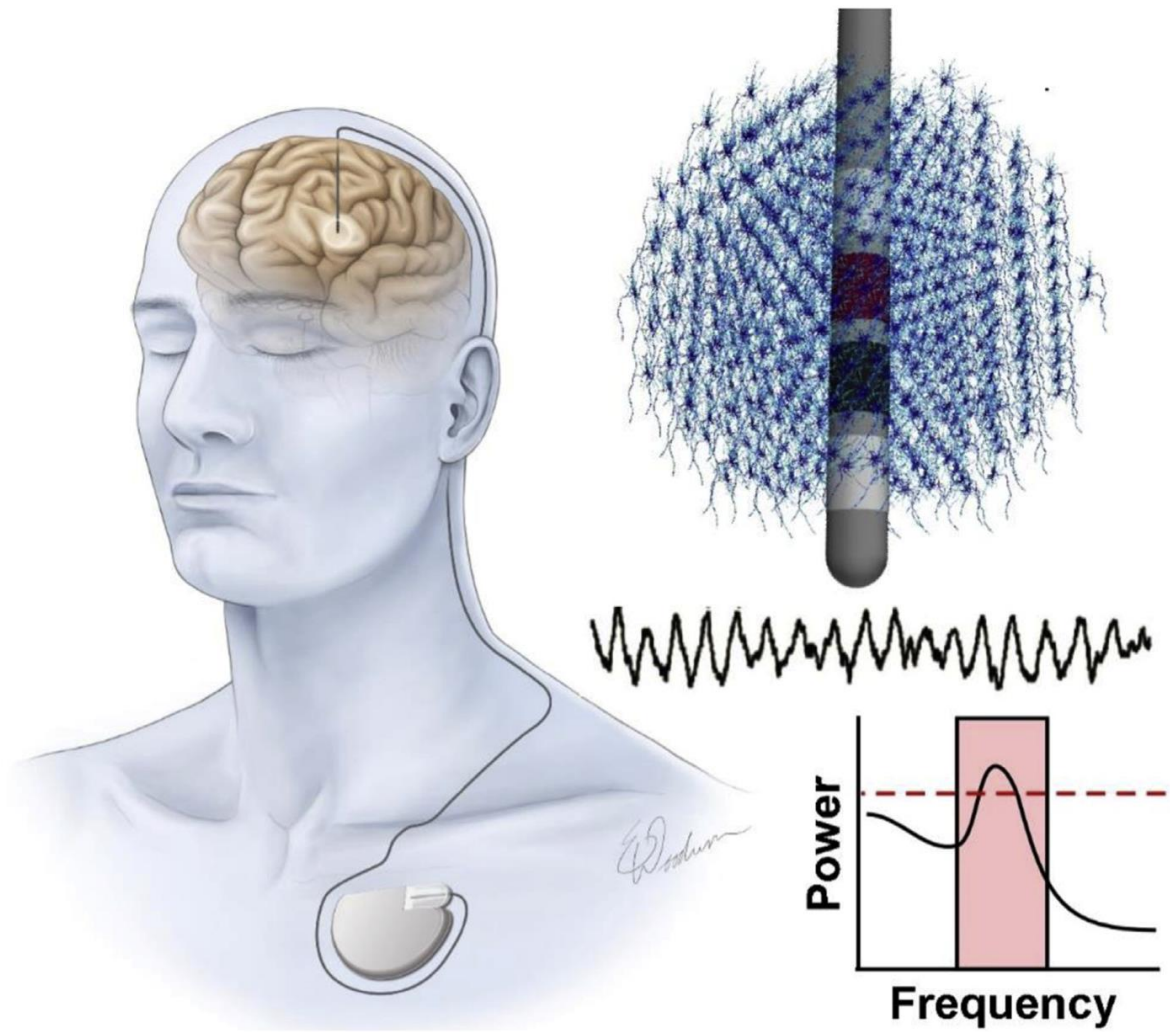
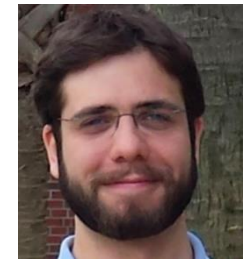


Figure 2. Closed-loop DBS. Electrophysiological biomarker signals are derived from the synchronous activity of large populations of neurons (and their synaptic inputs) surrounding the implanted recording electrodes. These signals summate into a local field potential (LFP) which can be analyzed as time series data. Typical closed-loop control systems covert the data into the frequency domain, monitor power in a specific frequency band (pink box), and trigger stimulation when that power exceeds a threshold (red dashed line). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

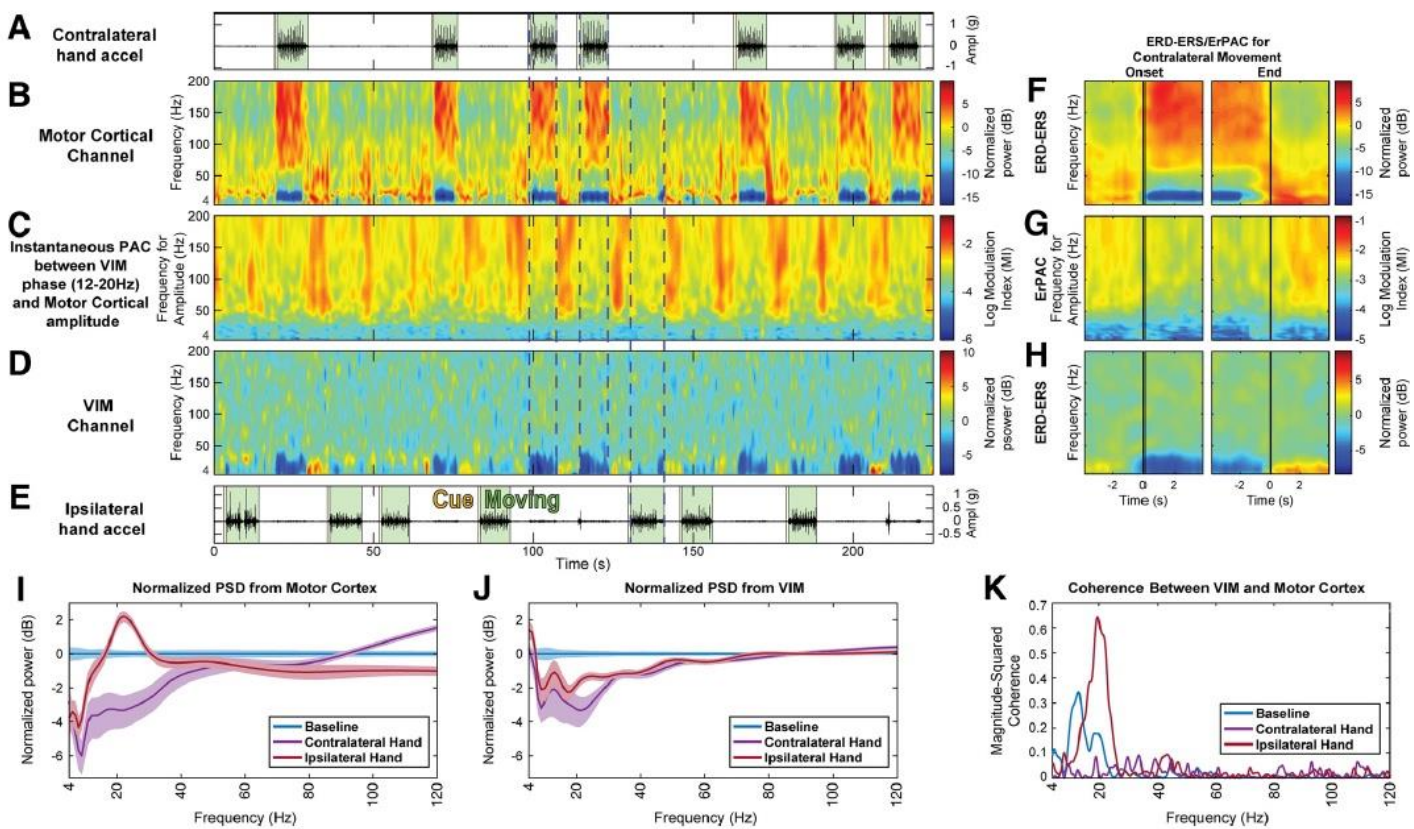
Behavioral/Cognitive



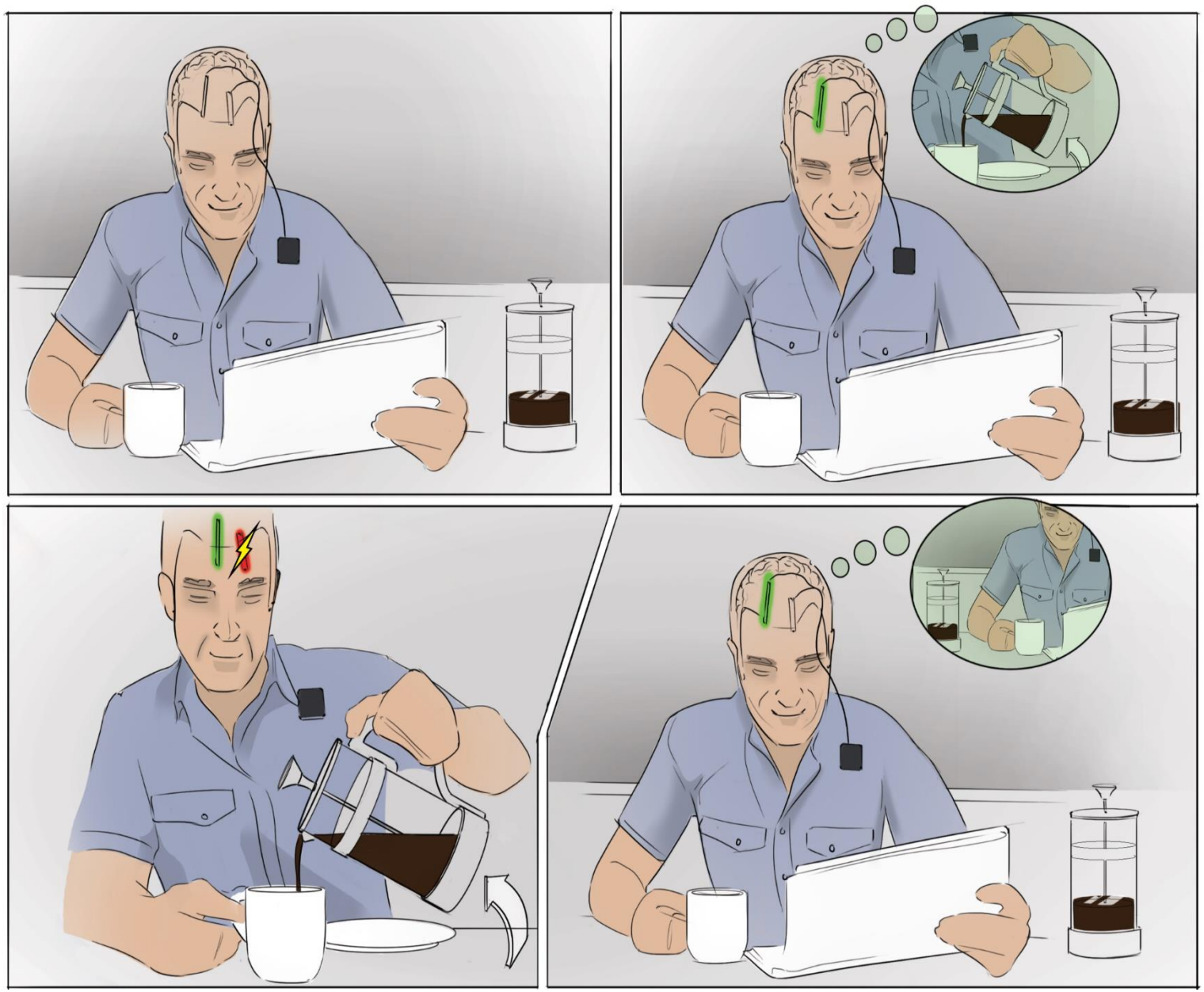
The Functional Role of Thalamocortical Coupling in the Human Motor Network

Enrico Opri,[1] Stephanie Cernera,[1] Michael S. Okun,[2] Kelly D. Foote,[2] and Aysegul Gunduz[1,2]

[1]J. Crayton Pruitt Family Department of Biomedical Engineering, and [2]Fixel Center for Neurological Diseases at UF Health, Departments of Neurology and Neurosurgery, University of Florida, Gainesville, Florida 32611

