Surgical Treatment of Parkinson's Disease



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UFHealth
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Parkinson's Foundation

Tourette Association of America

Tyler's Hope for a Dystonia Cure

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NIH Support

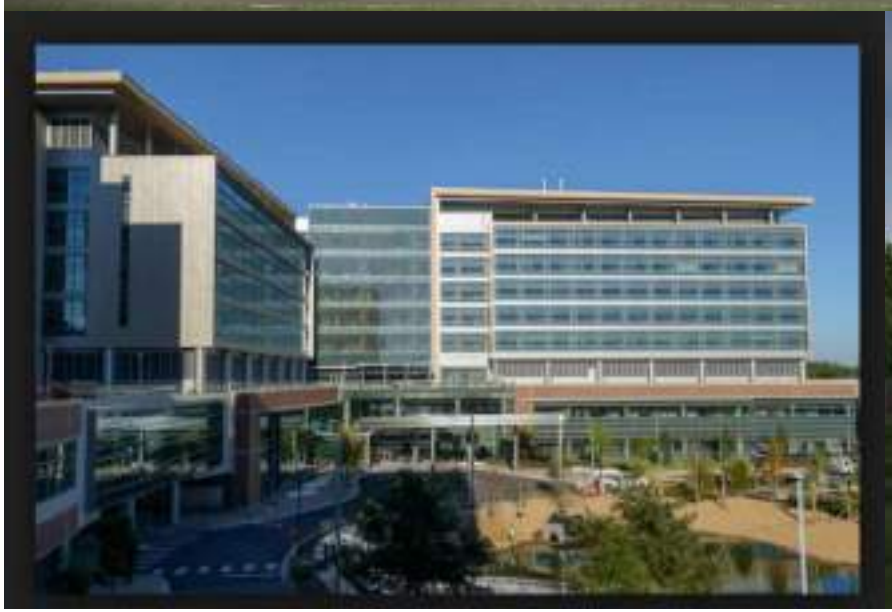
- UH3 NS18-023 Defining Targets for Tic Detection and Suppression in Tourette Syndrome Deep Brain Stimulation NS18-023
- R01NS131342 Thalamic DBS and Voice Tremor
- U01 Automated Image Differentiation of Parkinson's
- R25NS108939 University of Florida R25 Early Research Program for Neurology and Neurosurgery 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
- R21NS119849 Balance and Gait in Essential Tremor
- 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: www.pdplan.org









The ‘cypher’ for my talk



Clinical Pearl



New Paper



‘Hot’ Paper

‘Shout out’ to Fellows









JAMA | Review

Diagnosis and Treatment of Parkinson Disease
A Review

Melissa J. Armstrong, MD, MSc; Michael S. Okun, MD

JAMA PATIENT PAGE

Choosing a Parkinson Disease Treatment

Parkinson disease (PD) is the most common cause of parkinsonism, a syndrome of movement problems such as stiffness, slowness, and tremor.

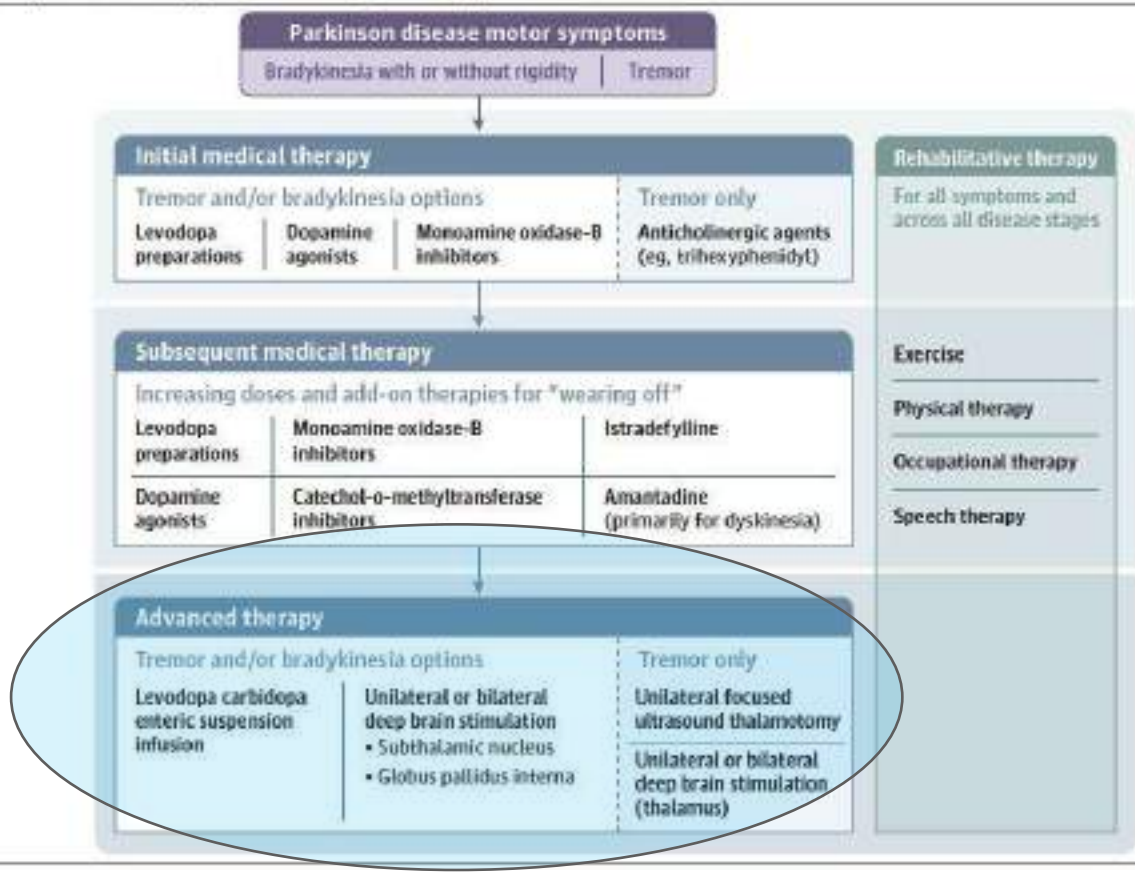
Less common causes of parkinsonism include other progressive brain diseases, medications, and stroke. An estimated 6.1 million people worldwide had a PD diagnosis in 2016, 2.4 times higher than in 1990. Choosing the right treatment is an important concern for people with PD.

Approaches to PD-Related Rehabilitative Therapy

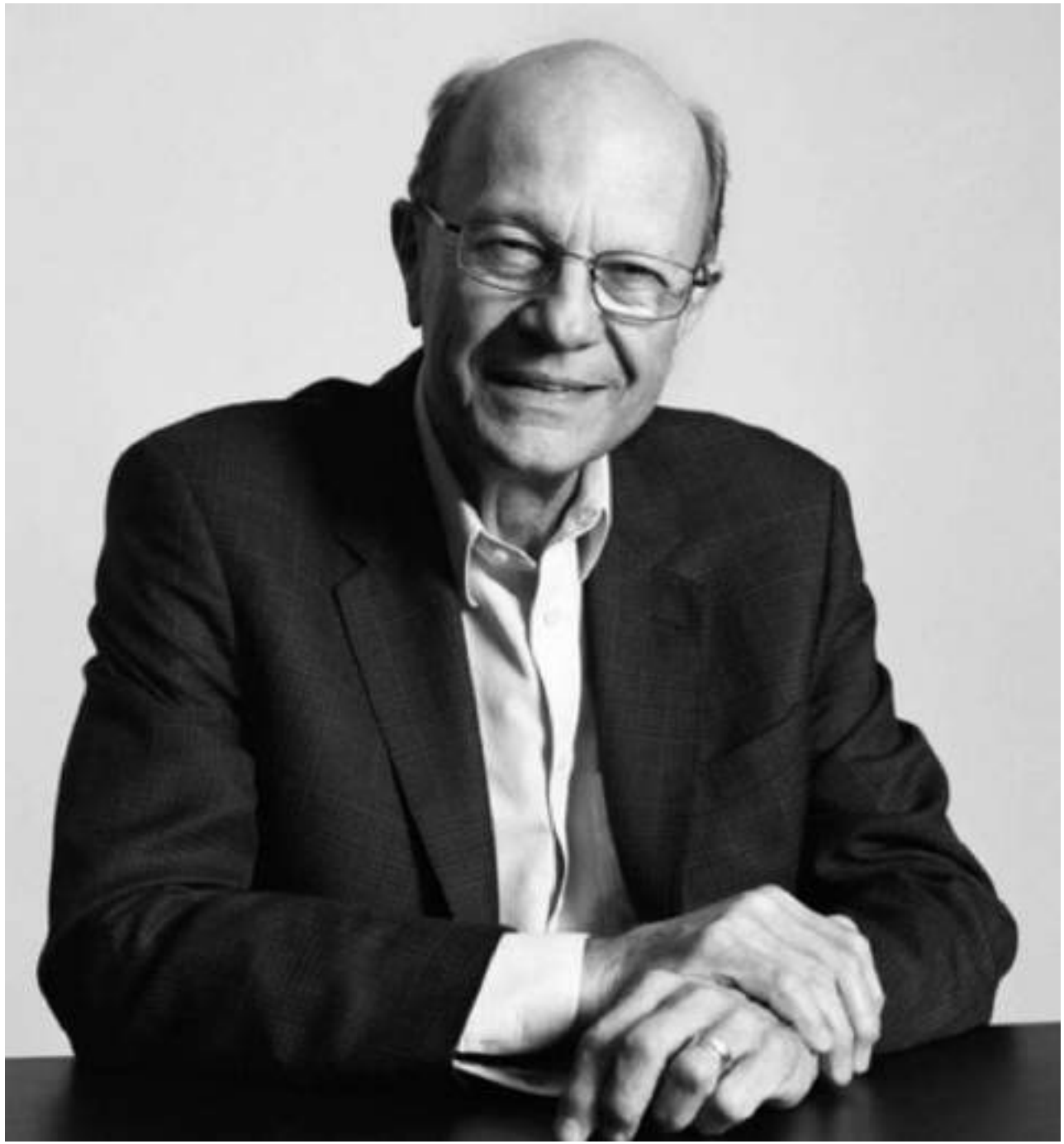
Rehabilitative therapy is important to start as soon as PD is diagnosed. Exercise is the most common therapy. Stretching, strength training, and aerobic exercise plans are all helpful. Dance and tai chi



Figure 5. Proposed General Approach to Treating Motor Symptoms in Parkinson Disease







What's 'new and hot' in surgical treatments for Parkinson's?





Article

Phase I trial of hES cell-derived dopaminergic neurons for Parkinson's disease

https://doi.org/10.1038/s41586-025-08845-y

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V. Tabar[1,2,3]✉, H. Sarva[4], A. M. Lozano[5,6], A. Fasano[6,7,8], S. K. Kalia[5,6], K. K. H. Yu[1], C. Brennan[1], Y. Ma[9,10], S. Peng[9], D. Eidelberg[9,10], M. Tomishima[11], S. Irion[11], W. Stemple[11], N. Abid[11], A. Lampron[11], L. Studer[2,12,14] & C. Henchcliffe[13,14]

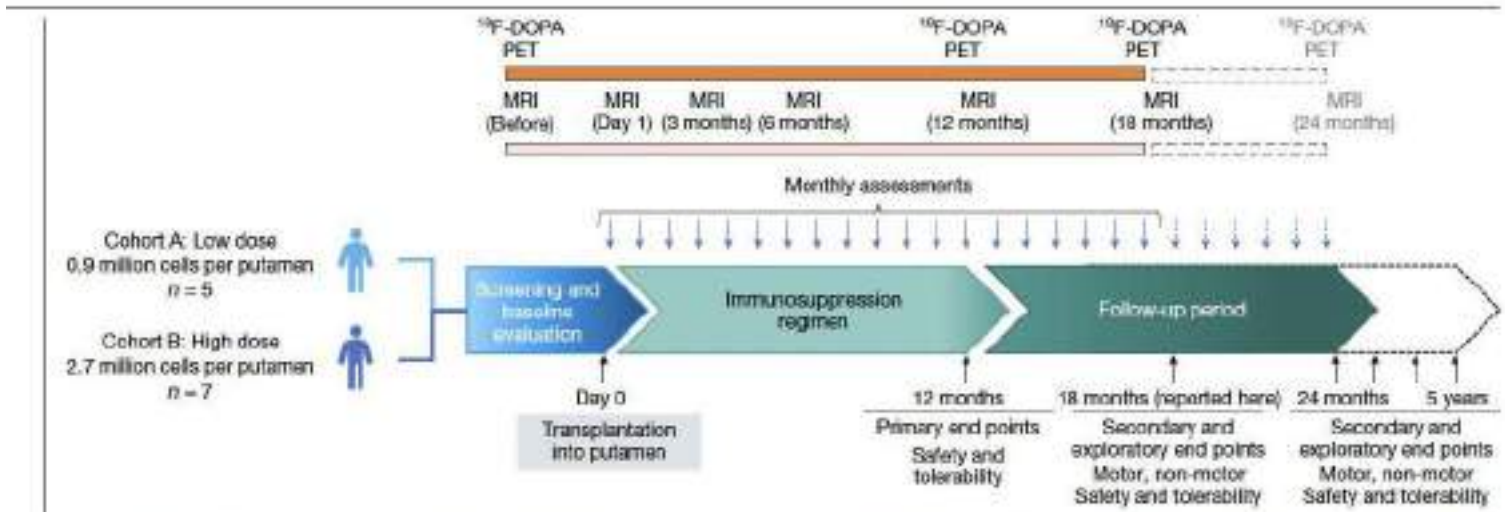
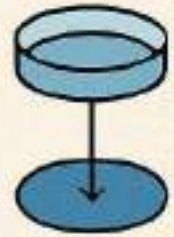


Fig. 1 | The study design. Summary of the study design. Patients were enrolled sequentially into a low-dose then a high-dose cohort. The diagram indicates the timeline of immunosuppression, monthly laboratory and clinical assessments, and imaging studies throughout the study. Ongoing follow-up is anticipated for a minimum of 5 years.

Sawamoto Study: iPSC-Derived Dopaminergic Neurons

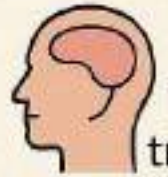


Cell Source
Induced pluripotent stem acIls (iPSCs) from adult cells

Immune Compatibility
(Autologous cells reduce rejection risk)

7

Patients



Intracerebral transplantatio

Key Findings
Demonstrated safety; further studies need for efficacy

Tabar-Study: hESC-Derived Dopaminergic Neurons



Human embryonic stem cells (iESCs)



12 Patients



12 Patients

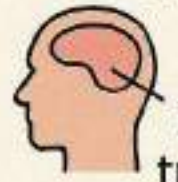
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Phase I

12 Patients (5 low-dose, 7 high-dose)



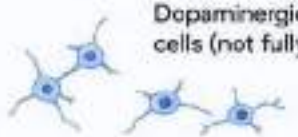
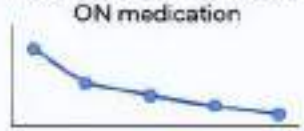
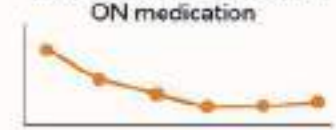
12 Patients



Intracerebral transplantation

Key Findings
Demonstrated safety; further studies needed for efficacy



	Sawamoto et al. *Nature, 2020*	Tabar et al. *NEJM, 2022*	Kim et al. *NEJM, 2024*
Cell source & product	 iPS cells (201B7 line) Floor plate–derived dopaminergic progenitors	 hESCs (H9 line) Midbrain progenitor cells (LMX1A+ FOXA2+)	 Integration-free iPS cells Midbrain dopaminergic neurons (fully differentiated)
What was transplanted	 Dopaminergic progenitor cells (not fully mature)	 Highly enriched midbrain dopaminergic progenitor cells	 Fully differentiated dopaminergic neurons (TH+)
Dose per putamen	2, 5, or 7.5 million cells 	2 or 5 million cells 	2, 5, or 10 million cells 
Patients (N)	 7	 12	 12
Results (UPDRS III)	Improved at 12–18 months ON medication 	Improved ON medication state at 12 months 	Improved at 6–12 months ON medication 
Follow-up	12–24 months	12–18 months	6–24 months (ongoing)
Key take-home	First clinical trial of hPSC-dopaminergic progenitors in PD; showed safety and signals of benefit.	Larger cohort confirmed safety of hESC-derived progenitors and showed clinical improvement.	First trial with terminally differentiated neurons; encouraging safety and early efficacy signals.



Bottom line: All three studies show that hPSC-derived dopaminergic cell therapies can be delivered safely to the putamen of PD patients, with signals of graft survival and clinical benefit.