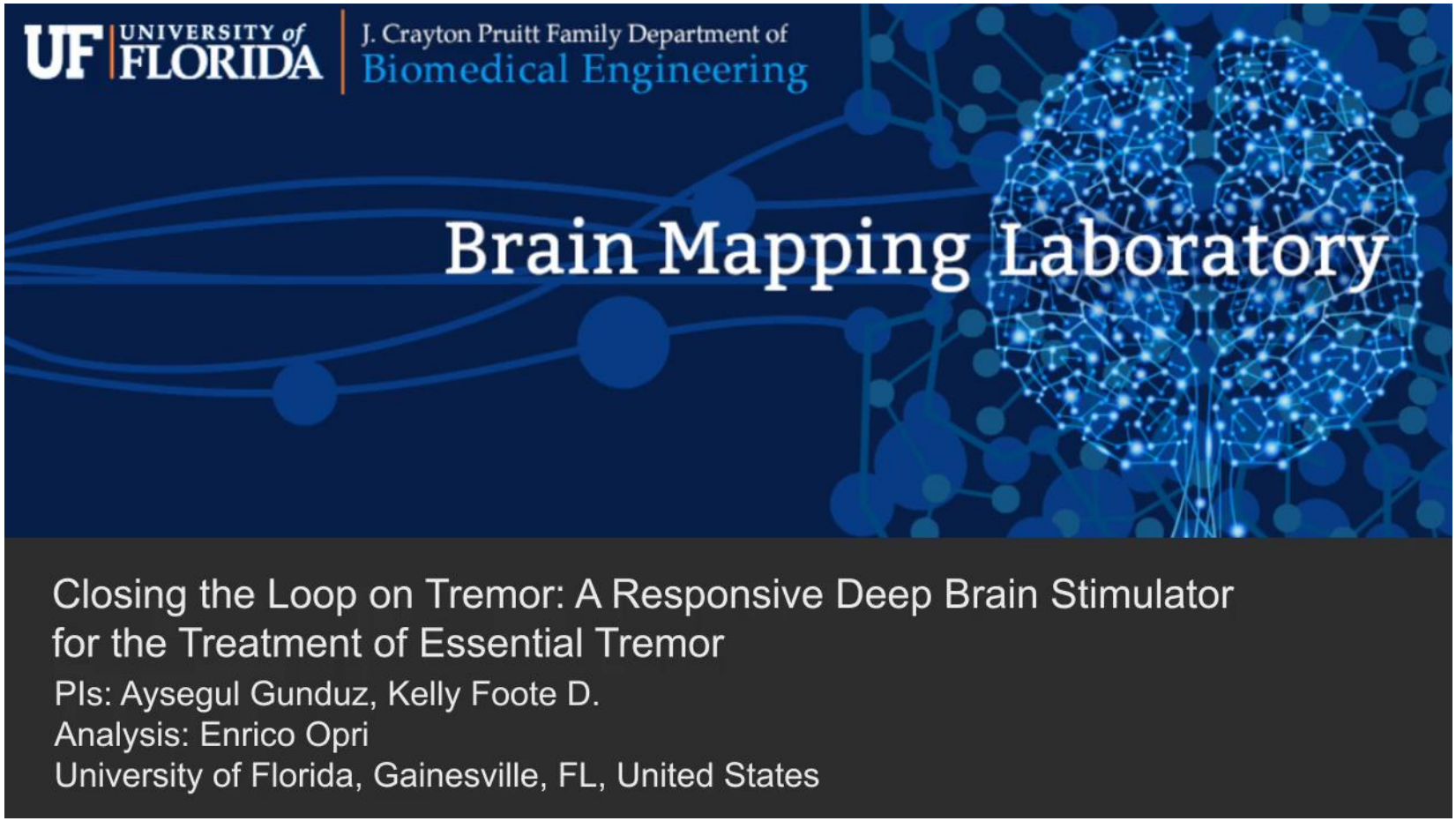


Common Scenario



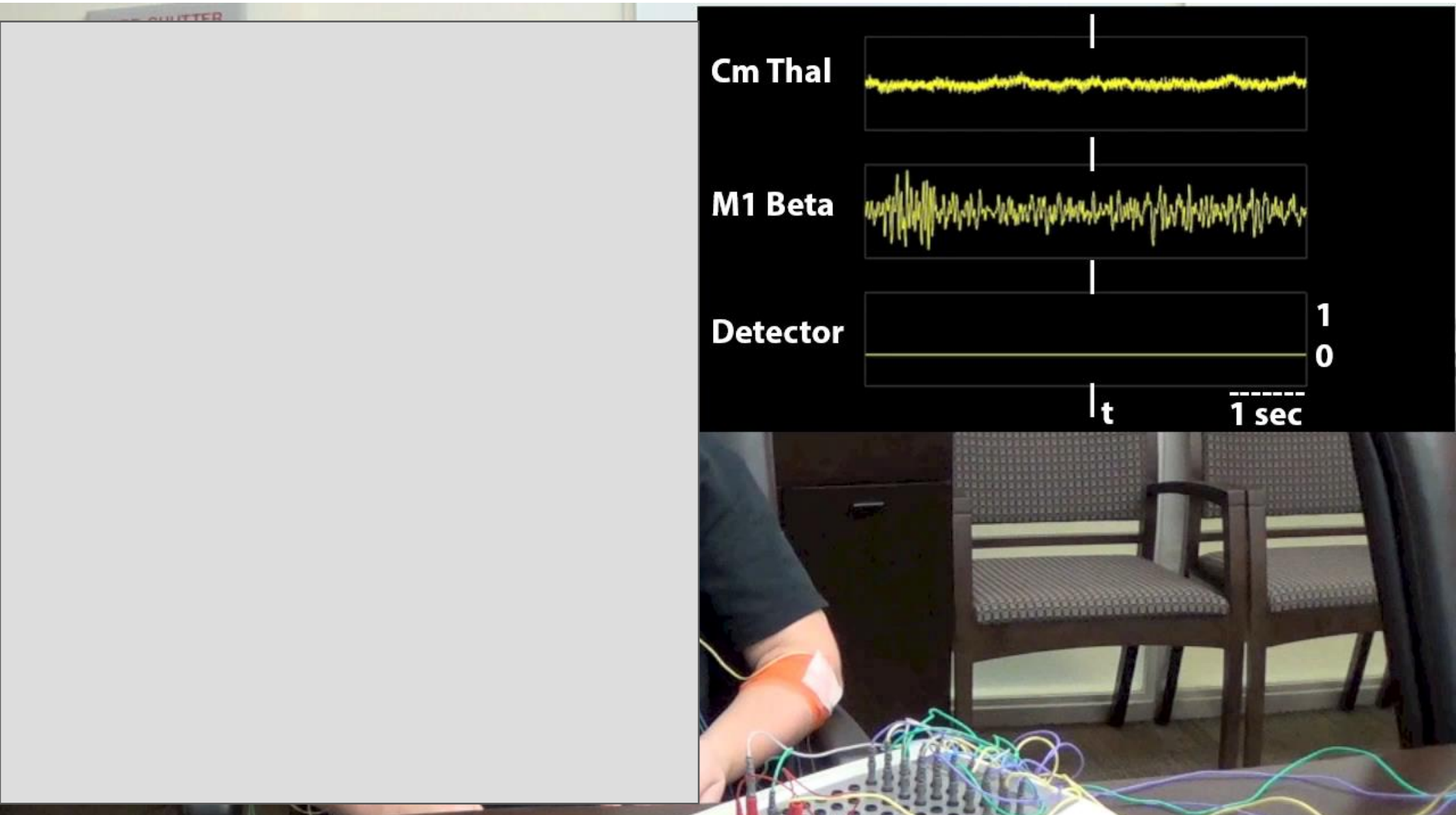
NIH Brain Initiative Gunduz, Foote, et. al.

Adaptive Deep Brain Stimulation



Gunduz and Foote, NIH UH3 Brain Initiative Grant

The Human 'Tic' Detector

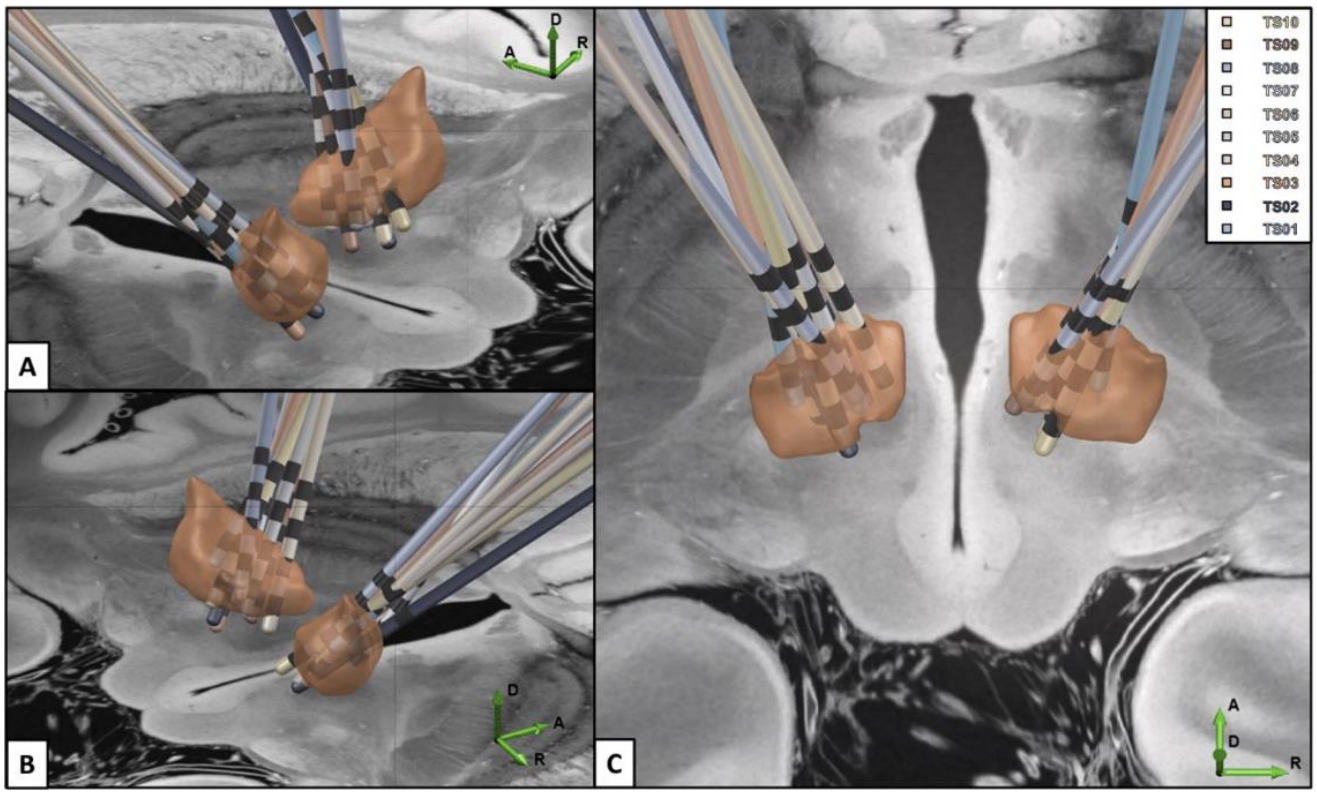


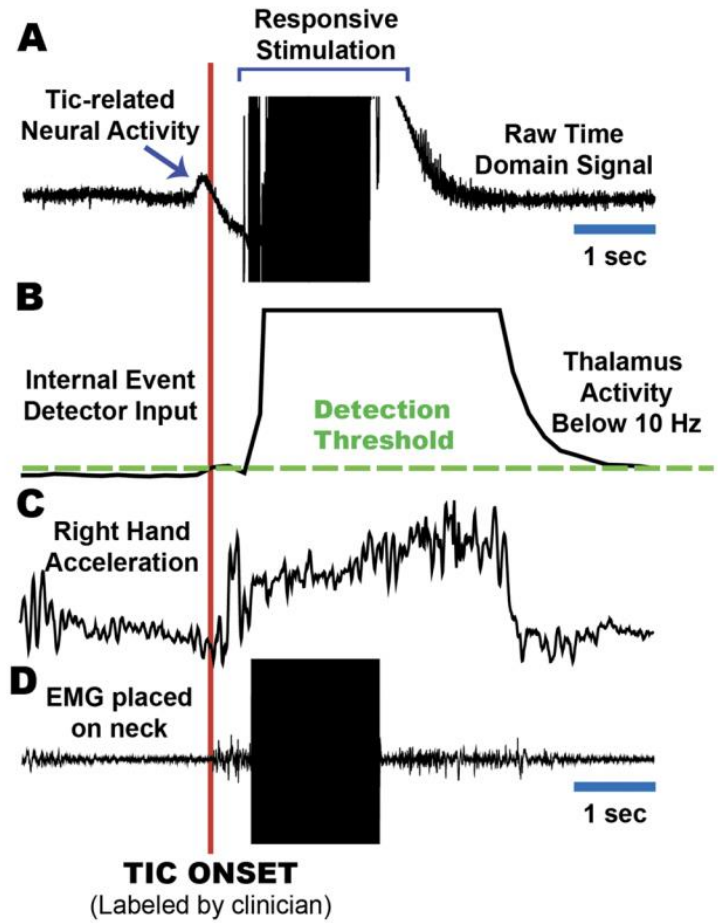
scientific reports

OPEN

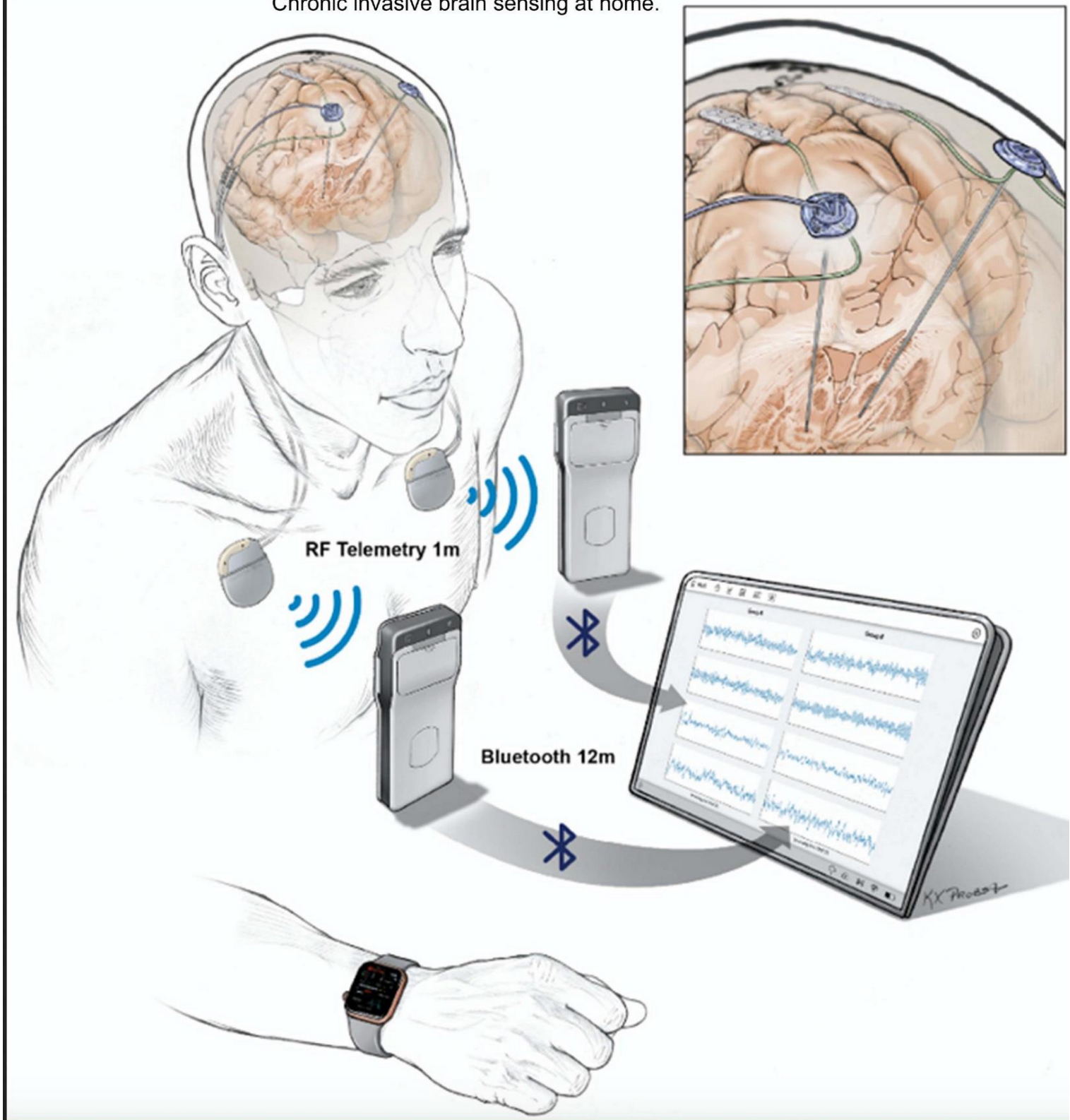
Responsive deep brain stimulation for the treatment of Tourette syndrome

Michael S. Okun[1,2]✉, Jackson Cagle[1], Julieth Gomez[3], Dawn Bowers[4], Joshua Wong[1], Kelly D. Foote[1,2] & Aysegul Gunduz[1,4]



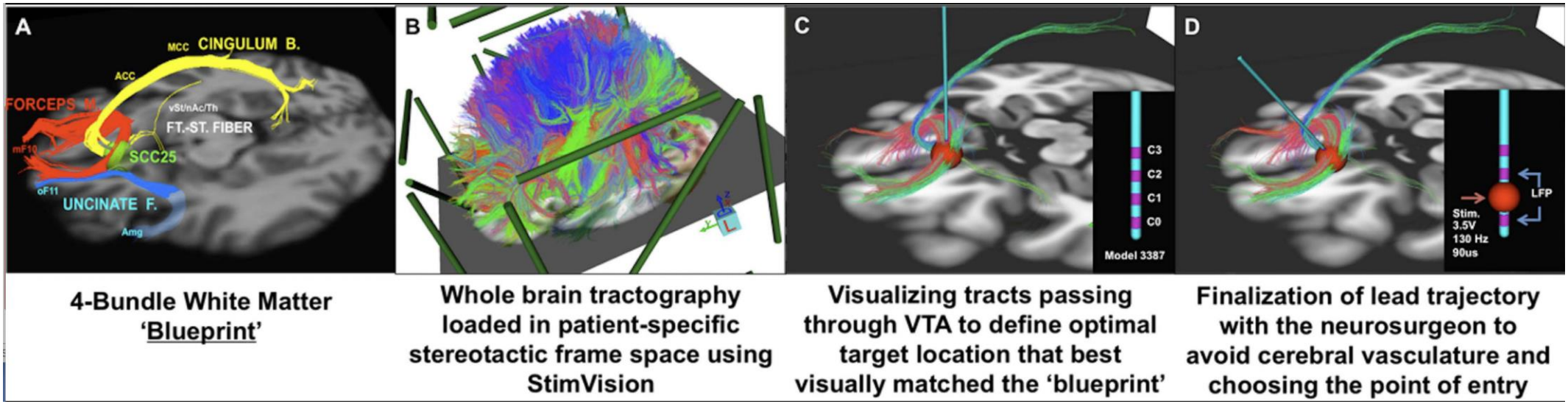


Chronic invasive brain sensing at home.



Is it time to more effectively use imaging to target?

The 'Reboot' of a new multi-center depression trial will depend on it



4-Bundle White Matter 'Blueprint'

Whole brain tractography loaded in patient-specific stereotactic frame space using StimVision

Visualizing tracts passing through VTA to define optimal target location that best visually matched the 'blueprint'

Finalization of lead trajectory with the neurosurgeon to avoid cerebral vasculature and choosing the point of entry

Article

Cingulate dynamics track depression recovery with deep brain stimulation

https://doi.org/10.1038/s41586-023-06541-3

Received: 12 September 2021

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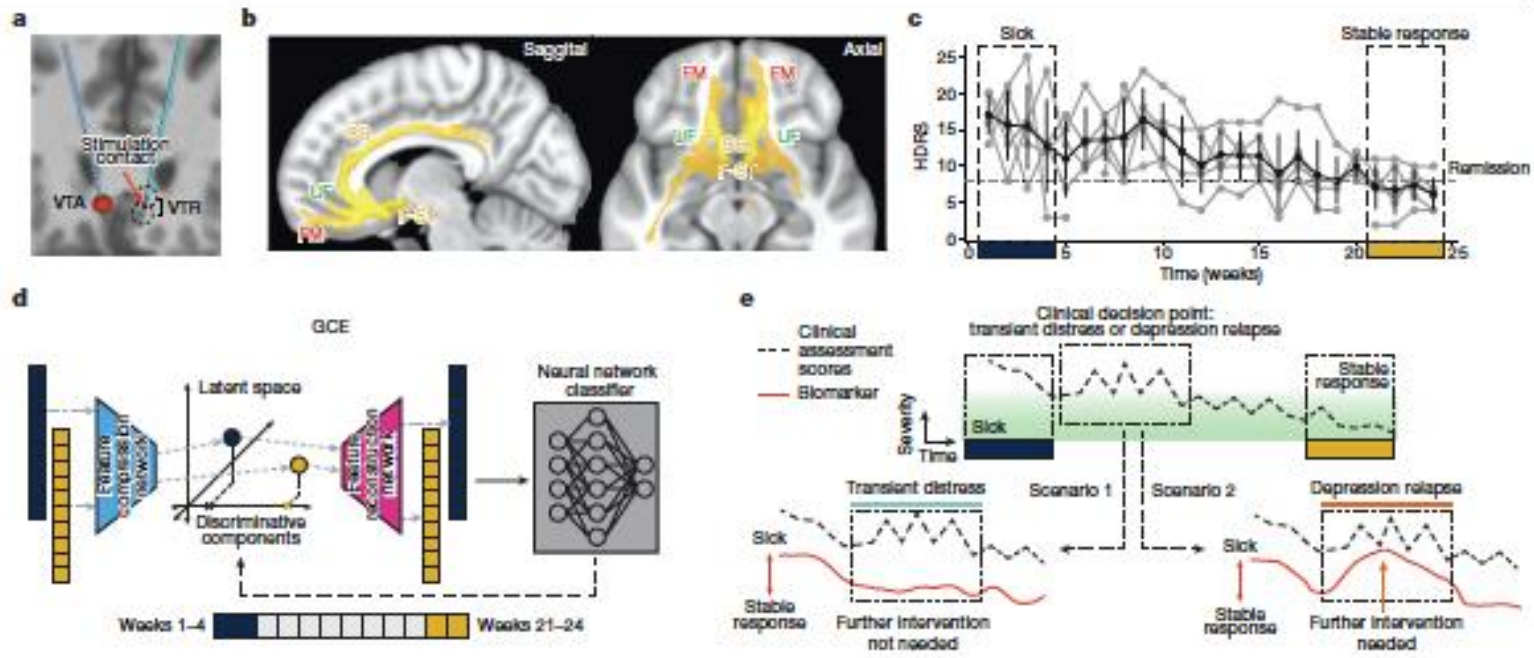
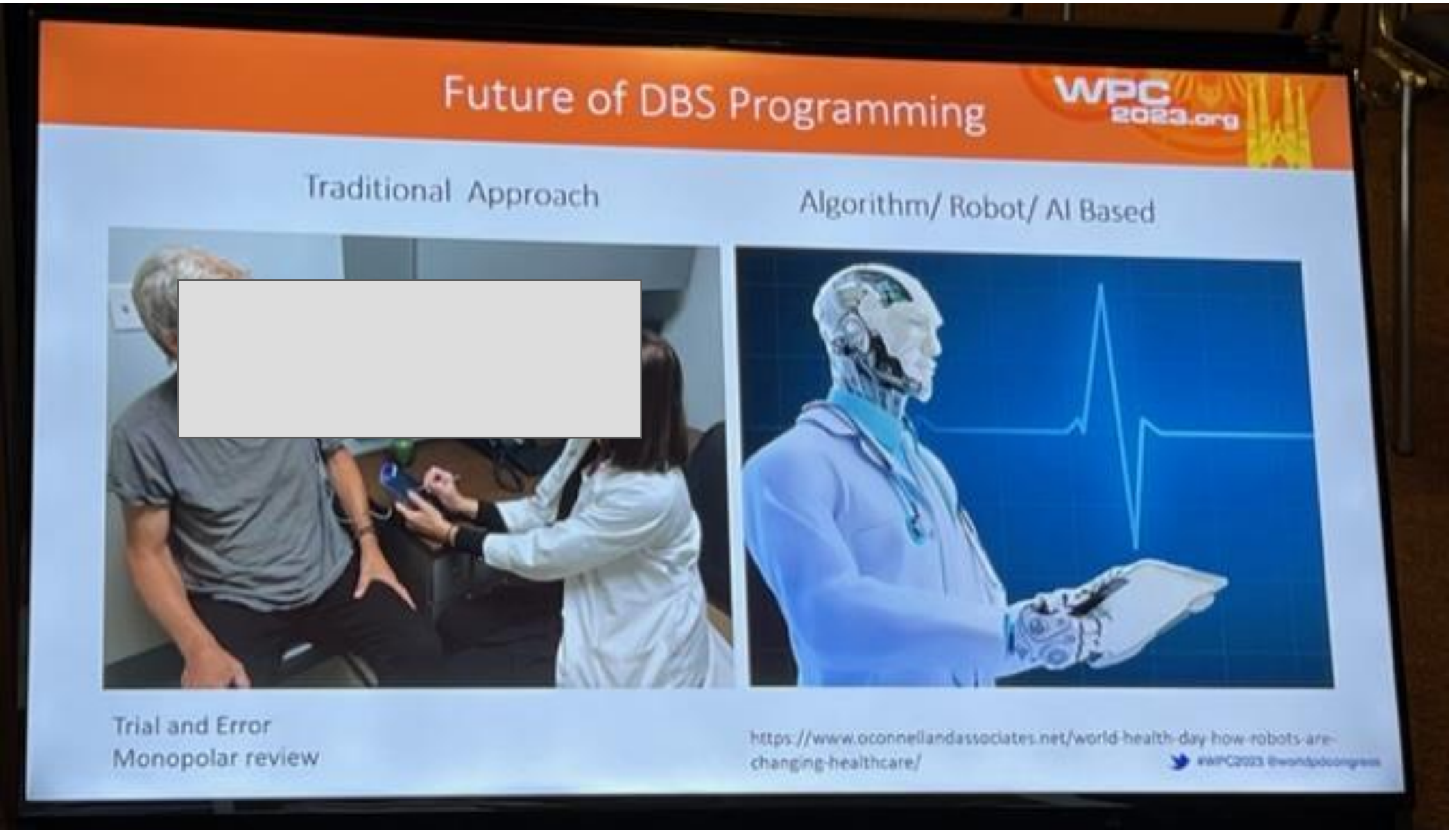
Open access