Parkinson Canada

Japan grants conditional, limited approval to a stem cell-based therapy for Parkinson's



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JUN 3, 2026

Global ideas, shared hope

JUN 1, 2026

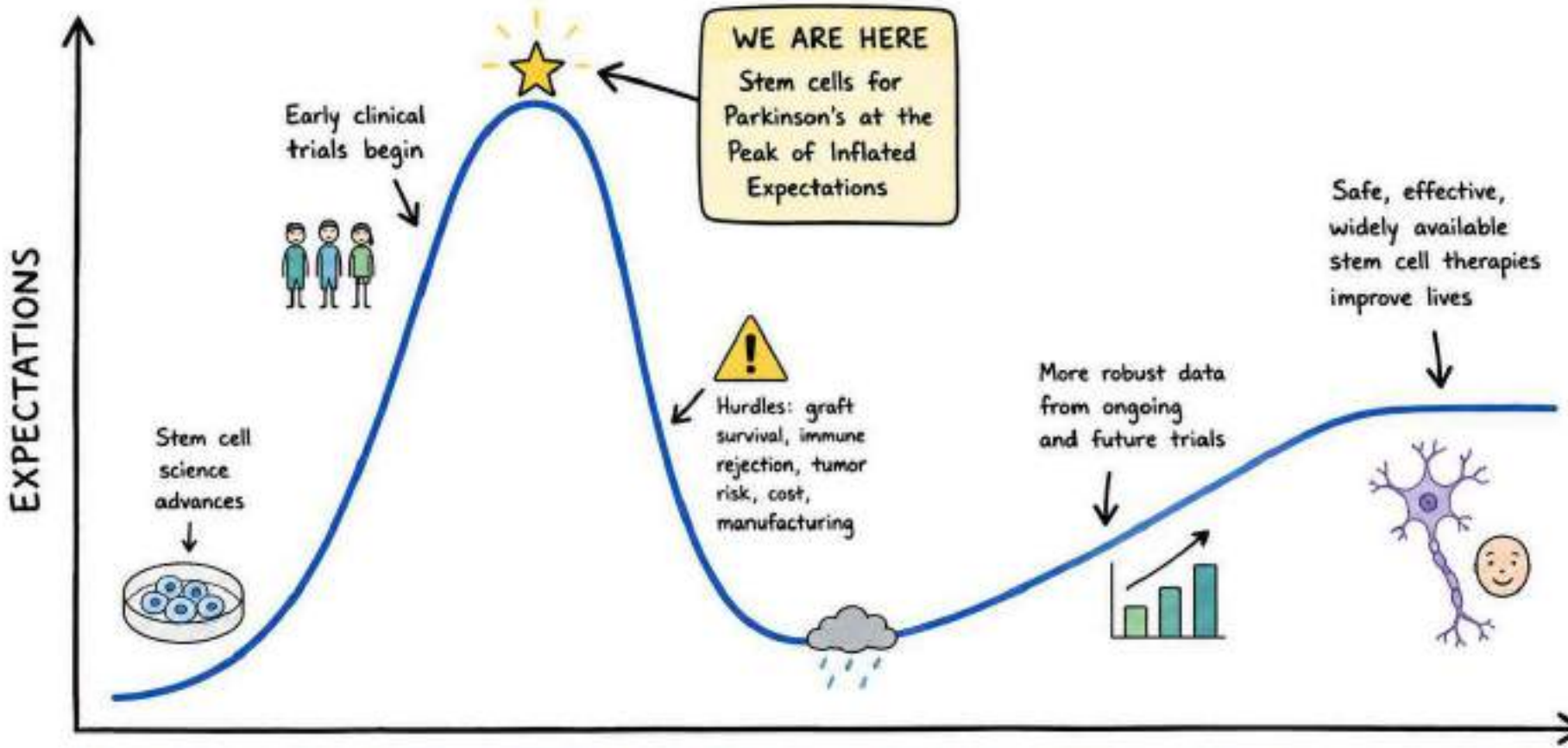
LUMA trial: A setback, not a defeat

MAY 27, 2026

Landmark funding. Bold research. A brighter future for Parkinson's.

GARTNER HYPE CYCLE

STEM CELLS FOR PARKINSON'S DISEASE



1. TECHNOLOGY TRIGGER

Breakthroughs in stem cell biology and differentiation for dopaminergic neurons

2. PEAK OF INFLATED EXPECTATIONS

Excitement around clinical trials and potential to transform PD treatment

3. TROUGH OF DISILLUSIONMENT

Challenges emerge: variability, scale-up, cost, long-term safety and efficacy questions

4. SLOPE OF ENLIGHTENMENT

Better data, standardization, improved delivery, patient selection and trial design

5. PLATEAU OF PRODUCTIVITY

Proven safe, effective stem cell therapies become integrated into standard care for PD

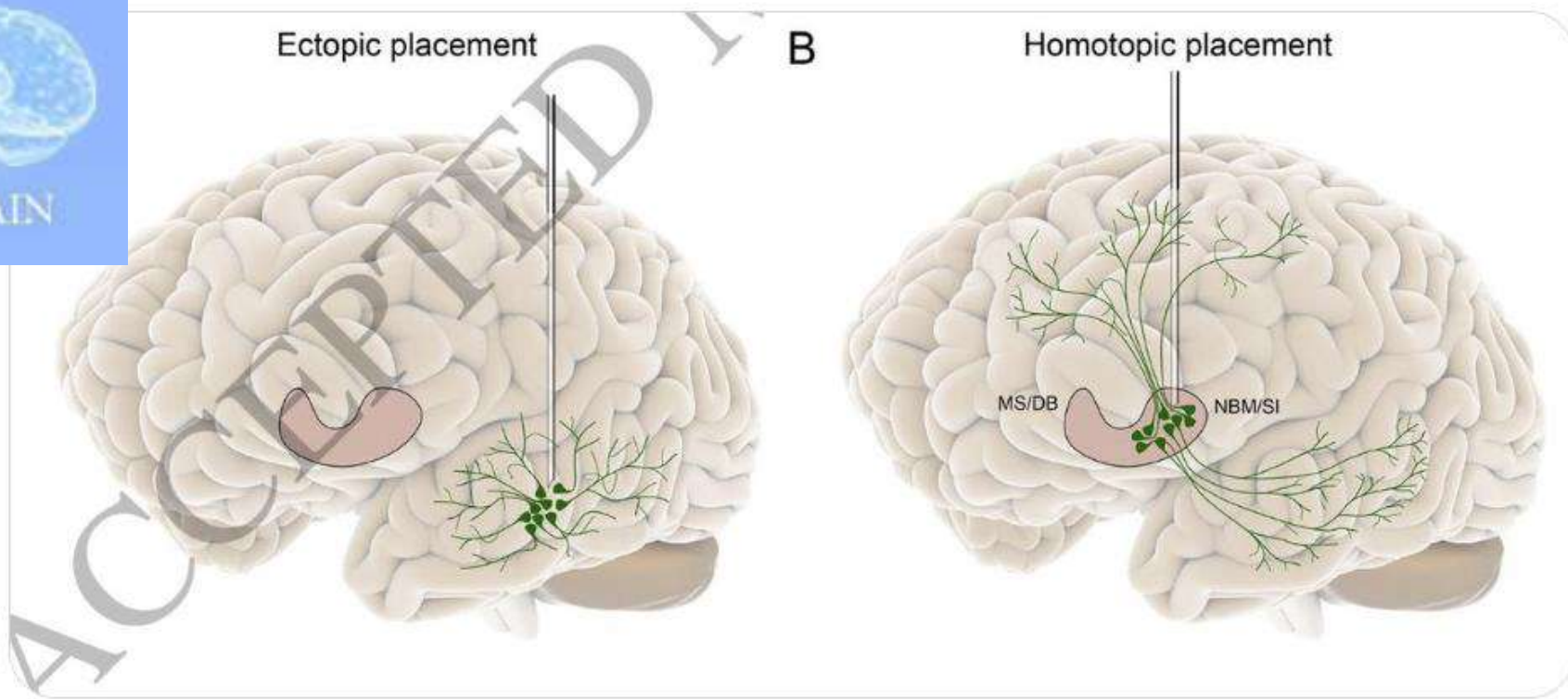


Michael Okun @MichaelOkun · Mar 1

Do you know the two **transplant approaches** being considered for **regenerative medicine** restoration of **memory** and **thinking** in **Parkins disease?** Anders Björklund, and Roger Barker @Brain1878 teach us abou the basal forebrain cholinergic system as a serious target for **cell**

Show more

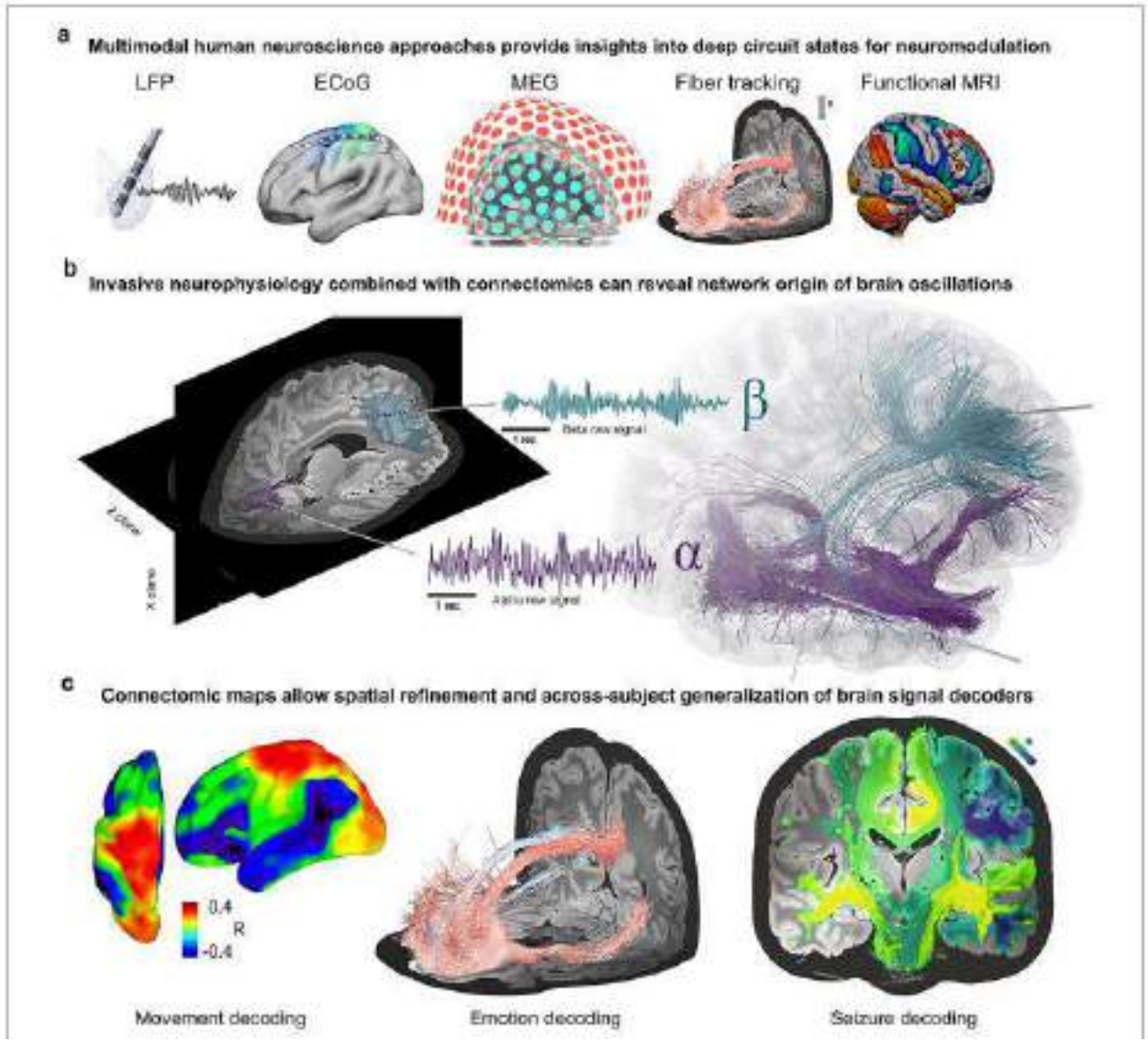
ACCEPTED



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frontiers | Frontiers in Human Neuroscience

Proceedings of the 13th annual deep brain stimulation think tank: the evolving landscape



npj | parkinson's disease

Article

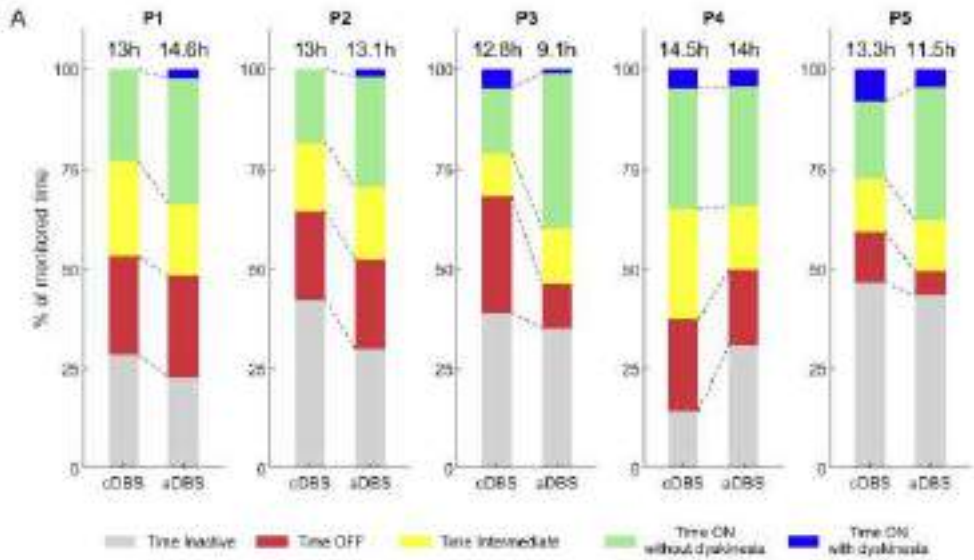
Published in partnership with the Parkinson's Foundation

https://doi.org/10.1038/s41531-025-01369-z

Chronic adaptive deep brain stimulation in Parkinson's disease: ADAPT-START findings and programming principles

Check for updates

Simone Cascino[1,2], Fabrizio Luiso[1,3], Laura Caffi[3,4], Chiara Palmisano[1,3], Elena Contaldi[1], Gianni Pezzoli[1,3], Ioannis Ugo Isaias[4,5] ✉ & Salvatore Bonvegna[4]



npj | parkinson's disease

Article

Published in partnership with the Parkinson's Foundation

Chronic adaptive deep brain stimulation for Parkinson's disease: clinical outcomes and programming strategies

Johannes L. Busch[1,2], Jonathan Kaplan[1,2], Jennifer K. Behnke[1,2], Victoria S. Wittig[1], Luise Drescher[1], Jeroen G. V. Habets[1,2] & Andrea A. Kühn[1,2,3]

Preparation

Evaluate patient
Residual fluctuations
Contact selection
Stimulation limits

Evaluate LFPs
Frequency selection
Modulation
Artifacts

Record Timeline
Constant stimulation settings

Setup

Set LFP thresholds
Evaluate Timeline
- Discard artifacts
- Focus on daytime

Set stimulation limits

Assess aDBS
Side effects
Artifacts

Optimization

Evaluate symptoms
Timing of fluctuations
Night-time symptoms

Evaluate Timeline
Stimulation adaptation
Link symptoms and LFPs
LFP thresholds
Artifacts

Adjust LFP thresholds
↑ Lower threshold if stimulation high
↓ Upper threshold if stimulation low