Check for updates

Sankaraleengam Alagapan[1], Ki Sueng Choi[2,3,4,14], Stephen Heisig[2,14], Patricio Riva-Posse[5], Andrea Crowell[5], Vineet Tiruvadi[6,7], Mosadoluwa Obatusin[2], Ashan Veerakumar[8], Allison C. Waters[2,9,10], Robert E. Gross[6,11,12], Sinead Quinn[5], Lydia Denison[7], Matthew O'Shaughnessy[1], Marissa Connor[1], Gregory Canal[1], Jungho Cha[2], Rachel Hershenberg[5], Tanya Nauvel[2], Faical Isbaine[11], Muhammad Furqan Afzal[2], Martijn Figee[2,9,10], Brian H. Kopell[2,4,9,10,13], Robert Butera[1,6], Helen S. Mayberg[2,4,9,10,13,15] ✉ & Christopher J. Rozell[1,15] ✉

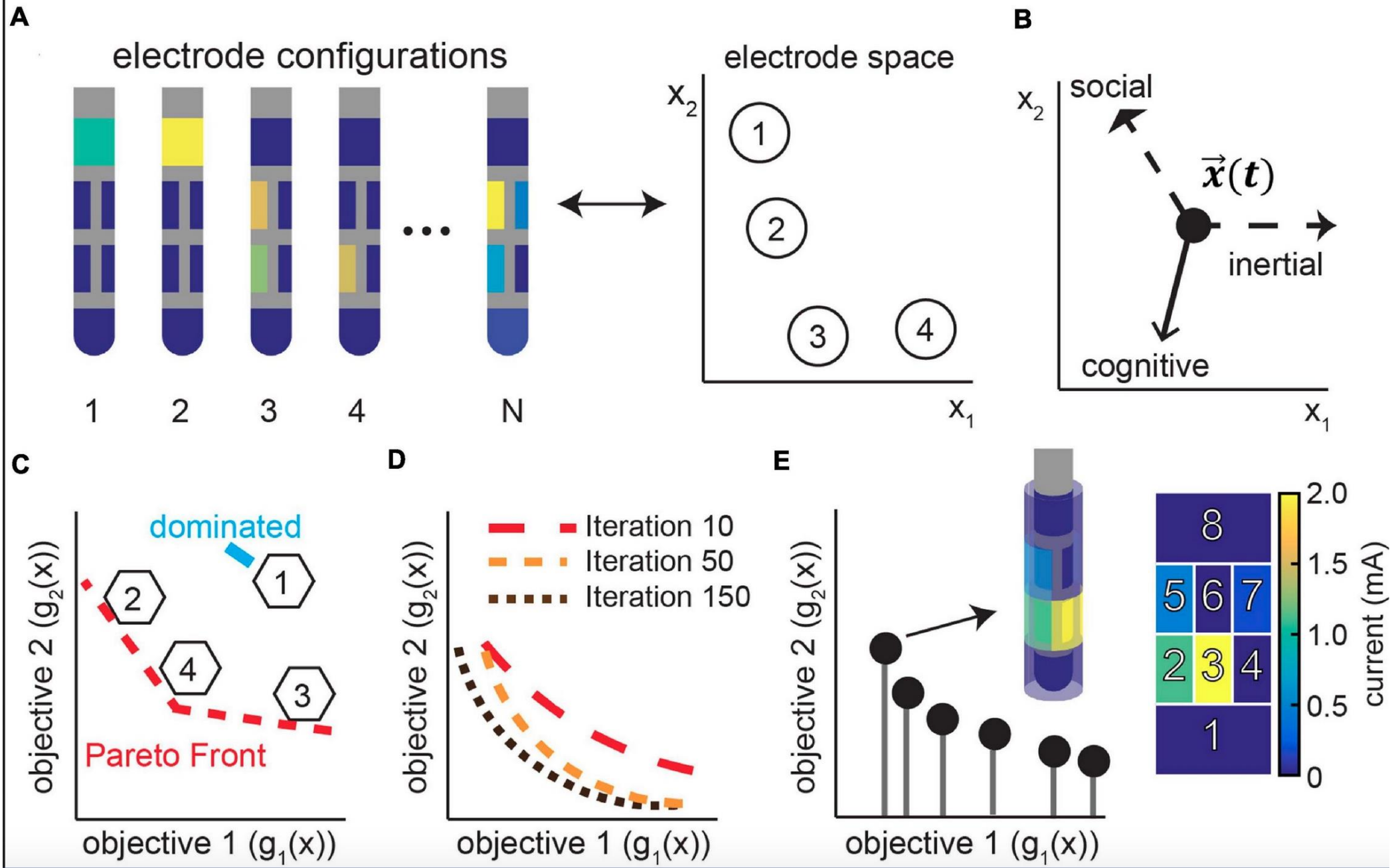


Will ‘AI’ solve the ‘practicalities’ of patient selection and later management of hundreds of thousands of devices?



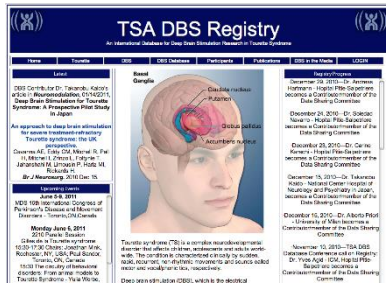
Jill Ostrem 2023 World Parkinson Congress

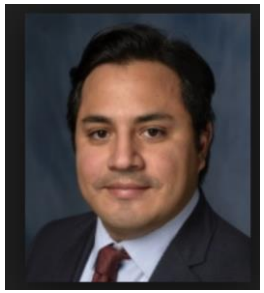
Model-based algorithms for optimizing DBS therapy



How do we track diseases/symptoms when very few cases are being performed across many continents and expert centers?

To Improve Our Understanding:
“Collect Outcomes”





New Online Views **4,822** | Citations **0** | Altmetric **587**

Original Investigation ONLINE FIRST

January 16, 2018

Efficacy and Safety of Deep Brain Stimulation in Tourette Syndrome

The International Tourette Syndrome Deep Brain Stimulation Public Database and Registry

Daniel Martinez-Ramirez, MD[1]; Joohi Jimenez-Shahed, MD[2]; James Frederick Leckman, MD[3]; et al

» Author Affiliations

JAMA Neurol. Published online January 16, 2018. doi:10.1001/jamaneurol.2017.4317

Approaches for Personalization in Targeting

	Mt. Sinai	Baylor/UCLA	UCSF
	Stim: SGC; Sense: SGC	Stim: SGC, VC/VS; Sense: 10 temporary sEEG electrodes in pre-frontal & temporal regions	Stim + Sense: SGC, VC/VS, Amy, HPC, OFC; 2 sites selected from sEEG electrodes in 10 brain regions
Select Brain Region			
Targeting	Tractography	Tractography (3D/holographic) Network effects using directional current steering	Tractography Clinical + functional network mapping
Inpatient Stage	No	Yes: explore and narrow parameter space, examine network effects	Yes: identify stimulation and sensing sites, determine eligibility for chronic device
Therapeutic Implant	Implanted during first/only surgery	Implanted at initial surgery	Implanted at second surgery
Device	Medtronic RC+S	Boston Scientific Cartesia/Gevia	NeuroPace RNS System
Stimulation	Continuous	Continuous	Intermittent
Biomarker	Target engagement Exploratory depression recovery tracking	Targeting, network activity	Personalized marker of depressed state Drives closed-loop stimulation
Personalization	Individualized tractography guided targeting using predefined network blueprint and intraoperative CT/DTI and behavioral verification	Individualized network targeting and parameter optimization	Targeting based on individualized clinical + functional network mapping. Stimulation driven by personalized biomarkers.

9th DBS Think Tank Proceedings

Who is going to pay for the devices, battery replacements and maintenance/removal?

Are we doing a good job performing informed consent procedures?

JAMA Neurology

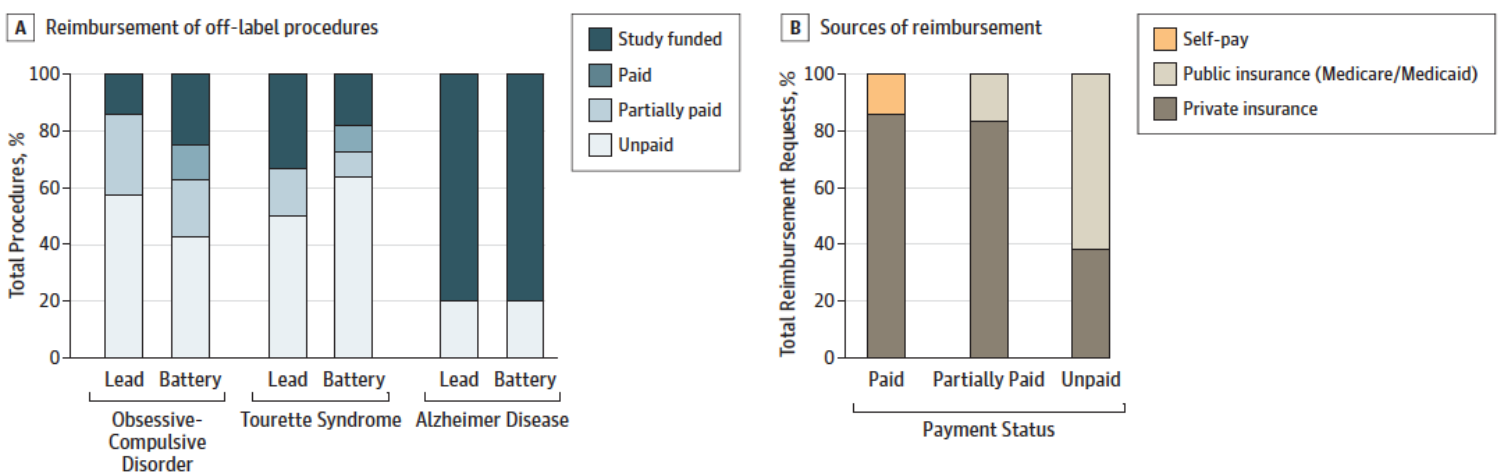
VIEWPOINT

The Problem of Funding Off-label Deep Brain Stimulation

Bait-and-Switch Tactics and the Need for Policy Reform

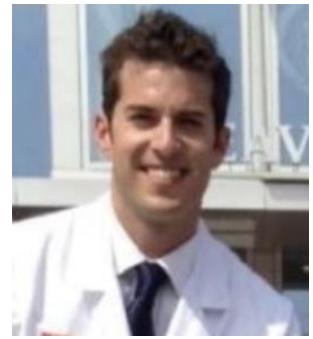
JAMA Neurology Published online November 7, 2016

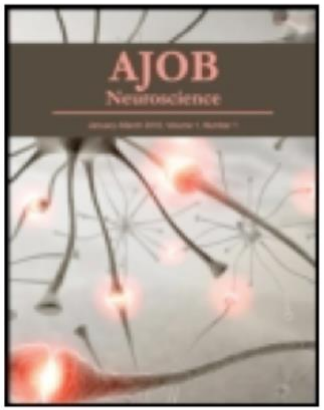
Figure. Reimbursement Information for Off-label Deep Brain Stimulation Procedures, 2005-2015



No Path Forward Dilemma

***JAMA Neurology* Viewpoint Manuscript Revision Submission**
Revision Date: November 19, 2013
Title:
Medicare Coverage of Investigational Devices: The Troubled Path Forward for Deep Brain Stimulation





AJOB Neuroscience
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/uabn20

Translational Imperatives in Deep Brain Stimulation Research: Addressing Neuroethical Issues of Consequences and Continuity of Clinical Care

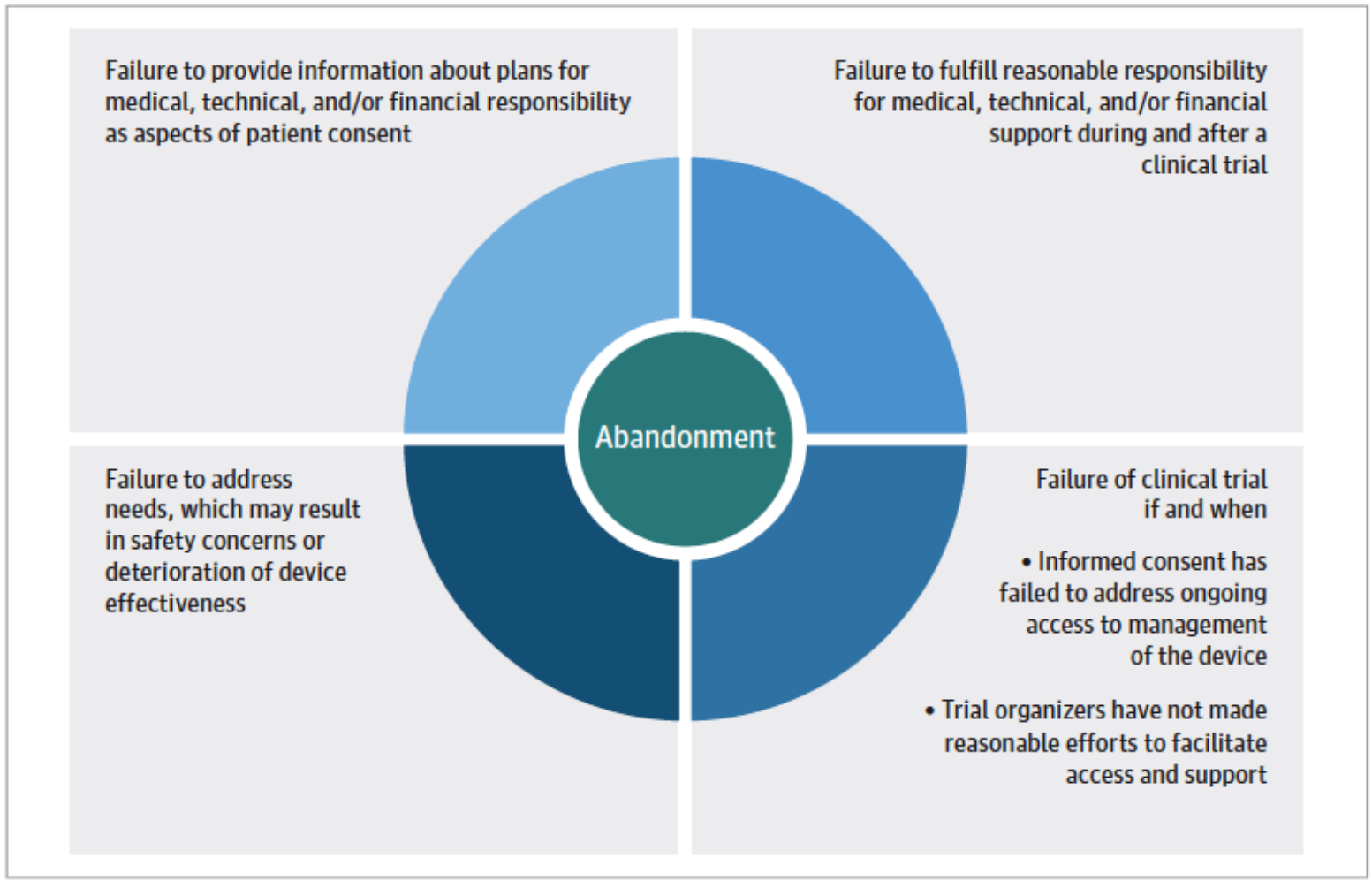
P. Justin Rossi [a] , Michael Okun [a] & James Giordano [b]
[a] University of Florida
[b] Georgetown University Medical Center and Ludwig-Maximilians Universität
Published online: 30 Jan 2014.

JAMA Network Open

Consensus Statement | Health Policy

Definition of Implanted Neurological Device Abandonment
A Systematic Review and Consensus Statement

Michael S. Okun, MD; Timothy Marjenin, BS; Jinendra Ekanayake, MBBS, PhD; Frederic Gilbert, PhD; Sean P. Doherty, PhD; Jack Pilkington, MSc; Jennifer French, BS, MBA; Cynthia Kubu, PhD; Gabriel Lázaro-Muñoz, PhD; Timothy Denison, PhD; James Giordano, PhD, MPhil



VIEWPOINT

Reforming the Process for Deep Brain Stimulation and Neurologic Device Approval in Rare Diseases

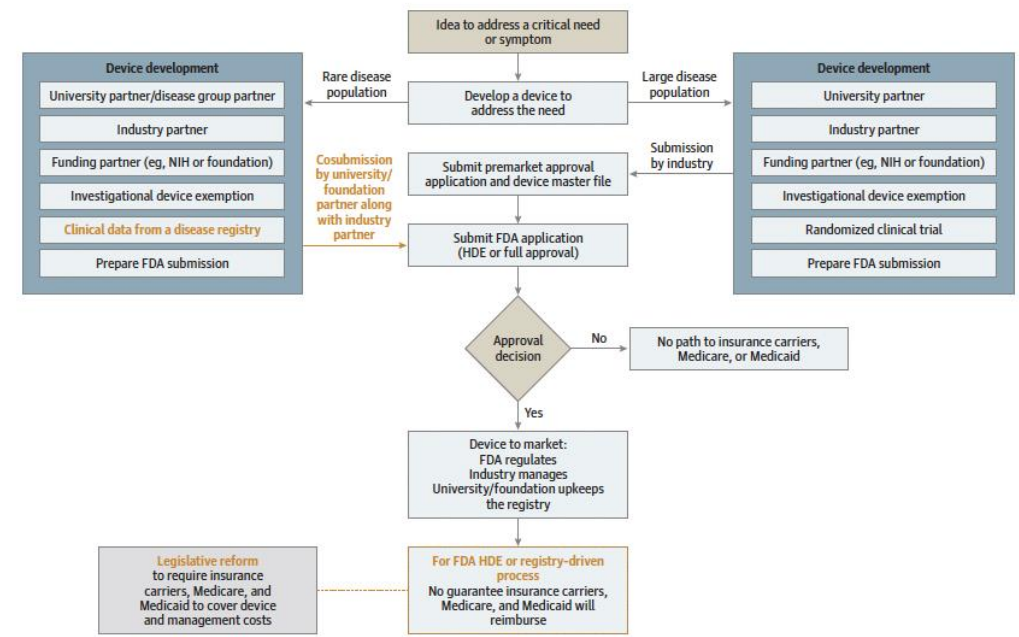
JAMA Neurology

VIEWPOINT

Michael S. Okun, MD
Norman Fixel Institute for Neurological Diseases, University of Florida Health, Gainesville; and Associate Editor, *JAMA Neurology*.

James Giordano, PhD
Neuroethics Studies Program, Pellegrino Center for Clinical Bioethics, Department of Neurology, Georgetown University Medical Center, Washington, DC.

Figure. Device Approval Process for Rare vs Large Disease Populations



frontiers in Psychiatry

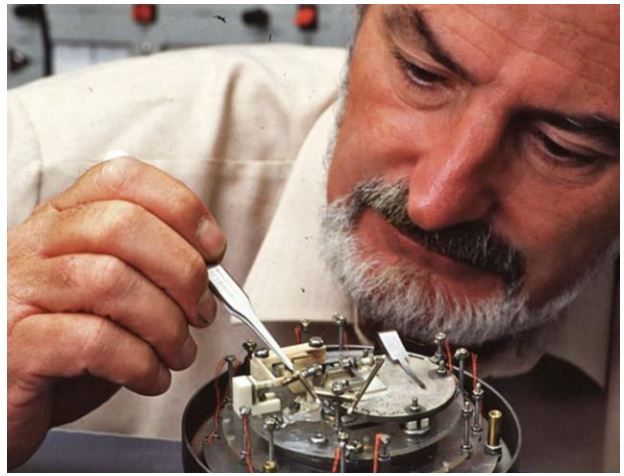
Restriction of Access to Deep Brain Stimulation for Refractory OCD: Failure to Apply the Federal Parity Act

Rachel A. Davis[1*], James Giordano[2], D. Brian Hufford[3], Sameer A. Sheth[4], Peter Warnke[5], Alik S. Widge[6], R. Mark Richardson[7,8], Joshua M. Rosenow[9], Peter Justin Rossi[10], Eric A. Storch[11], Helena Winston[1,12], JoAnne Zboyan[13], Darin D. Dougherty[8,14], Kelly D. Foote[15], Wayne K. Goodman[11], Nicole C. R. McLaughlin[16,17,18], Steven Ojemann[19], Steven Rasmussen[16,17,18,20], Aviva Abosch[21†] and Michael S. Okun[22†]

- The Mental Health Parity and Addiction Equity Act of 2008
- Banned the use of differential rules in the provision of mental health care
- U.S. federal mandate large-group employer health insurance plans to cover mental health benefits
- Equivalent coverage for mental health and physical health treatments.
- Patient Protection and Affordable Care Act (PPACA or “ACA”) extended to
- individual and small-group plans
- Behavioral health as one of the “essential benefits”

“Science means constantly walking a tightrope between blind faith and curiosity; between expertise and creativity; between bias and openness; between experience and epiphany; between ambition and passion; and between arrogance and conviction – in short, between and old today and a new tomorrow.”

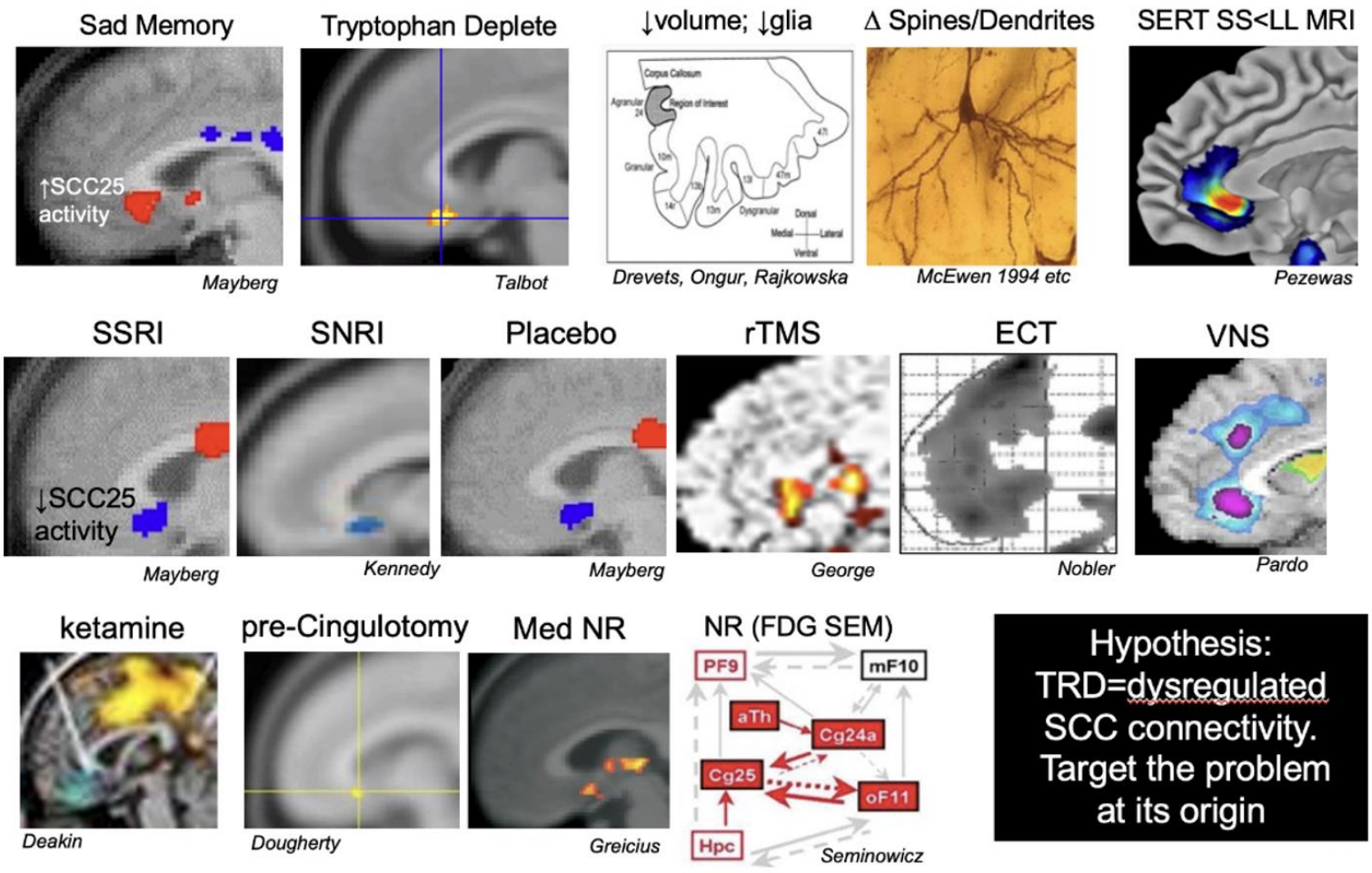
— Henrich Rohrer



Nobel Prize Winner 1986 (Swiss)
Scanning Tunneling Microscope

Result of MDD Treatment/Biomarker Studies

Converging Evidence of a Network Hub



Mayberg, 10th Annual DBS Proceedings, Unpublished with permission

‘You may have the best treatment in the world however if no one can access it, how good is it really?’
-Okun

nature medicine

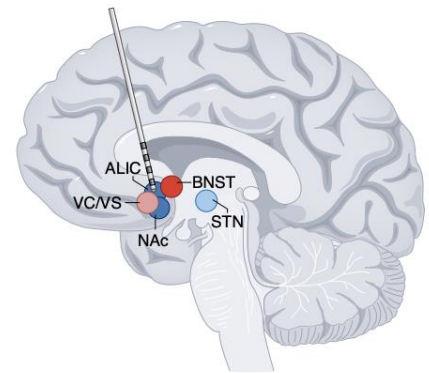
Deep brain stimulation for obsessive–compulsive disorder: a crisis of access

Deep brain stimulation is an effective treatment for obsessive–compulsive disorder but is rarely used. Action is needed by psychologists, psychiatrists and insurers so that patients with otherwise intractable cases can receive this therapy to improve their mental health.