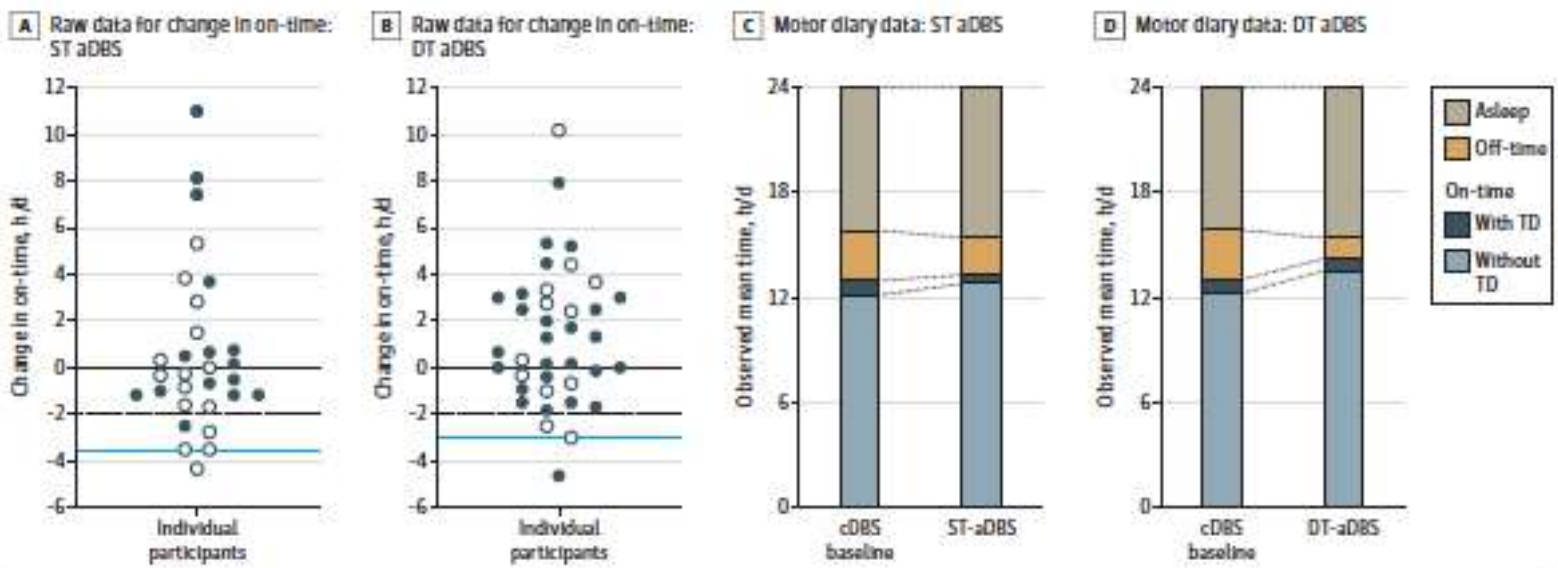
Adjust stimulation limits
↑ Stimulation if hypokinetic
↓ Stimulation if hyperkinetic

JAMA Neurology | Original Investigation

Long-Term Personalized Adaptive Deep Brain Stimulation in Parkinson Disease
A Nonrandomized Clinical Trial

Helen M. Bronte-Stewart, MD, MSE; Martijn Beudel, PhD; Jill L. Ostrem, MD; Simon Little, PhD; Leonardo Almeida, MD; Adolfo Ramirez-Zamora, MD; Alfonso Fasano, MD, PhD; Travis Hassell, MD, PhD; Kyle T. Mitchell, MD; Elena Moro, MD, PhD; Michal Gostkowski, DO; Gaurav Chattree, MD; Rob M. A. de Bie, MD, PhD; Martijn de Neeling, MD; Dan Piña-Fuentes, MD, PhD; Bart Swinnen, MD, PhD; Philip A. Starr, MD, PhD; Lauren H. Hammer, MD, PhD; Kelly D. Foote, MD; R. Mark Richardson, MD, PhD; Alice Flaherty, MD, PhD; Alexandra Boogers, MD, PhD; Qais Sa'di, MD; Sara Meoni, MD, PhD; Anna Castrioto, MD, PhD; Scott Stanslaski, MS; Rebekah L. S. Summers, DPT, PhD; Lisa Tonder, MS; Ye Tan, MD, MS; Helen Berrier, BSN; Tim J. Goble, PhD; Robert S. Raike, PhD; Todd M. Herrington, MD, PhD; for the ADAPT-PD Investigators

Figure 2. Changes in Motor Diary

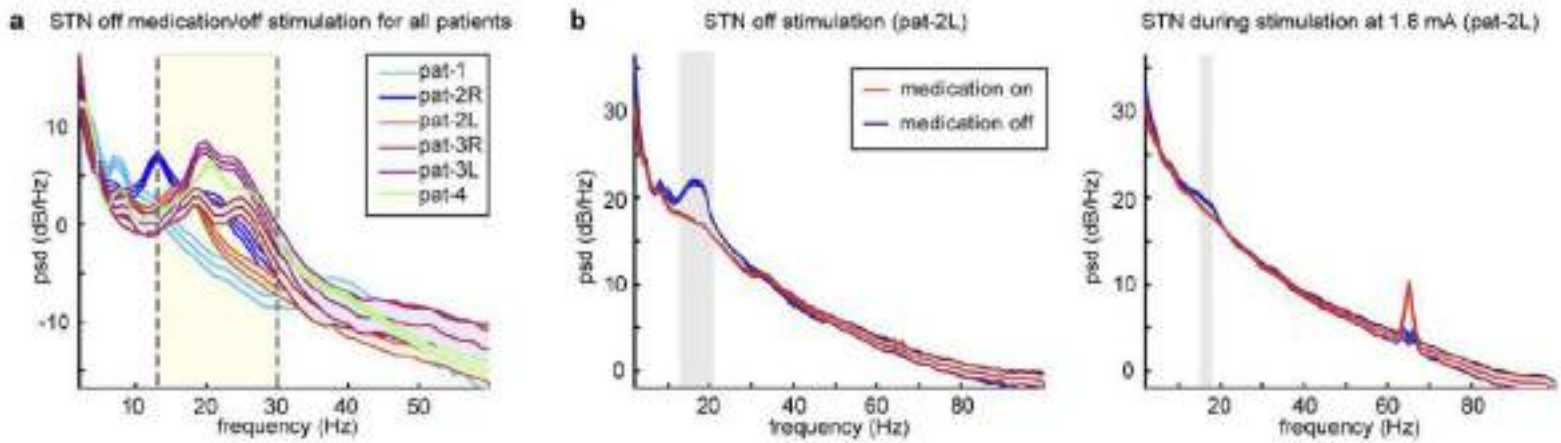


nature medicine

Published in final edited form as:
Nat Med. 2024 November ; 30(11): 3345–3356. doi:10.1038/s41591-024-03196-z.

Chronic adaptive deep brain stimulation versus conventional stimulation in Parkinson's disease: a blinded randomized feasibility trial

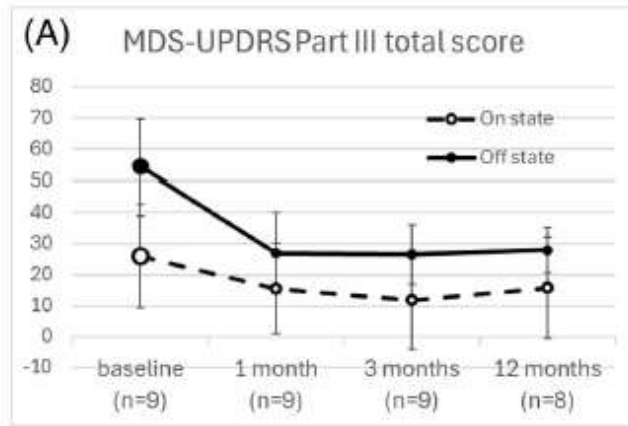
Carina R Oehrn[1,*], **Stephanie Cernera**[1,*], **Lauren H Hammer**[2,*], **Maria Shcherbakova**[1], **Jiaang Yao**[1,3], **Amelia Hahn**[1], **Sarah Wang**[2,4], **Jill L Ostrem**[2,4], **Simon Little**[2,3,4,**], **Philip A Starr**[1,3,4,**]

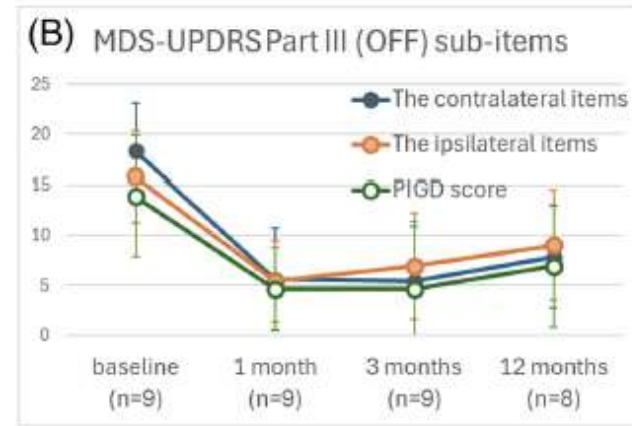


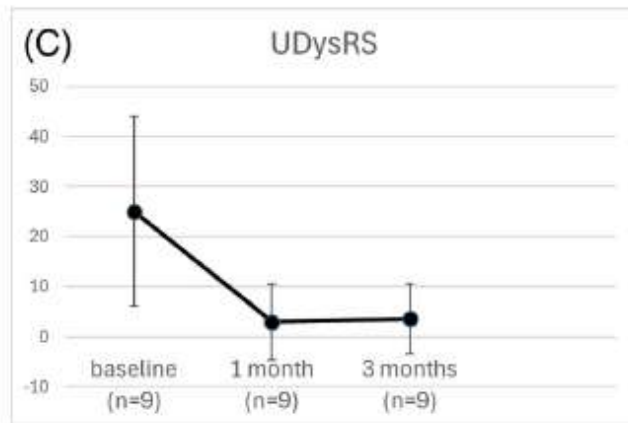
BRIEF REPORT

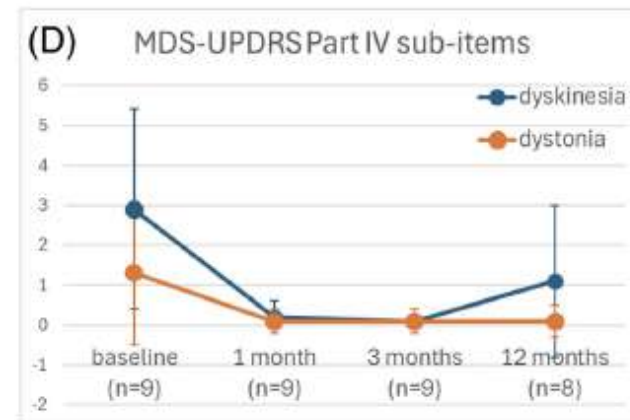
Bilateral Effects of Unilateral Pallidothalamic Tractotomy Using Focused Ultrasound in Parkinson's Disease

Jun Ikezawa, MD, PhD,[1] Fusako Yokochi, MD, PhD,[1] Toshio Yamaguchi, MD, PhD,[2,3] Keiichi Abe, MD, PhD,[4] Tsutomu Kamiyama, MD, PhD,[1] Tomoya Kawazoe, MD, PhD,[1] Shiro Horisawa, MD,[4] Jinichi Sasanuma, MD, PhD,[5] Tomokatsu Hori, MD, PhD,[5] Hiroki Hori, PhD,[6] Toru Kakegawa, MD,[7] Ryoichi Okiyama, MD,[1] Kazushi Takahashi, MD, PhD,[1] and Takaomi Taira, MD, PhD[4*]





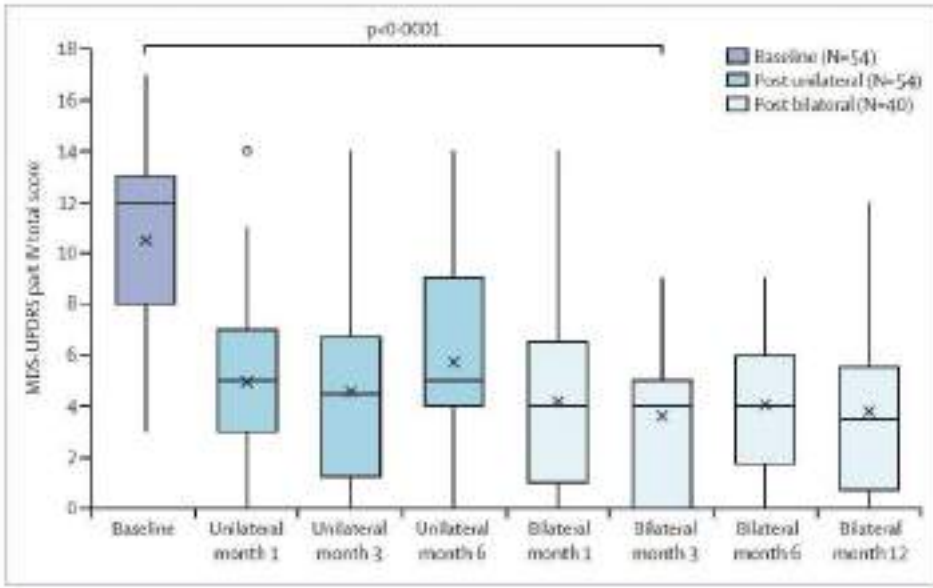




THE LANCET
Neurology

Safety and efficacy of staged, bilateral magnetic resonance-guided focused ultrasound pallidothalamic tractotomy for motor complications of Parkinson's disease: a prospective, multicentre, single-arm trial

Arif Deka, Howard M Eisenberg, Peihan Wu, Lloyd Zeidler, Wei Chieh Chang, Harini Sarva, Paul S Fishman, Vivek P Buch, Michele Matarazzo, Mario del Alamo, Maria Cruz Rodriguez-Oroz, Lein Hermes González-Quarante, Sepehr Sani, Pejman Ghanouni, Neepa Patel, Michael Rosenfeld, Alon Mogilner, Jose A Obeso, Michael G Kaplitt



	Adverse event at any timepoint		Persistent at 6 months	
	Not clinically significant	Clinically significant	Not clinically significant	Clinically significant
Unilateral treatment (n=54)				
Confusion	0	1 (2%)	0	0
Gait unsteadiness	3 (6%)	0	1 (2%)	0
Dyskinesia	0	1 (2%)	0	0
Hypophonia	3 (6%)	0	3	0
Somnolence	2 (4%)	0	0	0
Fatigue	4 (7%)	0	2 (4%)	0
Reduced levodopa effect	0	1 (2%)	0	0
Weight gain	0	1 (2%)	0	1* (2%)
Staged, bilateral treatment (n=40)				
Confusion	0	1 (3%)	0	0
Decreased short-term memory	0	1 (3%)	1 (3%)	0
Imbalance or unsteadiness	1 (3%)	1 (5%)	0	2 (5%)
Gait abnormality	1 (3%)	1 (3%)	0	1 (3%)
Anarthria	0	1† (3%)	0	1† (3%)
Dysarthria	4 (10%)	1 (3%)	2 (5%)	1 (3%)
Slurred speech	2 (5%)	0	2 (5%)	0
Hypophonia	2 (5%)	1 (3%)	1 (3%)	1 (3%)
Stutter	0	1 (3%)	0	1 (3%)
Voice Handicap Index score elevated	2 (5%)	0	2 (5%)	0
Increased salivation or drooling	2 (5%)	0	2 (5%)	0
Dysphagia	1 (3%)	1 (3%)	1 (3%)	1 (3%)
Drowsiness	3 (8%)	0	0	0
Fatigue	3 (8%)	0	0	0
Lethargy	0	1 (3%)	0	0
Weakness	0	1 (3%)	0	1 (3%)
Weight gain	0	1 (3%)	0	1 (3%)

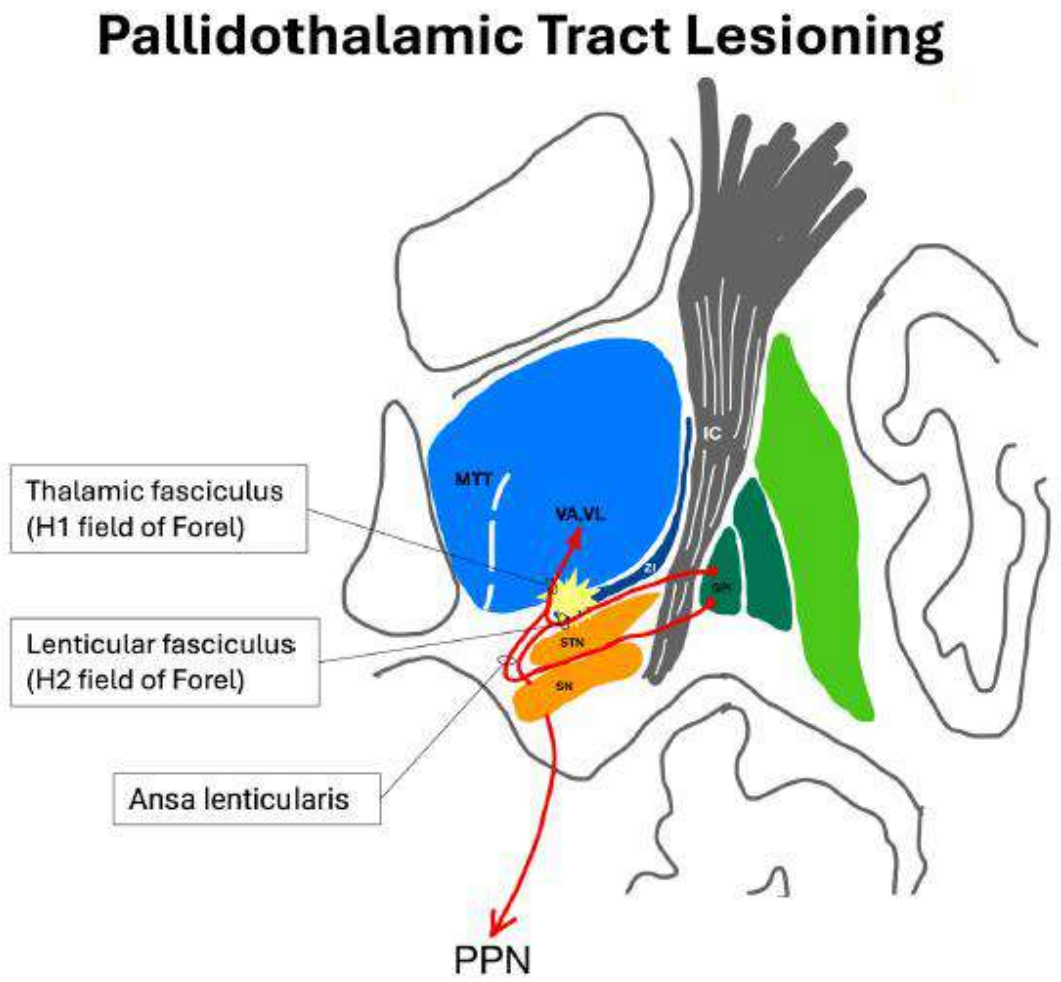
All reported related clinically significant adverse events (ie, moderate and severe), and any non-clinically significant adverse events (ie, mild) reported in two or more (≥5%) patients. *Resolved at 7 months. †Severe adverse event.