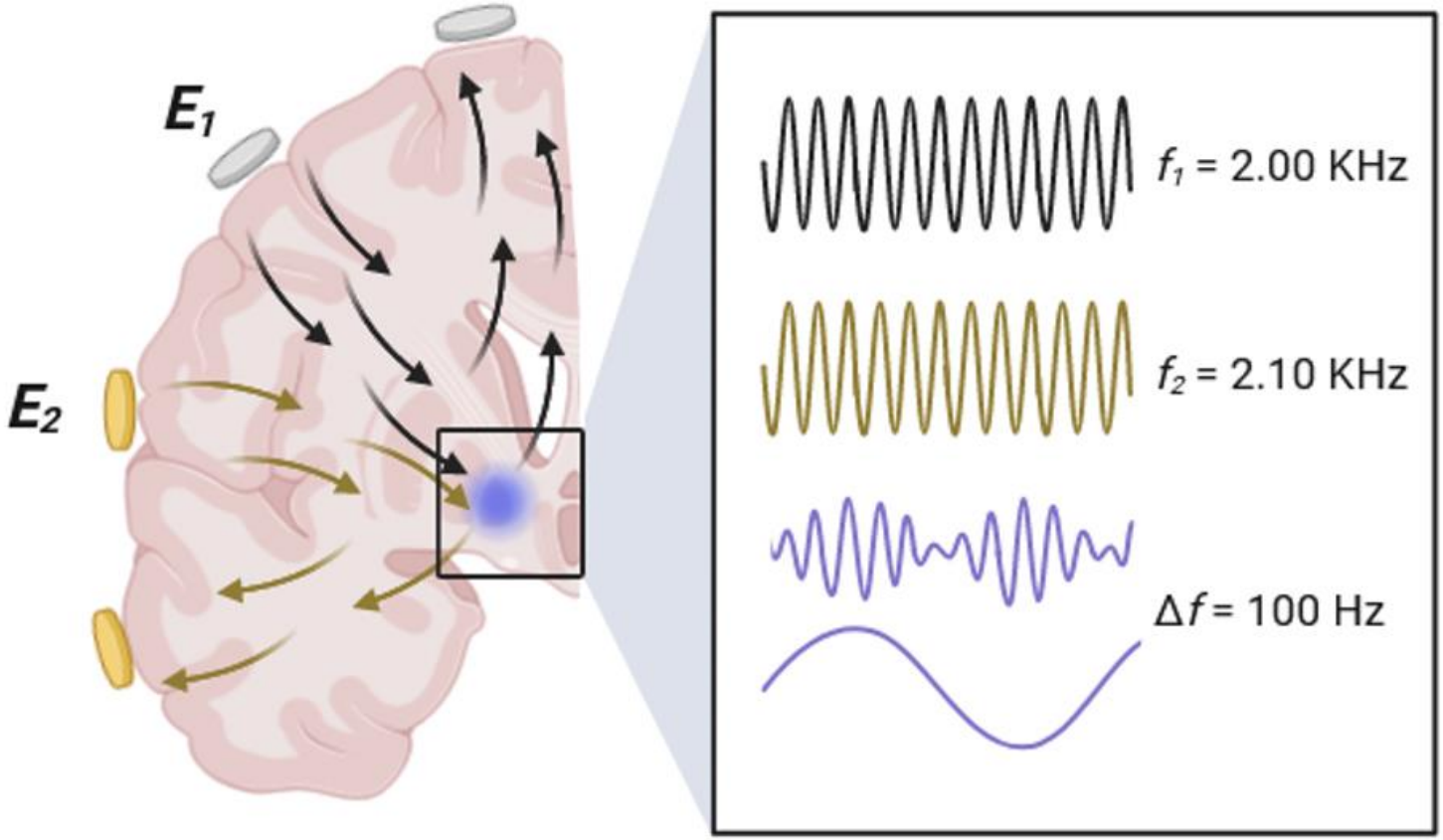
Veerle Visser-Vandewalle, Pablo Andrade, Philip E. Mosley, Benjamin D. Greenberg, Rick Schuurman, Nicole C. McLaughlin, Valerie Voon, Paul Krack, Kelly D. Foote, Helen S. Mayberg, Martijn Figee, Brian H. Kopell, Mircea Polosan, Eileen M. Joyce, Stephan Chabardes, Keith Matthews, Juan C. Baldermann, Himanshu Tyagi, Paul E. Holtzheimer, Chris Bervoets, Clement Hamani, Carine Karachi, Damiaan Denys, Ludvic Zrinzo, Patric Blomstedt, Matilda Naesström, Aviva Abosch, Steven Rasmussen, Volker A. Coenen, Thomas E. Schlaepfer, Darin D. Dougherty, Philippe Domenech, Peter Silburn, James Giordano, Andres M. Lozano, Sameer A. Sheth, Terry Coyne, Jens Kuhn, Luc Mallet, Bart Nuttin, Marwan Hariz and Michael S. Okun

Deep brain stimulation (DBS) is an approved therapy for obsessive–compulsive disorder (OCD), but it is rarely used despite its efficacy, which deprives people of effective treatment. OCD is characterized by distressing thoughts (obsessions) and repetitive mental or behavioral acts (compulsions). OCD affects 2–3% of the worldwide population and may cause substantial disability and adversely affect quality of life. First-line treatment consists of exposure and response prevention via cognitive–behavioral therapy (CBT) and pharmacotherapy, most commonly serotonin-reuptake inhibitors.

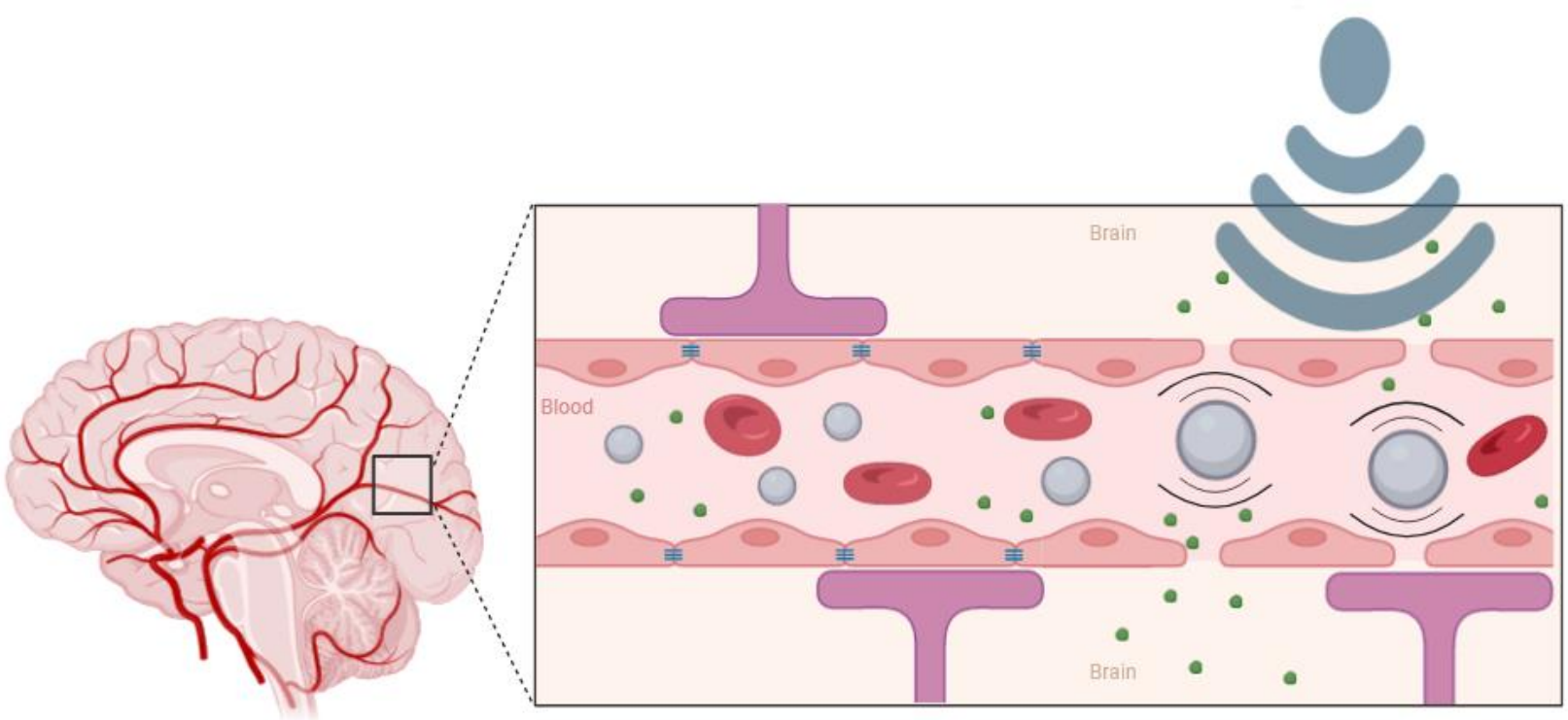
was developed in the 1940s and 1950s by Jean Talairach and Lars Leksell. The procedure consisted of using stereotactic methods to create thermal lesions in the anterior limb of the internal capsule (ALIC) to selectively dampen pathologically overactive fronto–thalamic circuits[3]. Due to its success in the treatment of movement disorders, DBS was introduced to the field of psychiatry decades later, when Bart Nuttin and colleagues used DBS to treat patients with refractory OCD, and also targeted the ALIC to offer an adjustable, programmable alternative to lesioning procedures[4]. Based on several subsequent DBS trials



What is on the horizon?



In Submission: Currie A, Wong J, Okun MS
Nature Parkinson's Journal



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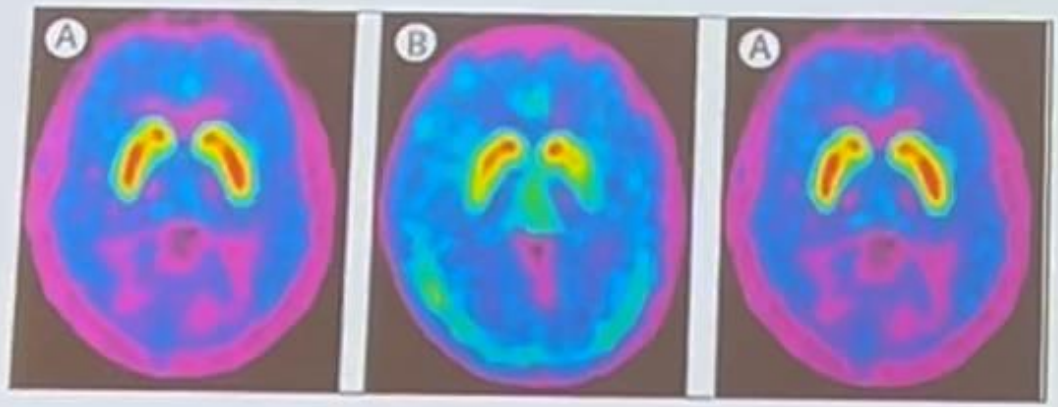
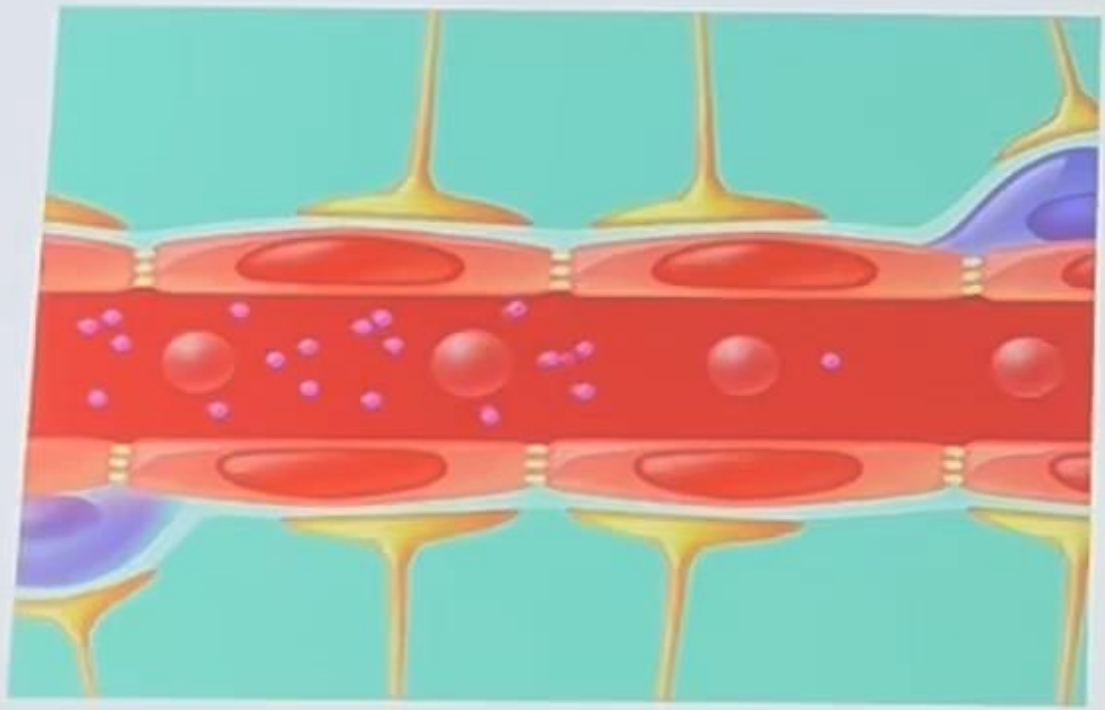
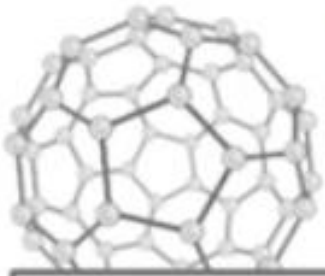