Table 2: Safety of unilateral and staged, bilateral treatment

european journal
of neurology

Immediate Motor Control Enhancement via Pallidothalamic Tract (PTT) Circuit Ablation: A Dual-Target MR-Guided Focused Ultrasound Approach for Tremor-Dominant Parkinson's Disease

Jui-Cheng Chen[1,2,3,4] | Chun-Ming Chen[1,5] | Yu Aoh[6,7] | Yu-Kai Cheng[1,8] | Ming-Kuei Lu[1,2,4,6,7] | Chon-Haw Tsai[1,2,6,7]



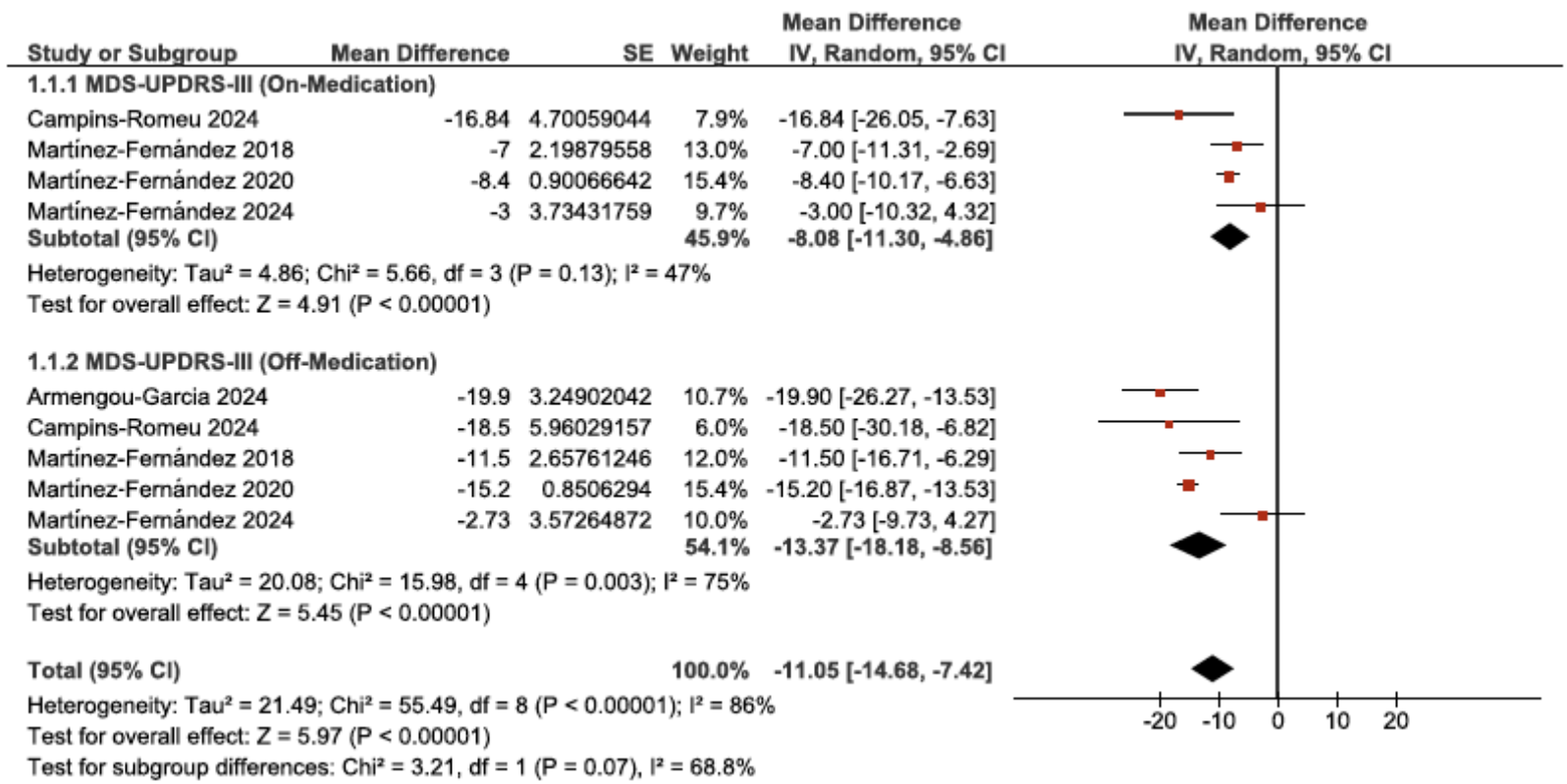
Neurosurgical Review

Neurosurgical Review (2026) 49:201
https://doi.org/10.1007/s10143-025-04045-4

RESEARCH

Magnetic resonance-guided focused ultrasound subthalamotomy for Parkinson's disease: a meta-analysis of effectiveness and safety

Abdallah Abbas[1] · Haneen Sabet[2] · Moaz Elsayed Abouelmagd[3] · Mahmoud Tarek Hefnawy[4] · Salma Bakr[5] · Basant Lashin[6] · Mohamed Ahmed Zanaty[2] · Mohamed El-Moslemani[1] · Mohamed Mohesn Helal[4] · Majed Aldehri[7,8] · Ibrahim Alnaami[9] · Ahmed M. Raslan[10]



Journal of Parkinson's Disease

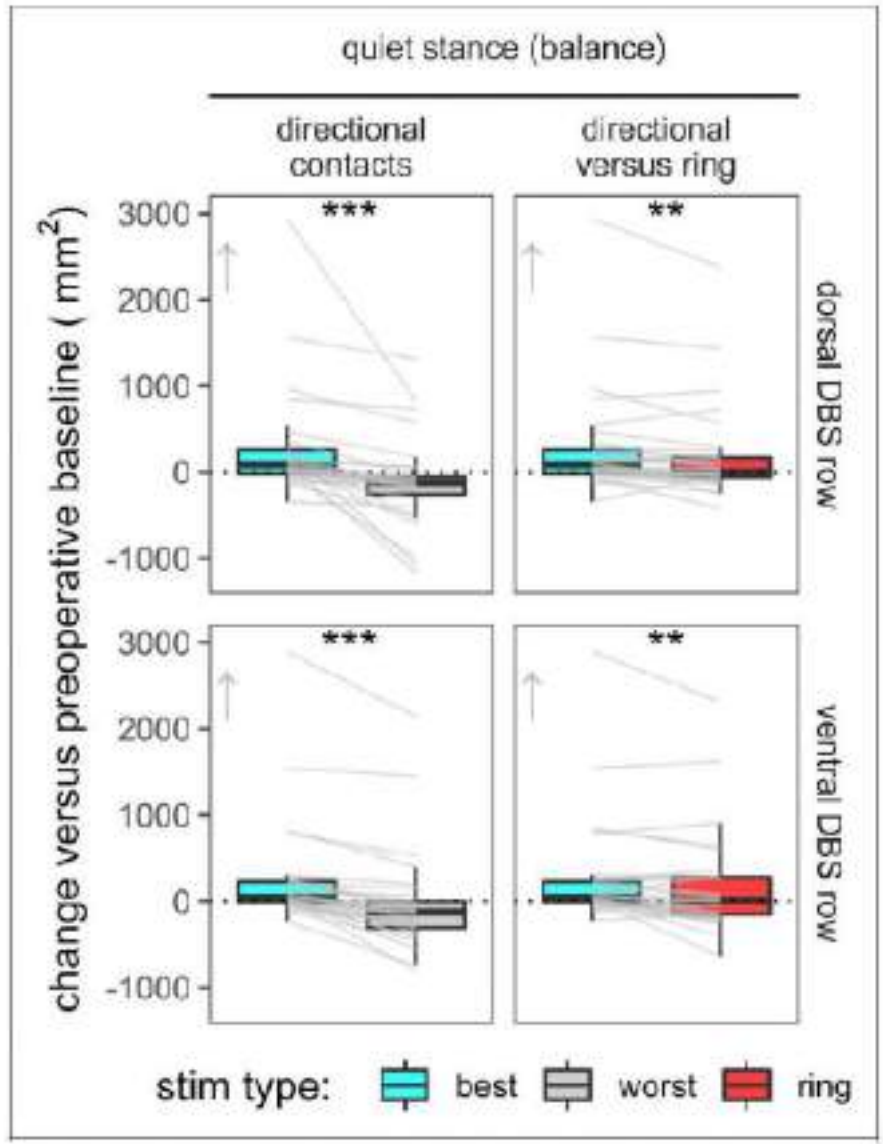
Research Article

Pointing in the right direction: Greater motor improvements with directional versus circular subthalamic nucleus deep brain stimulation for Parkinson's disease

Journal of Parkinson's Disease
2025, Vol. 15(1) 200–213
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DOI: 10.3233/JPD-240301
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Christopher P Hurt[1,2], Daniel J Kuhman[1], Alyson Moll[1], Barton L Guthrie[3], Joseph W Olson[4], Arie Nakhmani[5], Melissa Wade[4], Sarah A Brinkerhoff[1], Marshall T Holland[3] and Harrison C Walker[4,6]







JNS CLINICAL ARTICLE
J Neurosurg MI:1567-1577, 2024

Precision targeting in the globus pallidus interna: insights from the multicenter, prospective, blinded VA/NINDS CSP 468 study

Shawn D'Souza, MD,[1] Vikram Seshadri, BS,[1] Jamie Toms, MD,[2] Pierre D'Haese, PhD,[3] Benoit M. Dawant, PhD,[4] Rui Li, MS,[4] Harsh P. Shah, MD,[5] Paul Koch, MD,[5,6] Paul Larson, MD,[7,8] and Kathryn L. Holloway, MD[5,6]

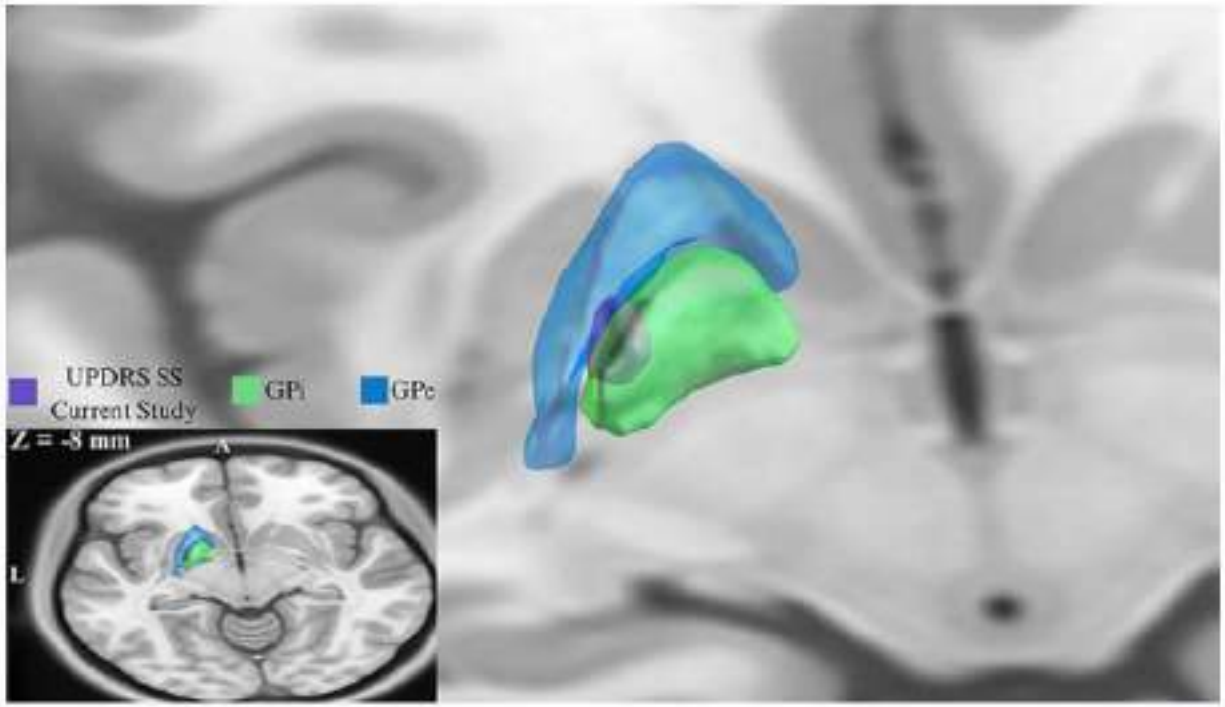


FIG. 5. 3D visualization of UPDRS-III sweet spot. The sweet spot for UPDRS-III in the current study is shown in an oblique, top-down view with the DISTAL atlas–defined GPi and GPe overlayed.[21] Structures were visualized on MNI152 ICBM Nonlinear Asymmetrical 2009b template space in Lead-DBS version 3.0.[17,23,24] The MRI backdrop is shown at an axial plane of −8 mm to provide perspective without covering the 3D object. Figure is available in color online only.

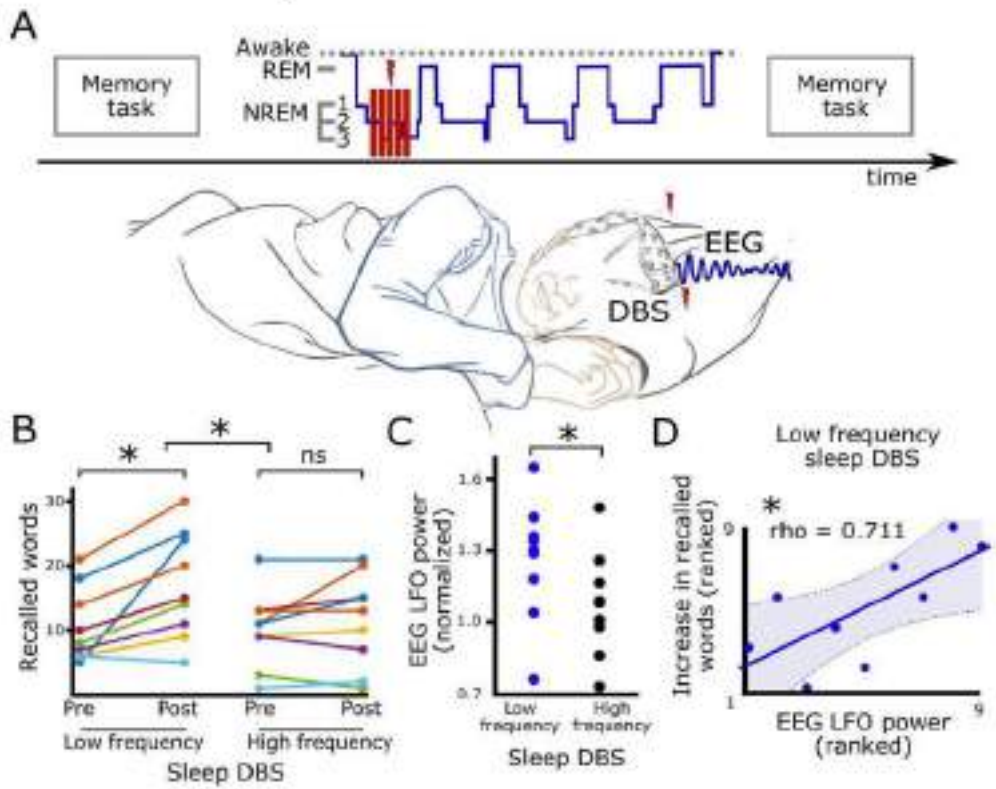


RESEARCH ARTICLE

Low-Frequency Deep Brain Stimulation in Non-Rapid Eye Movement Sleep Modifies Memory Retention in Parkinson's Disease

Damian M. Herz, MD, PhD,[1] Jenny Blech,[1] Yaroslav Winter, MD,[1] Gabriel Gonzalez-Escamilla, PhD,[1,2] and Sergiu Groppa, MD, MBA[1,2*]

LOW-FREQUENCY BRAIN STIMULATION FOR MEMORY



brain sciences 2025 MDPI



Review

AI-Driven Advances in Parkinson's Disease Neurosurgery: Enhancing Patient Selection, Trial Efficiency, and Therapeutic Outcomes

José E. Valerio [1,2,3,4], Guillermo de Jesús Aguirre Vera [1,5], María P. Fernández Gómez [1], Jorge Zumaeta [1] and Andrés M. Alvarez-Pinzon [1,6,7,8,*]

AI Architecture	Input Modality	Diagnostic Output	Performance Metrics	Metrics Reference
CNN with Attention Mechanism	Nocturnal Breathing Signals	PD Detection and Severity Estimation	AUC: 0.90 (held-out), 0.85 (external)	Yang et al., 2022 [12]
SVM Classifier	18F-FDG PET Radiomic Features	PD vs. Healthy Classification	Accuracy: 90.97%, 88.08%	Wu et al., 2019 [114]
Multi-scale CNN (MCNN)	EEG Signals (PSD & PLV Features)	PD Classification	Accuracy: >99%	Qiu et al., 2022 [115]
AlexNet CNN with TFR	EEG Signals	PD Diagnosis	High Accuracy (Specific metrics not provided)	Li et al., 2024 [116]

Article	Article Description	Conclusion	Recommendations
Johnson, KA et al. [74]	This article provides an overview of the key findings from the Deep Brain Stimulation Think Tank XI. The focus is on the latest technologies in neuromodulation and new hypotheses regarding the integrative networks that support DBS treatment. The discussions also covered cutting-edge advances in other areas including physiology, translational neuromodulation, neuroethical dilemmas, algorithmic modeling, and artificial intelligence.	The meeting highlighted significant advancements in neuromodulation, particularly in understanding the mechanisms of Deep Brain Stimulation through animal models and human studies. It emphasized the importance of utilizing AI and large data-driven approaches to advance DBS as a widely used therapy.	The article recommends a continued emphasis on translational neuromodulation to gain a deeper understanding of this approach. It also suggests leveraging neurophysiological markers and machine learning algorithms to develop individualized treatments tailored to each patient, considering factors such as physiological changes, circadian rhythms, and sleep.



Michael Okun @MichaelOkun · Jun 10

How about a **brain implant** that when '**squeezed or pressed**' it powers a neuromodulation device? The word **piezo** is derived from the Greek word πιέζω: to squeeze or to press. Hou and colleagues have a new paper in @NatureComms on a **novel implantable piezoelectric ultrasound**

Show more



nature communications

Article | Open access | Published: 04 June 2024

An implantable piezoelectric ultrasound stimulator (ImPULS) for deep brain activation

Jason T. Hou, Md Osman Goni Naveen, Kian A. Caplan, Evan A. Ruesch, Albit Caban-Murillo, Ernesto Criado-Hidalgo, Sarah B. Ornellas, Brandon Williams, Ayella A. Pearce, Huseyin E. Dagdeviren, Michelle Surets, John A. White, Mikhail G. Shapiro, Fan Wang, Steve Ramirez & Canan Dagdeviren ✉

Nature Communications 15, Article number: 4601 (2024) | Cite this article

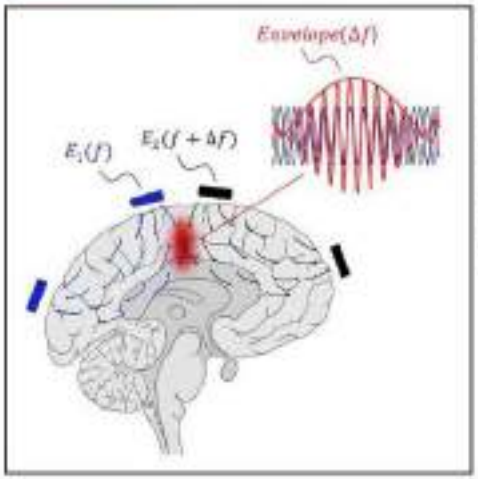
3068 Accesses | 61 Altmetric | Metrics



Cell

Noninvasive Deep Brain Stimulation via Temporally Interfering Electric Fields

Graphical Abstract



Authors

Nir Grossman, David Bono, Nina Dedic, ..., Li-Huei Tsai, Alvaro Pascual-Leone, Edward S. Boyden



THELANCETNEUROLOGY-D-17-00492
PII

In Context

Clinical preview

A new non-surgical approach for deep-brain stimulation

CellPress



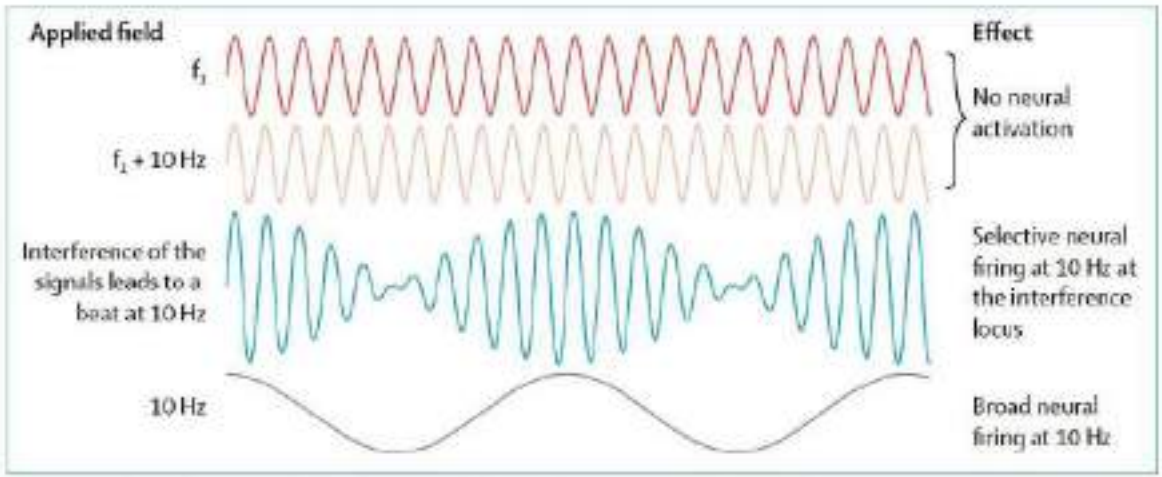


Figure: Model of temporal interference and its effects on neuronal activity
The interference of two oscillating electric fields with slightly varying frequencies (f_1 [red trace] and f_1 + 10 Hz [pink trace]) creates a beat at 10 Hz (where f_1 >1 kHz; not drawn to temporal scale). The interference field (blue trace) and a 10 Hz field (purple trace) both lead to 10 Hz neural firing, but the interference field leads to selective activation and the 10 Hz field leads to broad activation. f=frequency.

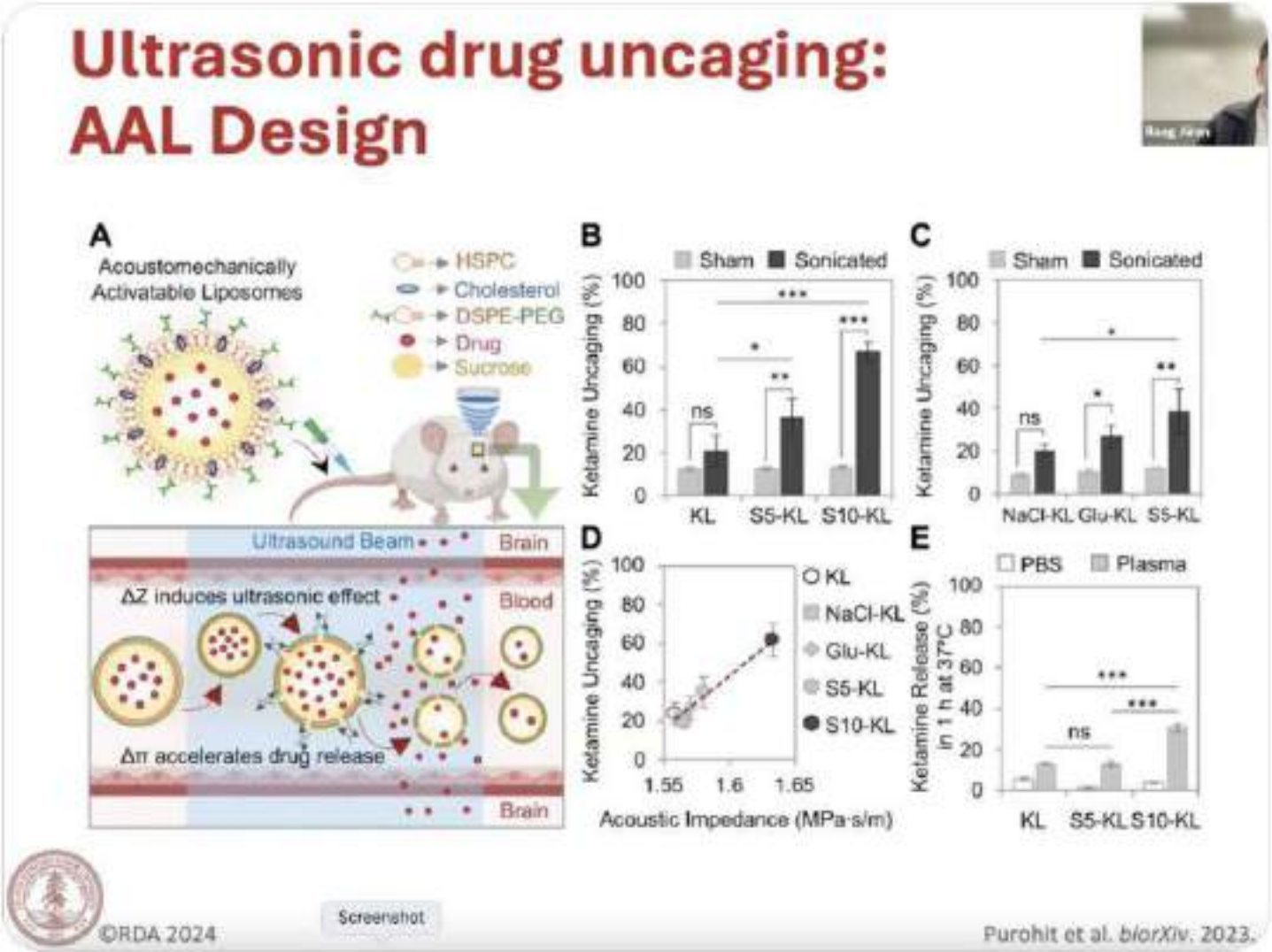






Michael Okun @MichaelOkun · May 6

Introducing the acoustomechanically activated liposome. Just add sugar and watch the drug delivered to the brain when hit with an ultrasound beam. Nice work by Raag Airan @Stanford.



6 14 2.4K





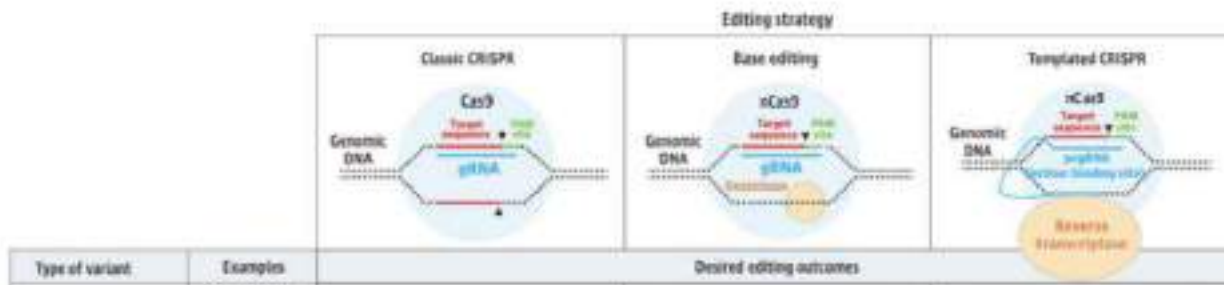
Michael Okun @MichaelOkun · Feb 4

Can you name **3 'gene editing' strategies** which may use **CRISPR** technology to **target neurological diseases**? How about classic cutting, base editing or templated repair? Gene editing using clustered regularly interspaced short palindromic repeats (CRISPR) has arrived and we will all Show more

JAMA Neurology | Review

Building CRISPR Gene Therapies for the Central Nervous System
A Review

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



1 14 34 4.2K

Pumps vs. DBS or Both?

Motor fluctuations

“Off time”

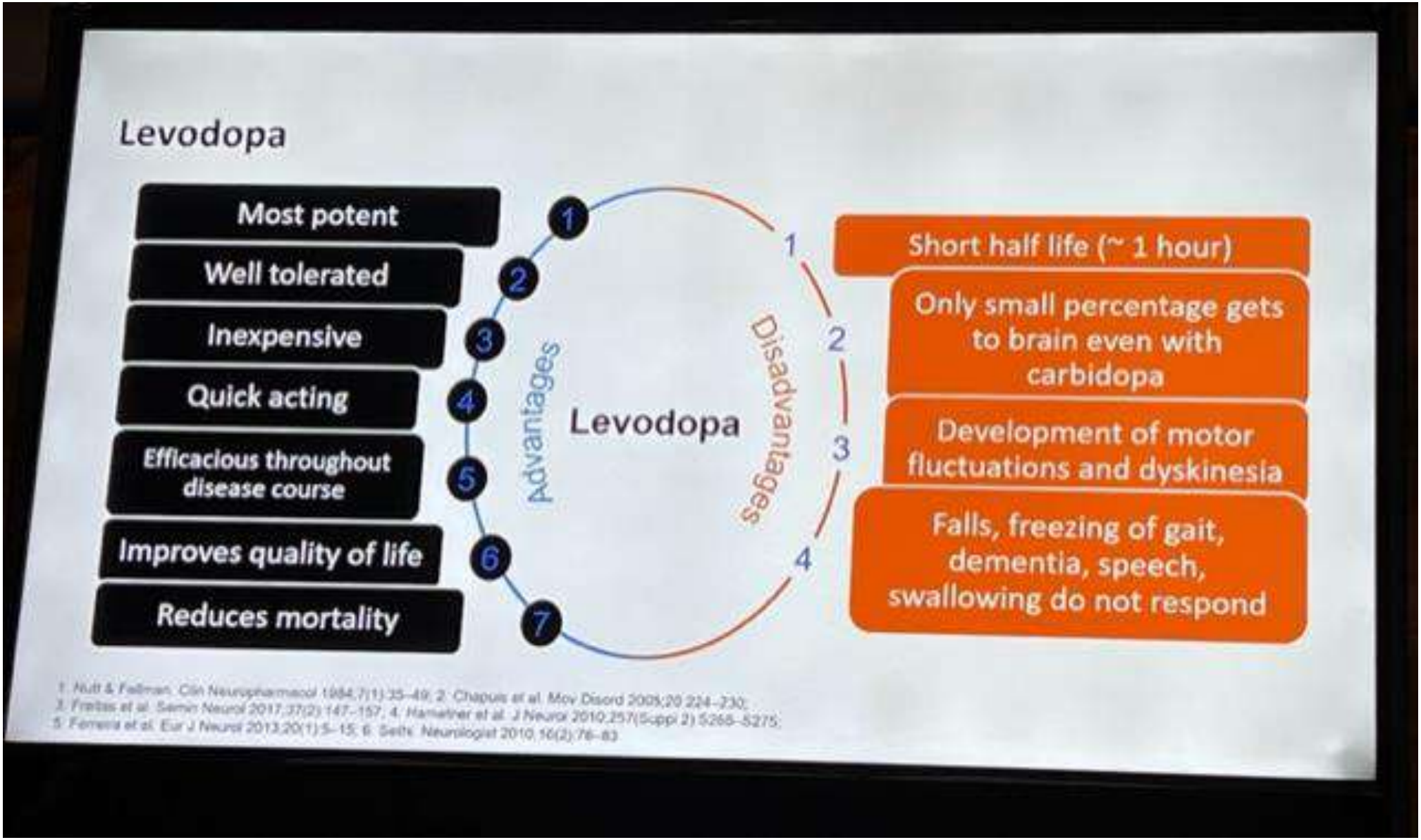
Dyskinesia

Levodopa responsive symptoms

Resistant Tremor



The ‘up-side’ and the ‘challenges’ of levodopa therapy



- Raj Pahwa World Parkinson Congress 2023

Don’t forget liquid levodopa, ‘Okun’s potion’