LOW-INTENSITY FOCUSED ULTRASOUND mediated-BBBo



NANOMEDICINE:

(NANOPARTICLES IN MEDICINE)

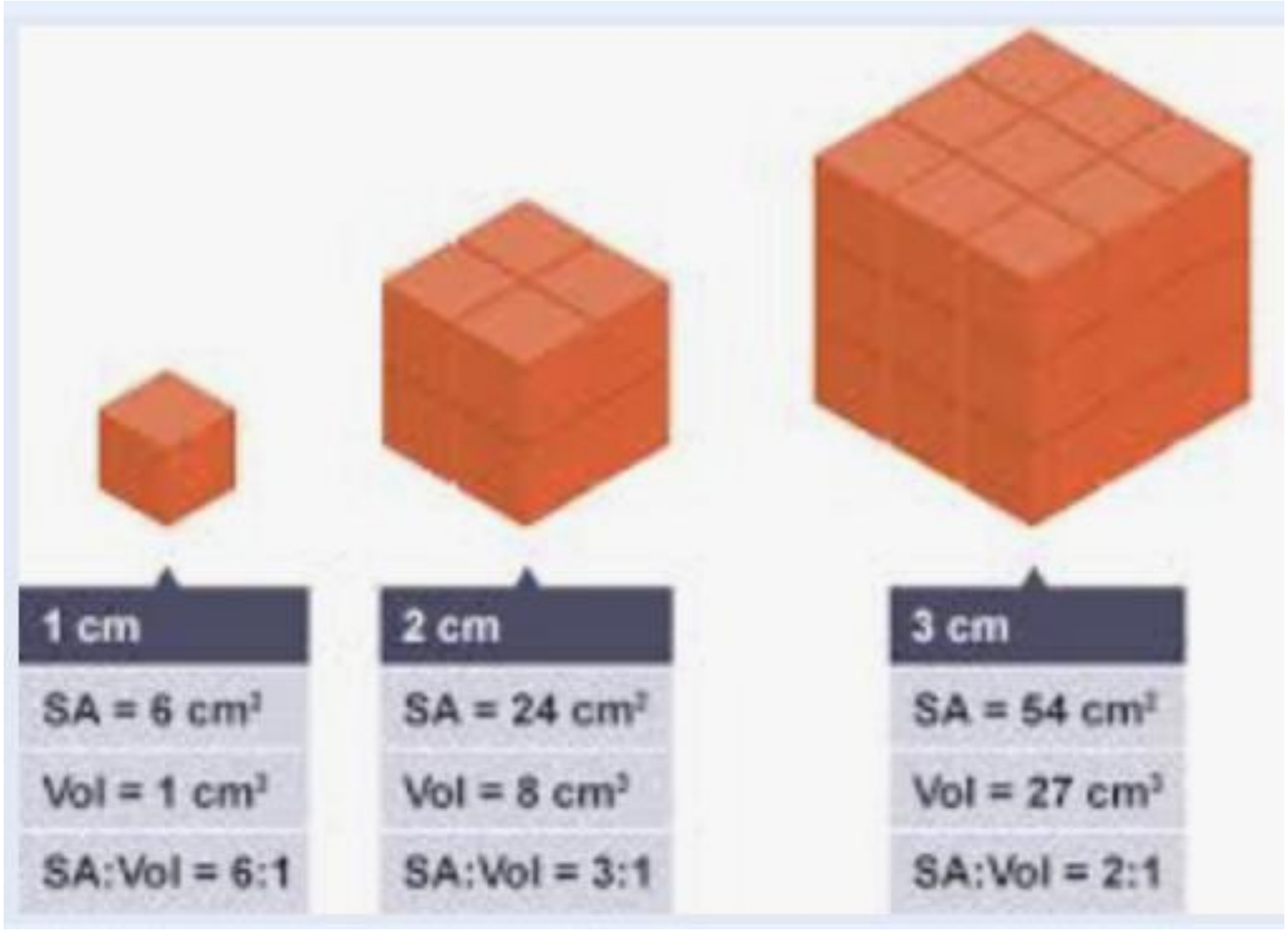


FULLERENES

(SO TINY)

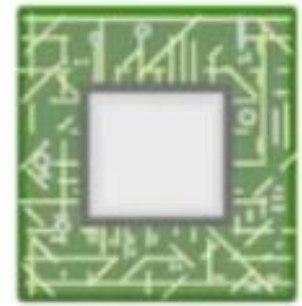
‘TO DELIVER DRUGS AROUND THE BODY

DELIVER DRUGS TO THE INSIDE OF CELLS



Surface Area to Volume Ratio

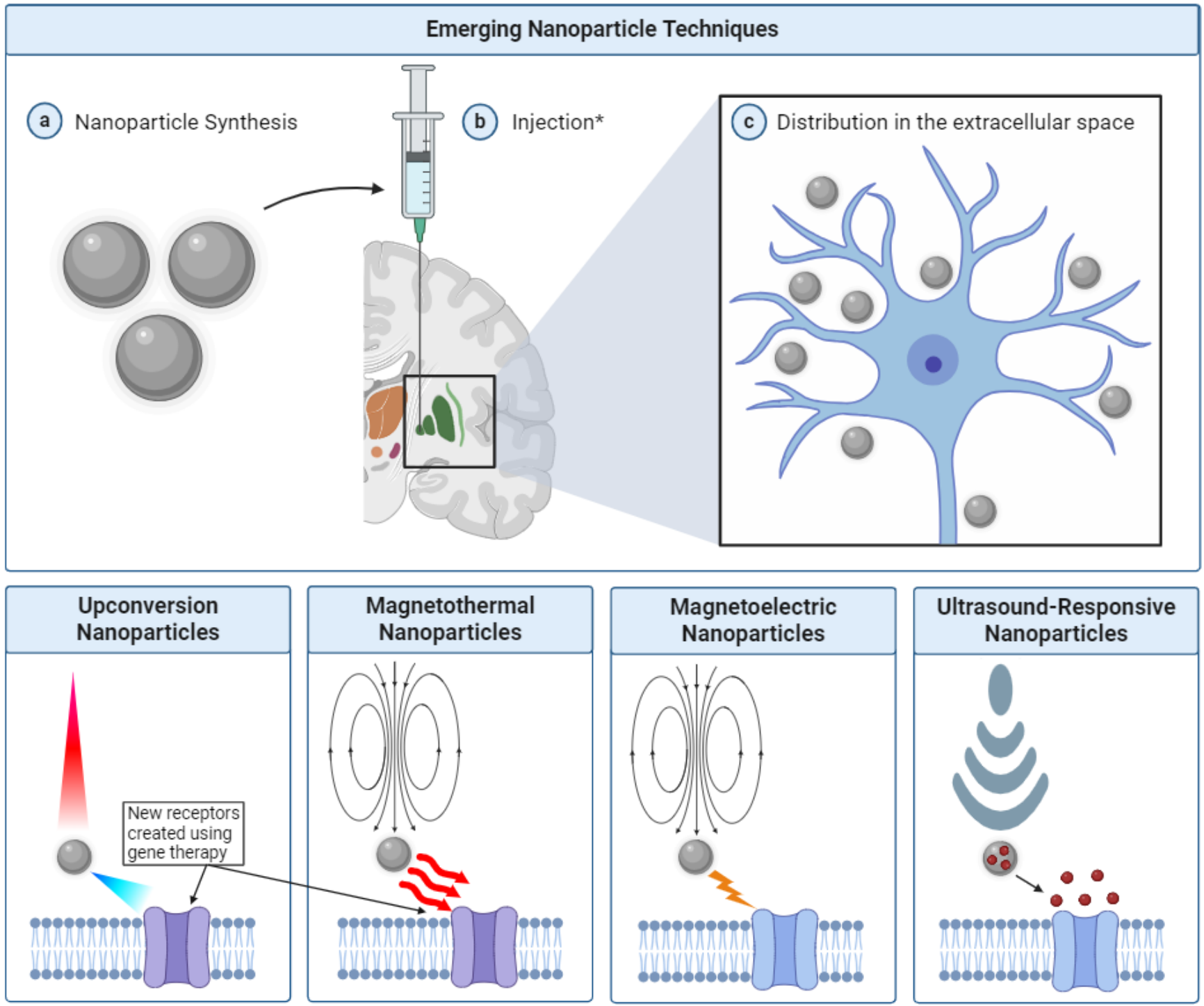
NANOPARTICLES IN ELECTRICAL CIRCUITS



TINY COMPUTER CHIPS

SOME OF THEM CAN CONDUCT ELECTRICITY

We are not focusing enough on ‘delivery systems/’



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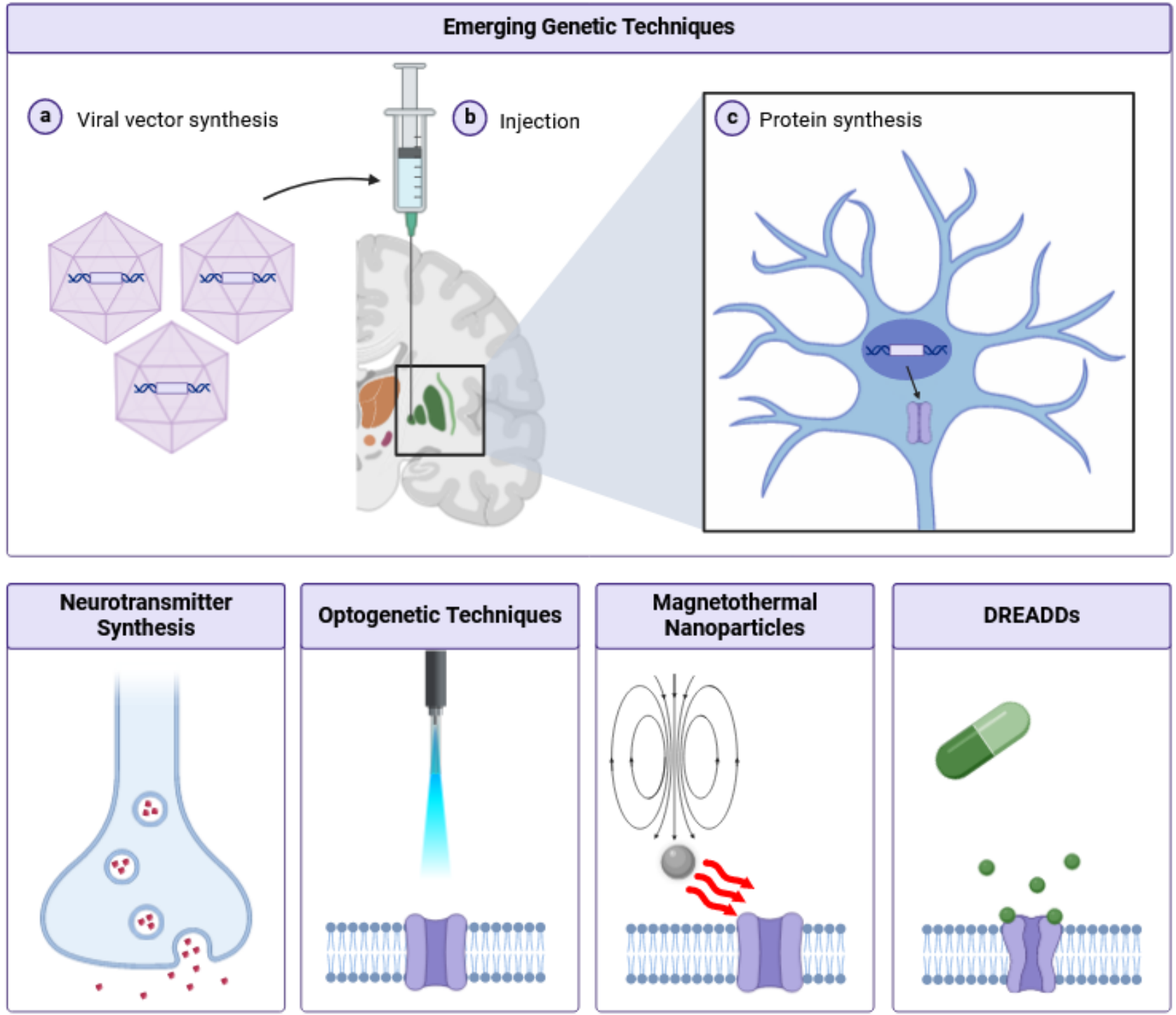