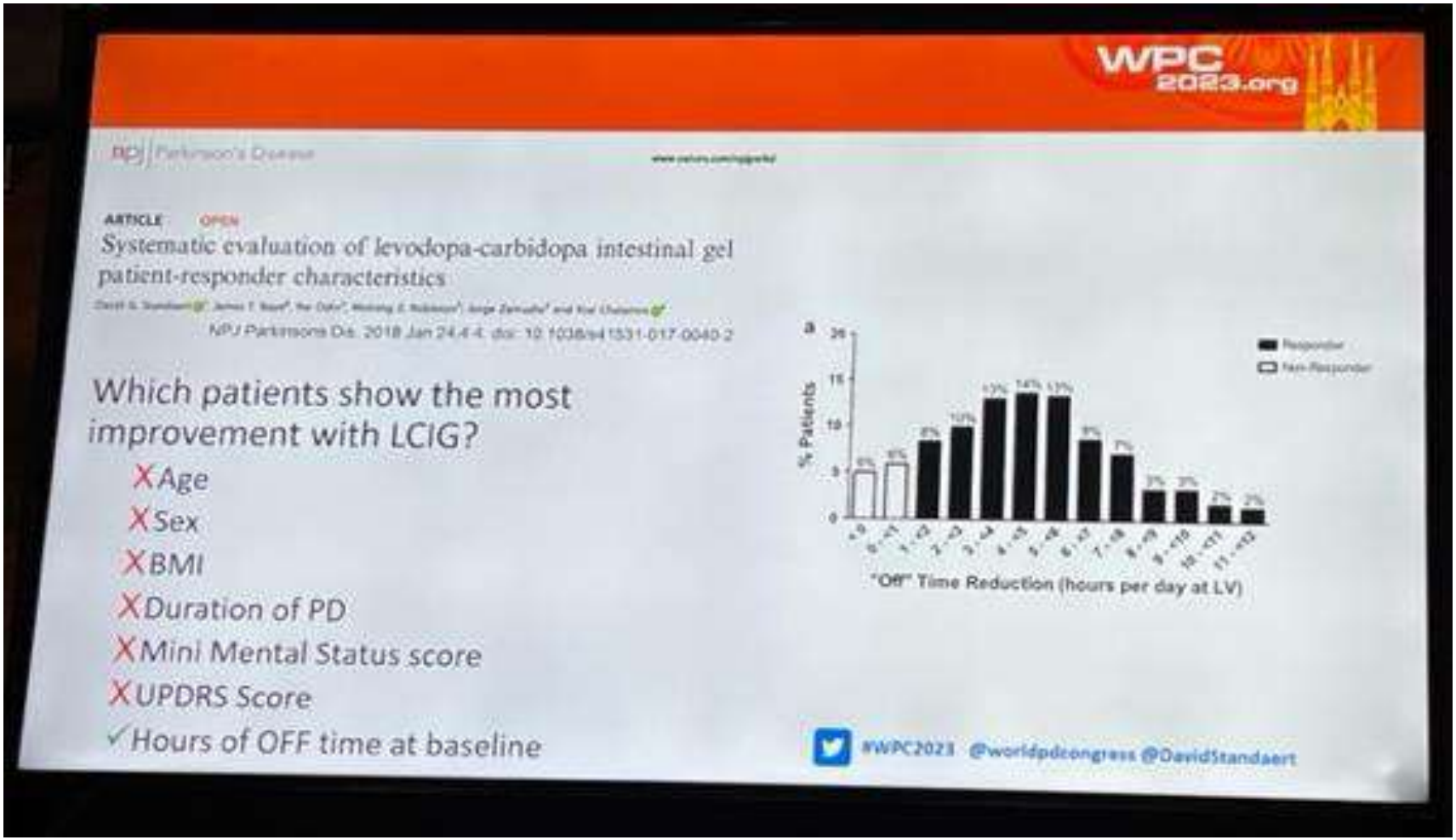
Journal of Parkinson's Disease 13 (2023) 609–617
DOI 10.3233/JPD-225117
IOS Press

Research Report

The Use of Liquid Sinemet in Routine Clinical Practice of Advanced Parkinson’s Disease: A Comparison of Available Options

Chee Boon Sung[a], Mary Danoudis[a,b], Eldho Paul[c] and Robert Iansek[a,b,*]
[a]*Clinical Research Centre for Movement Disorders and Gait, Parkinson's Foundation Center of Excellence, Monash Health, Kingston Centre, Melbourne, Australia*
[b]*Faculty of Medicine, Nursing and Health Sciences, School of Clinical Sciences, Monash University, Clayton, Australia*
[c]*Monash Centre for Health Research and Implementation, School of Public Health and Preventive Medicine, Monash University, Monash Medical Centre, Clayton, Australia*

What factor is the most important Pre-pump therapy: ‘Hours of Off time’



- David Standaert WPC 2023

Apomorphine Pump

Apomorphine subcutaneous infusion in patients with Parkinson's disease with persistent motor fluctuations (TOLEDO): a multicentre, double-blind, randomised, placebo-controlled trial

Regina Katzenschlager, Werner Poewe, Olivier Rascol, Claudia Trenkwalder, Günther Deuschl, K Ray Chaudhuri, Tove Henriksen, Tom van Laar, Kevin Spivey, Senthil Vel, Harry Staines, Andrew Lees

- Reduce 'Off Time'
- Improve Quality of Life

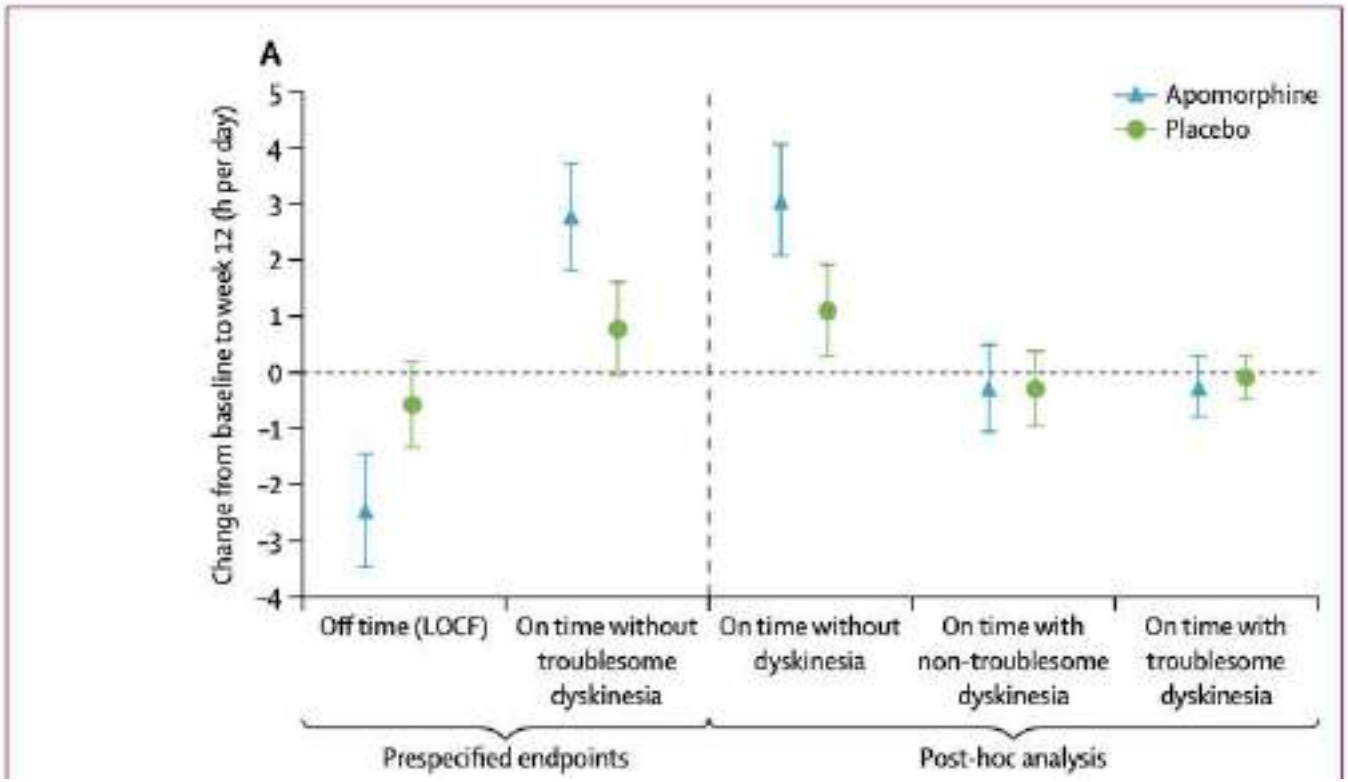
- This is a retrospective analysis on apomorphine in a large Dutch cohort.
- Long-term outcomes of apomorphine on motor and non-motor symptoms were reviewed.
- The efficacy on motor symptoms seems to be directly related to LEDD reduction.
- Apomorphine can be prescribed safely to PD patients with pre-existing visual hallucinations.
- Apomorphine seems to improve nighttime sleeping problems.



- Lees et. al. TOLEDO Trial.

~1.9 hours beyond levodopa ‘off time’

	Apomorphine (n=53)	Placebo (n=53)	Treatment difference (95% CI)	p value
Primary outcome				
Off time (h per day)	−2·47 (3·70)	−0·58 (2·80)	−1·89 (−3·16 to −0·62)	0·0025



Foslevodopa/Foscarbidopa SQ Pump Approach
1.7 hrs on time

Safety and efficacy of continuous subcutaneous foslevodopa-foscarbidopa in patients with advanced Parkinson's disease: a randomised, double-blind, active-controlled, phase 3 trial

Michael J Soileau, Jason Aldred, Kumar Budur, Nahome Fisseha, Victor SC Fung, Anna Jeong, Thomas E Kimber, Kevin Klos, Irene Litvan, Daniel O'Neill, Weining Z Robieson, Meredith A Spindler, David G Standaert, Saritha Talapala, Eleni Oikeanis Vasu, Hui Zheng, Maurizio F Facheris, Robert A Hauser

	Oral levodopa-carbidopa group (n=67)	Foslevodopa-foscarbidopa group (n=74)	Treatment difference (SE; 95% CI)	p value
Primary efficacy measure				
On time without troublesome dyskinesia, h/day	0·97 (0·50)	2·72 (0·52)*	1·75 (0·65; 0·46 to 3·05)	0·0083

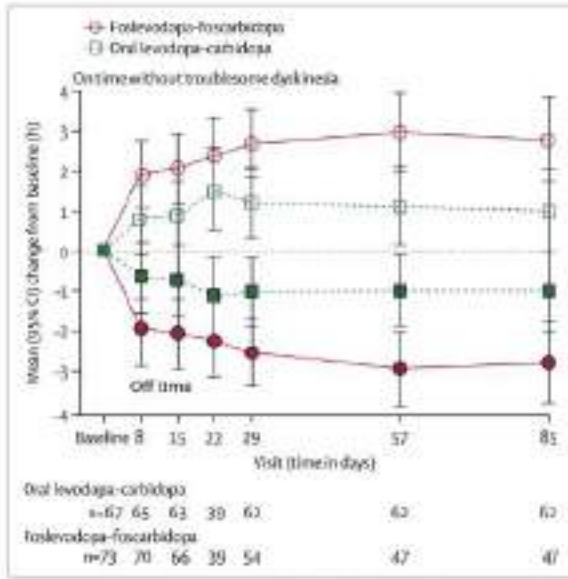


Figure 2: Least squares mean (95% CI) of change from baseline in average daily on time without troublesome dyskinesia and off time (full analysis set)
Assessed using a 24-h Parkinson's disease diary and normalised to a 16-h waking day. On time without troublesome dyskinesia is the sum of on time without dyskinesia and on time with non-troublesome dyskinesia. Error bars represent the 95% CI of the least squares mean change from baseline. Day 22 was an optional visit at the investigator's discretion and based on the participant's Parkinson's disease symptoms.

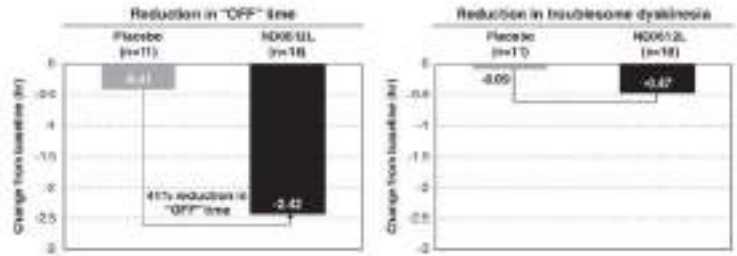
- ~1.7-1.8 hours of benefit beyond levodopa



(ND0612) Neuroderm SQ Pump 1.7 hours on time

- ND0612 had 1.72 hours in “Good ON” time (w/o troublesome dyskinesia).
- “OFF” time improved.
- Some data AAN 2023 Boston
- Some data SEC filing
- Limited to ~720mg dopamine administered through the pump

Moreover, when ND0612L was compared to the standard of care in the first period of our Phase II trial, treatment with ND0612L demonstrated major clinical benefits over the placebo in all objective, in-clinic, pre-specified, exploratory efficacy end points, including off-time reduction. A mean reduction of two hours versus placebo was observed in the ND0612L treated group. Moreover, the reduction in "off" time was not accompanied by an increase in troublesome dyskinesia.





- As filed with the Securities and Exchange Commission on July 13, 2015 and Olanow J Parkinson’s Disease 2021

Dopamine Pump Using a ‘Tube Based’ Approach

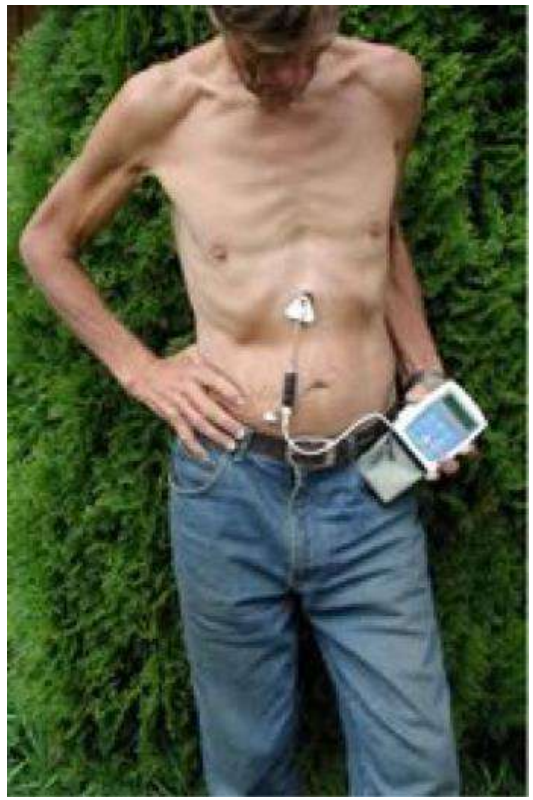
Articles

Continuous intrajejunal infusion of levodopa-carbidopa intestinal gel for patients with advanced Parkinson's disease: a randomised, controlled, double-blind, double-dummy study

Prof C Warren Olanow, MD, Karl Kieburtz, MD, Per Odin, MD, Alberto J Espay, MD, David G Standaert, MD, Hubert H Fernandez, MD, Arvydas Vanagunas, MD, Ahmed A Othman, PhD, Katherine L Widnell, MD, Weining Z Robieson, PhD, Yili Pritchett, PhD, Krai Chatamra, PhD, Janet Benesh, BSMT, Robert A Lenz, MD, Angelo Antonini, MD, for the LCIG Horizon Study Group

Published Online: 20 December 2013

- Mean off-time decreased by 4·04 hours vs. 2·14 h (0·66) immediate-release medication (3 months)
- Mean on-time without troublesome dyskinesia increased by 4·11 h (SE 0·75) vs 2·24 h (0·76) w/medication
- AE’s mainly associated with percutaneous gastrojejunostomy tube



Dopamine Pump: ~2.1 Hours of on time

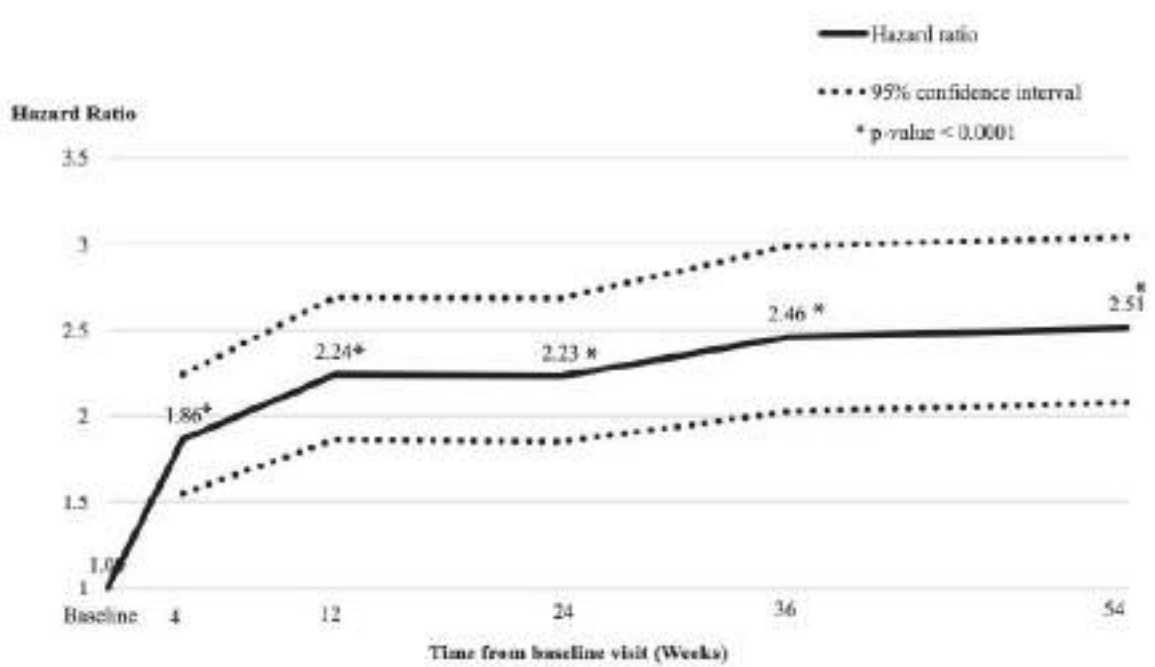


Fig. 1. ON-woTD onset timing after waking: Hazard ratios compared to baseline over 54 weeks.



Clinical Parkinsonism & Related Disorders

Long-term results of carbidopa/levodopa enteral suspension across the day in advanced Parkinson's disease: Post-hoc analyses from a large 54-week trial

Rajesh Pahwa, Jason Aldred, Aristide Merola, Nidhin Gupta, Emi Terazawa, Viviana Garcia-Horton, David R. Steffen, Prasanna L. Kandukuri, Yanjun Bao, Omar Ladhani, Connie H. Yan, Vivek Chaudhari, Stuart H. Isaacson

‘DUOGLOBE Duopa Study’



- 195 patients, 15 centers
- Off time and dyskinesia improve
- AE’s most common tube placement
- AE’s most common first 2 weeks
- Most common AE was abdominal pain
- 10% discontinue per year
- 30% by 5 years need a tube replaced

DUOGLOBE: One-Year Outcomes in a Real-World Study of Levodopa Carbidopa Intestinal Gel for Parkinson’s Disease

David G. Standaert, MD, PhD,[1]* Jason Aldred, MD,[2] Marleta Anco-Herschkovitsch, MD,[3] Paul Bourgeois, MD,[4] Esther Cubo, MD, PhD,[5] Thomas L. Davis, MD,[6] Robert Jansek, BMedSci, MBBS, PhD, FRACP, CHM,[7] Norbert Kovács, MD, DSc,[8] Francesco E. Pontieri, MD,[9] Mustafa S. Siddiqui, MD,[10] Mihaela Simu, MD,[11] Lars Bergmann, MD,[12] Pavnit Kukreja, PharmD,[12] Weining Z. Robieson, PhD,[12] and K. Ray Chaudhuri, MD, DSc[13]



- Movement Disorders journal; tube picture David Standaert WPC

Neurol Ther (2022) 11:851–861
https://doi.org/10.1007/s40120-022-00351-x

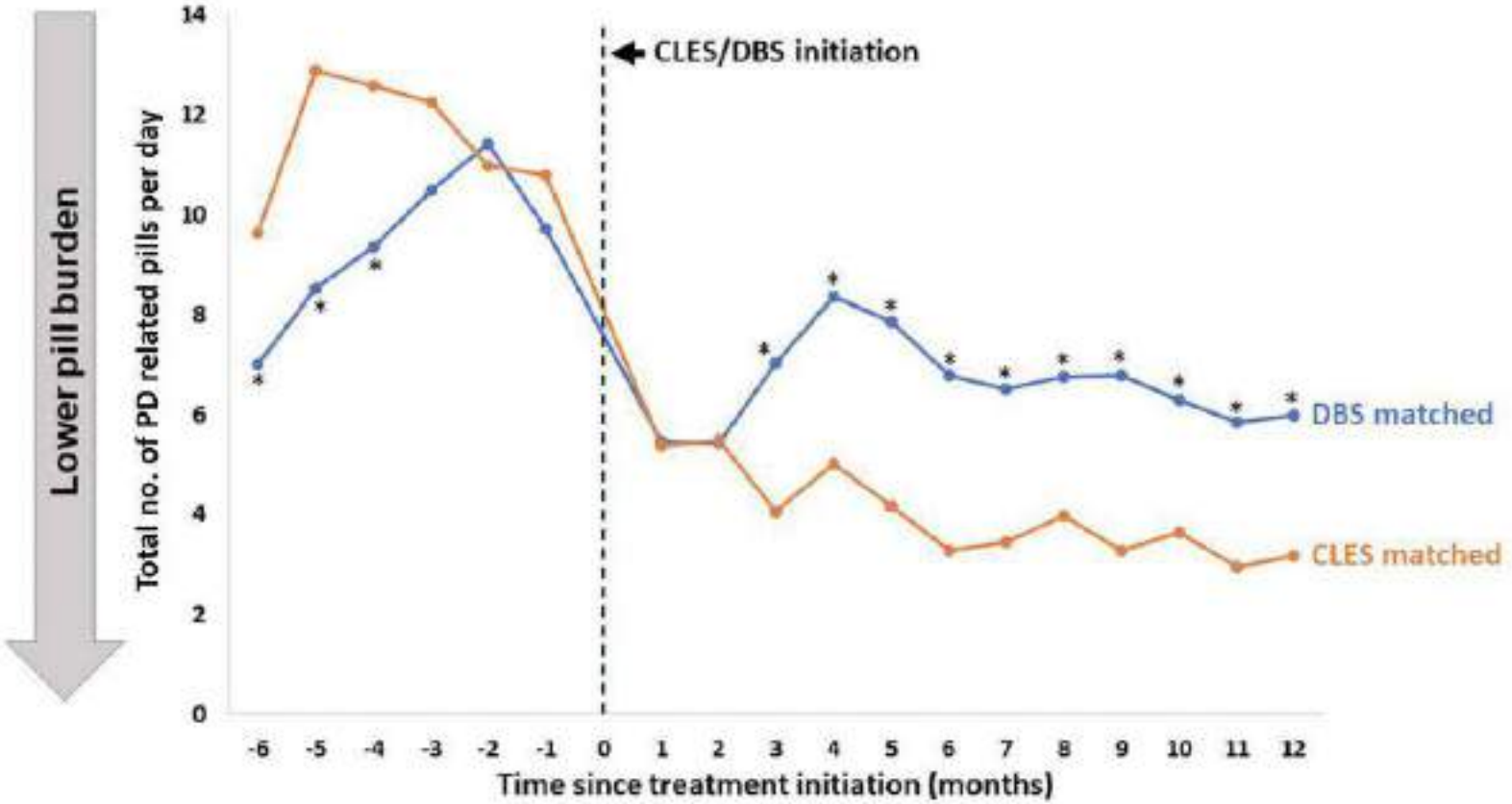
ORIGINAL RESEARCH

Comparative Effectiveness of Carbidopa–Levodopa Enteral Suspension and Deep Brain Stimulation on Parkinson's Disease-Related Pill Burden Reduction in Advanced Parkinson's Disease: A Retrospective Real-World Cohort Study

Michael J. Soileau · Fernando Pagan · Alfonso Fasano · Ramon Rodriguez-Cruz · Lin Connie H. Yan · Ali Alobaidi Mok Oh · Mustafa S. Siddiqui



Lower Pill Burden



Duodenal Levodopa Infusion for Long-Term Deep Brain Stimulation–Refractory Symptoms in Advanced Parkinson Disease

Ignacio Regidor, MD, PhD,† Vicente Benita, MD,‡ Marta del Álamo de Pedro, MD,*§ Luis Ley, MD,§ and Juan Carlos Martinez Castrillo, MD, PhD||*

Clinical Neuropharmacology • Volume 40, Number 3, May/June 2017

Mixed Results, Benefits….

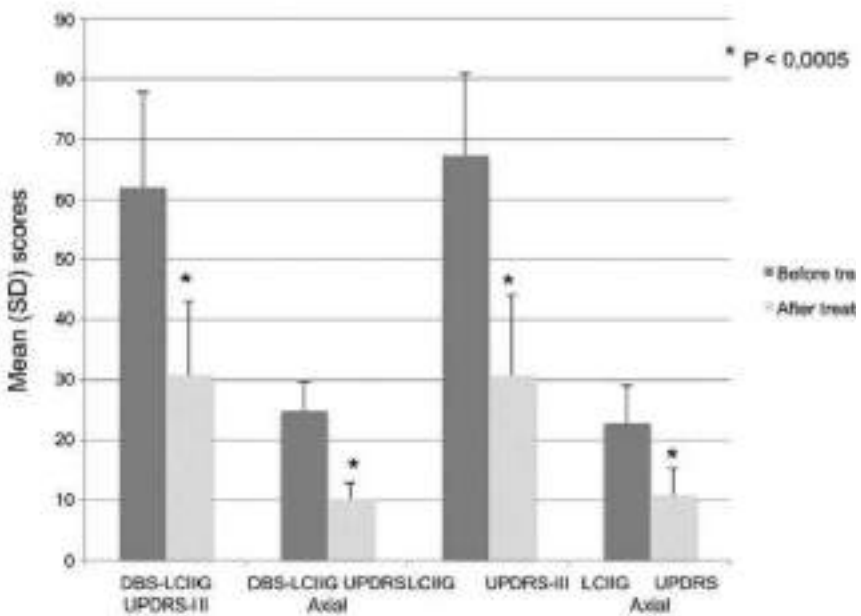


FIGURE 1. Changes in UPDRS-III and UPDRS axial subscales. Data were obtained in the drugs on, LCIIG on, DBS on, situation.

TABLE 2. Changes in UPDRS-III and UPDRS Axial Subscales in 19 Patients Treated With Double DBS-LCIIG Therapy According to Outcome of Treatment

Study Groups	Scales	Before LCIIG Treatment, Mean (SD)	After LCIIG Treatment Mean, (SD)	*P*
Discontinued DBS-LCIIG and returned to DBS monotherapy, n = 5	UPDRS-III	69.0 (14.7)	31.8 (12.3)	0.04
	UPDRS axial	24.0 (4.0)	11.2 (1.9)	0.04
Discontinued DBS and were maintained with LCIIG monotherapy, n = 5	UPDRS-III	60.6 (21.0)	36.2 (16.1)	0.04
	UPDRS axial	24.6 (7.3)	11.6 (3.3)	0.04
Continued with DBS-LCIIG double therapy, n = 9	UPDRS-III	58.9 (13.6)	27.6 (9.7)	0.00
	UPDRS axial	25.1 (4.3)	8.9 (2.3)	0.00

2,4 Rule for Device Based Therapy Improvement Increased ‘hours of on time improvement’ Beyond levodopa



- ~1.5-2 hours: Duopa Pump, SQ Infusions (Apomorphine, ND0612: Neuroderm or Foslevodopa/Foscarbidopa)
- ~4 hours: Bilateral deep brain stimulation
- Olanow et al CLES-Duopa: OFF time reduced by 4.04 with pump compared to 2.1 with levodopa (~2 hours); On time without Troublesome Dyskinesia (TD): 4.1 vs 2.2 (~2 hours)
- Soileau et al. Foslevodopa/FC: Ontime without TD 2.72 vs 0.97; difference of 1.75 hr;
  Off time: 2.75 vs 0.96 difference 1.79 hr
- Espay et al ND0612 On without TD difference: 1.72 hours; Off time difference of 1.4 hours
- Katzenschlager et al Apo SC: Off time 2.47 apo vs placebo 0.58 hours; difference of 1.89 hours

DBS Outcomes Comparison
*Different comparator from 'pump' trials



	NEJM 2006	Lancet Neurology 2012	Lancet Neurology 2020
# patients	156	136	160 (120 active/40 control)
Study Duration	6 months	3 months	3 months
Study Design	Prospective randomized pairs Open-label	Prospective randomized 3:1 Open-label	RCT – Sham control (3:1) Double-blind
Age	60.5 (7.4) yrs	61.7 (8.4) yrs	59.9 (7.95) yrs
Disease Duration	13.4 yrs	10.2 (7.4) yrs	10.1 (3.6) yrs
ON without troublesome dyskinesia	4.4 hours	4.3 hours	4.6 hours
UPDRS Motor Meds OFF vs Meds OFF/Stim ON	41% improvement	39% improvement	42% improvement
Device	Constant Voltage	Constant Current	Multiple Independent Current Control
Lead	Non-segmented	Non-segmented	Non-segmented (8 contact)

- Slide provided with permission from Dr. Raj Pahwa

5, 2, 1 Rule 'May be' Useful to Identify 'Device' Candidates?



Hindawi
Parkinson's Disease
Volume 2020, Article ID 7537924, 6 pages
https://doi.org/10.1155/2020/7537924

Research Article

5-2-1 Criteria: A Simple Screening Tool for Identifying Advanced PD Patients Who Need an Optimization of Parkinson's Treatment

D. Santos-García,[1] T. de Deus Fonticoba,[2] E. Suárez Castro,[2] A. Aneiros Díaz,[2] and D. McAfee[3]

- **Identify patients who require optimization**
- 5 times oral levodopa daily
- 2 hours of off time a day
- 1 hour troublesome dyskinesia a day
- *Used QOL

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

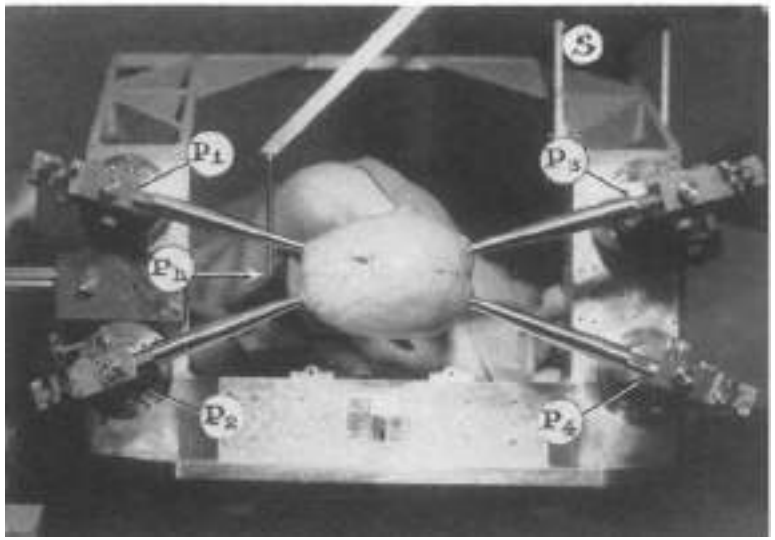
RUSSELL MEYERS, M.D.,† WILLIAM J. FRY, Sc.M.,‡ FRANK J. FRY, Sc.M.,‡ LEROY L. DREYER, Sc.B.,‡ DONALD F. SCHULTZ, M.D.,† and ROBERT F. NOYES‡

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.