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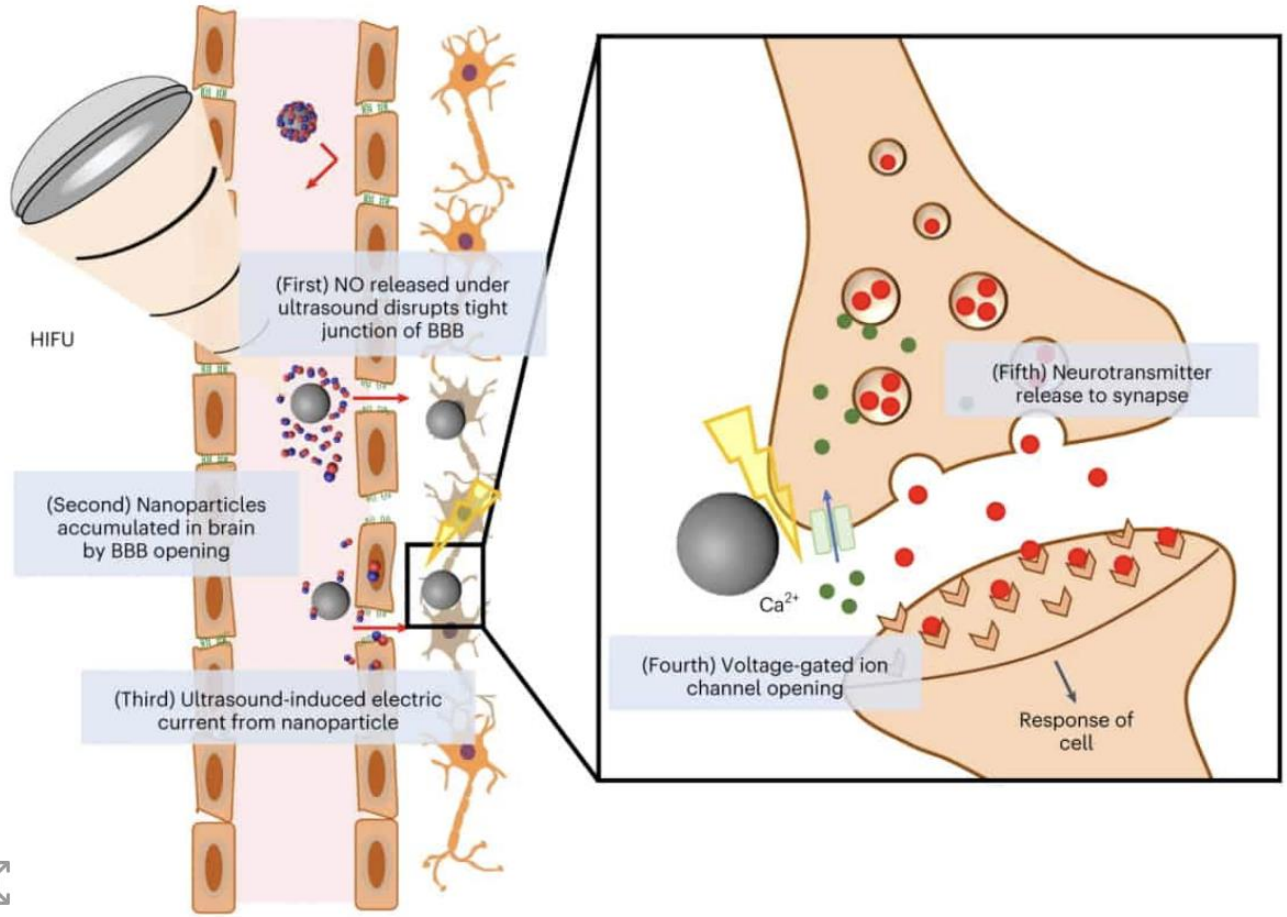
Piezoelectric nanoparticles provide deep brain stimulation without invasive surgery

04 Jan 2023 Tami Freeman

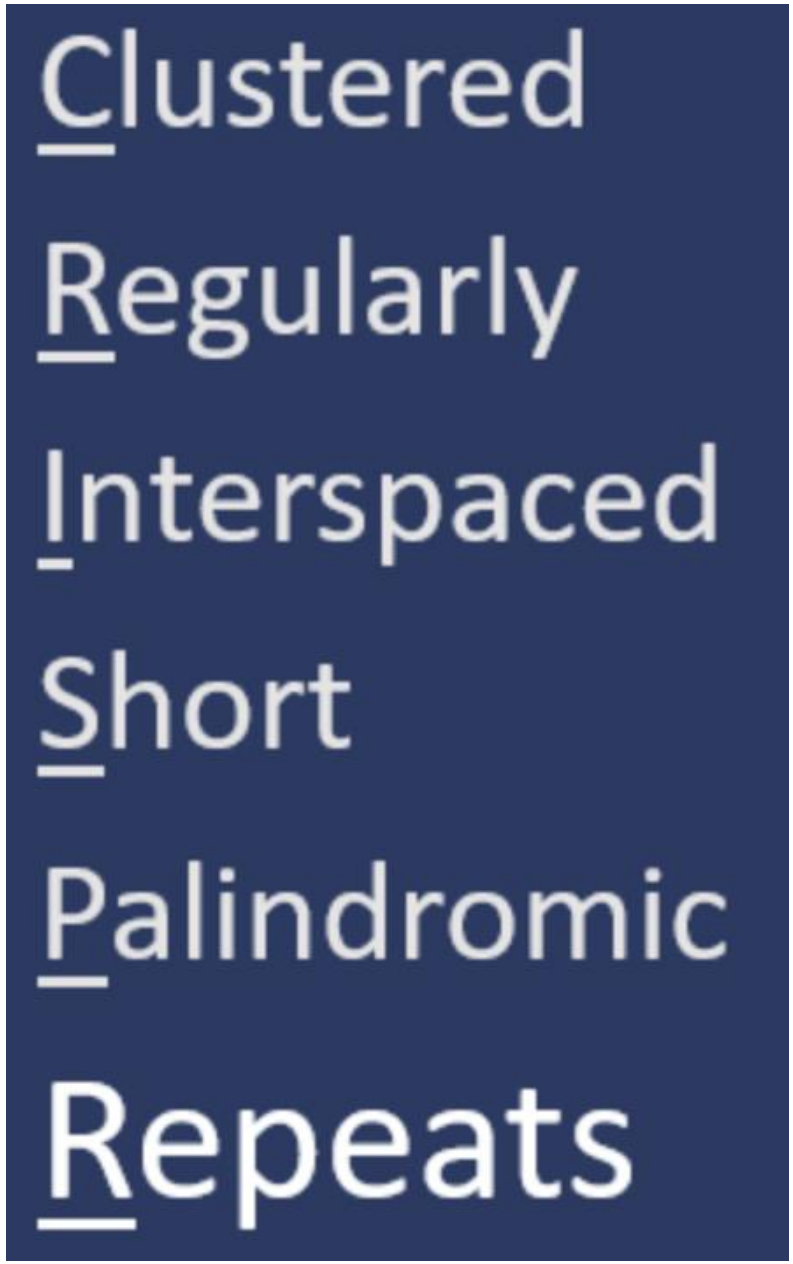


BBB opening and deep brain stimulation Schematic showing how systemically administered piezoelectric nanoparticles release NO locally in response to ultrasound and accumulate in the brain via BBB opening. The ultrasound-stimulated nanoparticles then generate current for neural stimulation, resulting in the release of neurotransmitters. (Courtesy ng. 10.1038/s41551-022-00965-4)

Screenshot

Greek word:
Piezein:
to squeeze
or press.


KAYAK
TACO CAT
RACECAR
NEVER ODD OR EVEN
STEP ON NO PETS
UFO TOFU
KAYAK
TACO CAT
RACECAR
NEVER ODD OR EVEN
STEP ON NO PETS
UFO TOFU

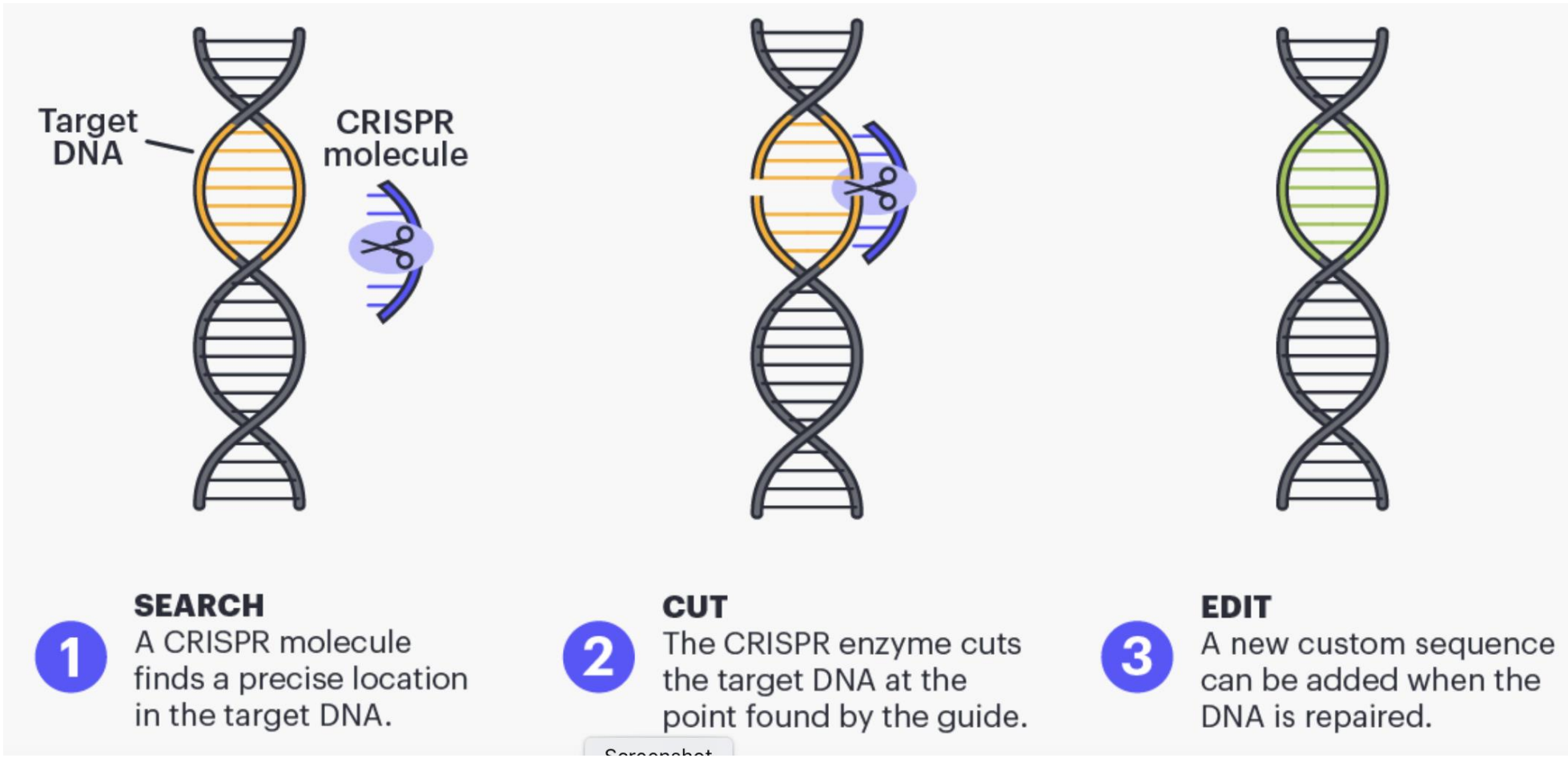

Clustered
Regularly
Interspaced
Short
Palindromic
Repeats

Clinical Review & Education

JAMA Neurology | Review

Building CRISPR Gene Therapies for the Central Nervous System
A Review

Sally E. Salomonsson, PhD; Claire D. Clelland, PhD, MD



Innovativegenomics

Concluding Thoughts

- A deeper understanding of the ‘normal state’ and the ‘diseased state’ will lead to more efficient and improved therapies.
- We need to think about ‘combinations’ of therapies and technologies.
- Delivery systems will need to improve.
- There is a world beyond deep brain stimulation.

How does the journey end?

NY Times

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@michaelokun on ‘X’ and Instagram