UF Center *for* Movement Disorders and Neurorestoration
College *of* Medicine

Slide provided by Jeff Elias

Research

JAMA Neurology | Original Investigation

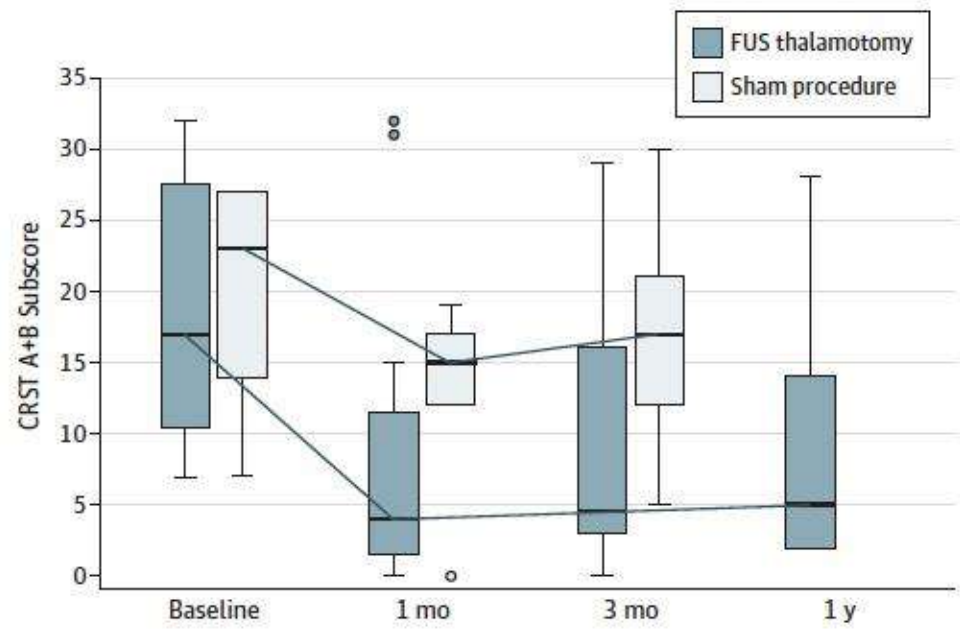
Safety and Efficacy of Focused Ultrasound Thalamotomy for Patients With Medication-Refractory, Tremor-Dominant Parkinson Disease

A Randomized Clinical Trial

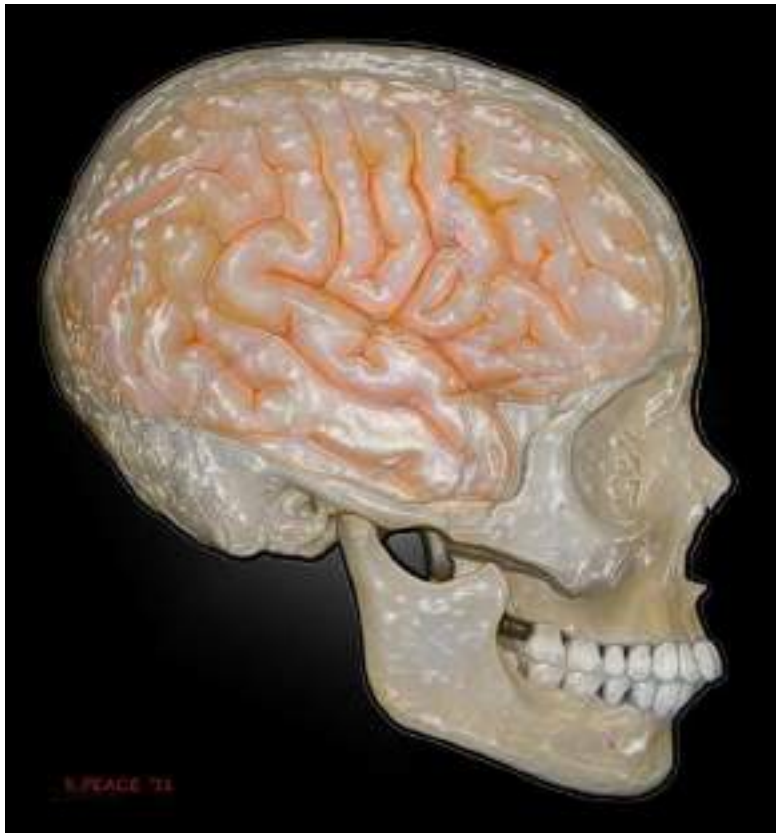
Aaron E. Bond, MD, PhD; Binit B. Shah, MD; Diane S. Huss, DPT, NCS; Robert F. Dallapiazza, MD, PhD; Amy Warren, MS; Madaline B. Harrison, MD; Scott A. Sperling, PsyD; Xin-Qun Wang, MS; Ryder Gwinn, MD; Jennie Witt, MD; Susie Ro, MD; W. Jeffrey Elias, MD

- 27 patients
- 62% improvement tremor

Figure 2. On-Medication Clinical Rating Scale for Tremor (CRST) A+B Treated Hand Tremor Subscore



Acoustic Spatial Heterogeneity of the Skull



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

Vyas, U. Med Phys 2016

Lesion or not? or sometimes? Does it matter?

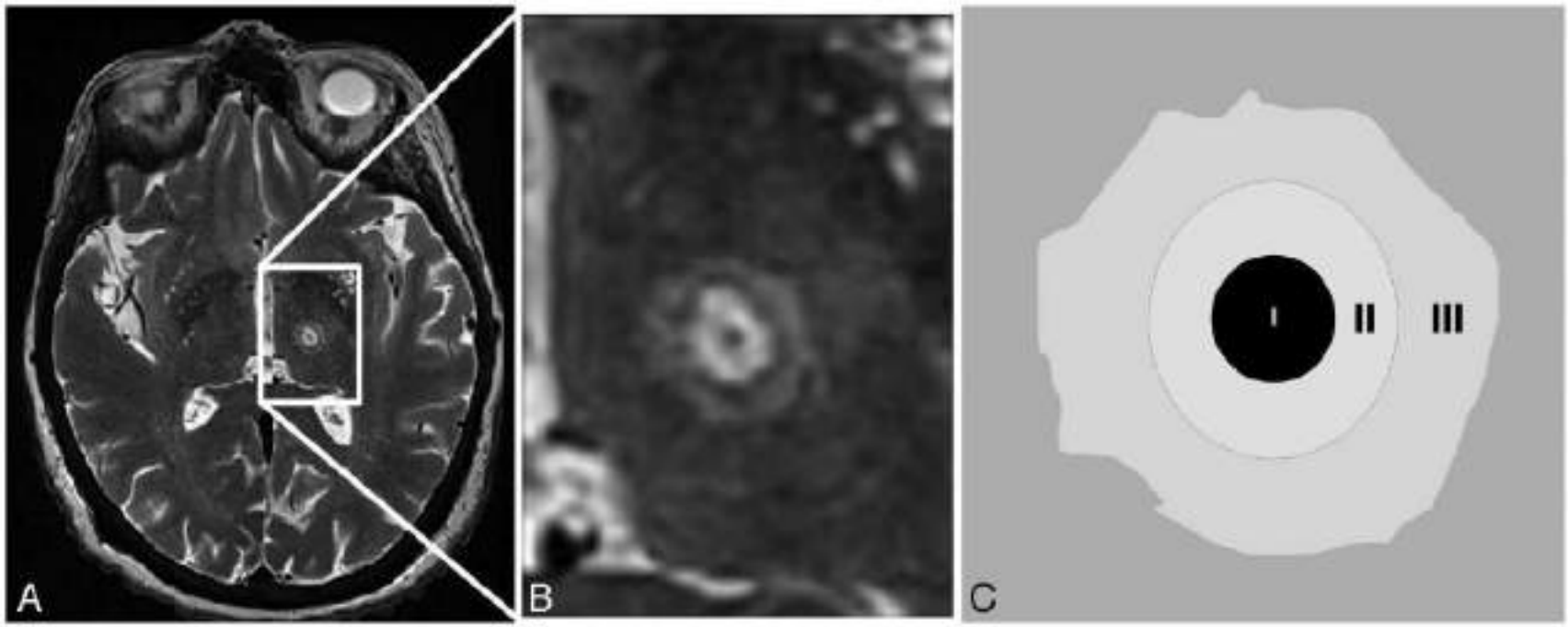


FIG 1. Schematic representation of zones I, II, and III visualized on T2-weighted imaging and the corresponding T2-weighted image of the lesion. On T2-weighted imaging, the patient developed 3 concentric zones at the site of lesioning: a hypointense zone I at the center, a strongly hyperintense zone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

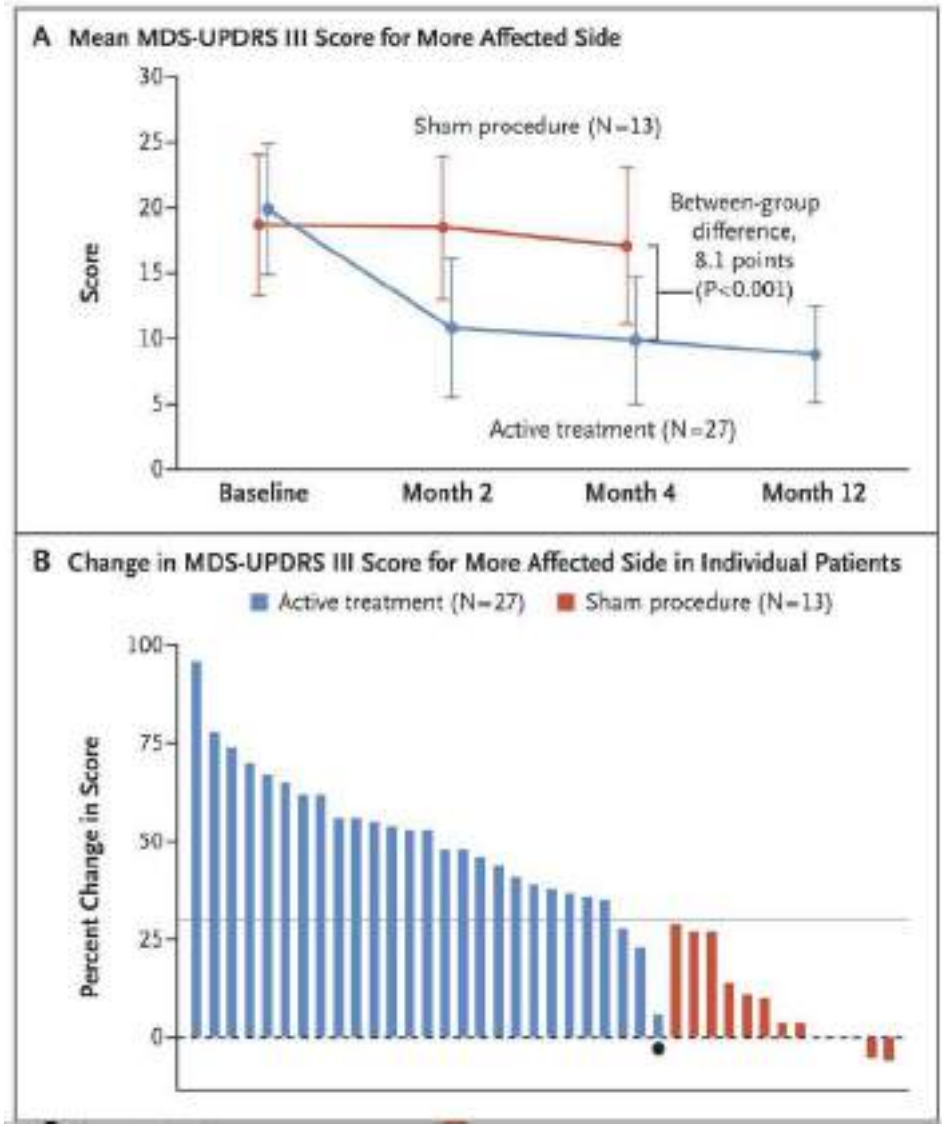
Penumbra- edematous brain is dysfunctional
Permanent efficacy (can you make it large enough) vs. (hopefully) temporary adverse effects

ORIGINAL ARTICLE

Randomized Trial of Focused Ultrasound Subthalamotomy for Parkinson's Disease

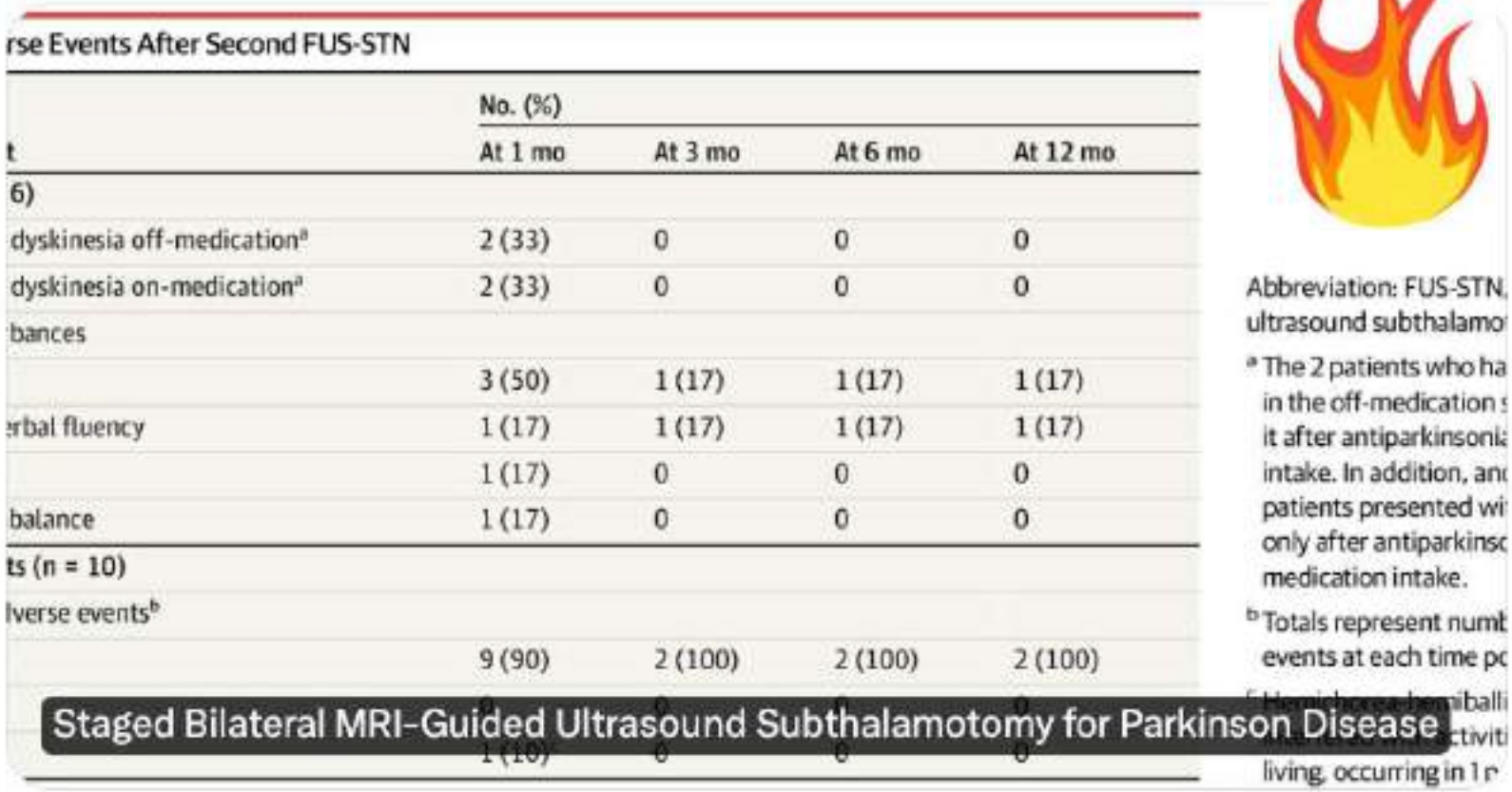
Raúl Martínez-Fernández, M.D., Ph.D., Jorge U. Máñez-Miró, M.D., Rafael Rodríguez-Rojas, Ph.D., Marta del Álamo, M.D., Binit B. Shah, M.D., Frida Hernández-Fernández, M.Sc., José A. Pineda-Pardo, Ph.D., Mariana H.G. Monje, M.D., Ph.D., Beatriz Fernández-Rodríguez, M.D., Scott A. Sperling, Psy.D., David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





JAMA Neurology @JAMANeuro · Jul 4

Staged bilateral MRI–guided focused ultrasound subthalamotomy was associated with significant motor improvement among patients with Parkinson disease, finds open-label case series.



rse Events After Second FUS-STN

t	No. (%) At 1 mo	At 3 mo	At 6 mo	At 12 mo
6)				
dyskinesia off-medication[a]	2 (33)	0	0	0
dyskinesia on-medication[a]	2 (33)	0	0	0
bances				
	3 (50)	1 (17)	1 (17)	1 (17)
rbal fluency	1 (17)	1 (17)	1 (17)	1 (17)
	1 (17)	0	0	0
balance	1 (17)	0	0	0
ts (n = 10)				
lverse events[b]				
	9 (90)	2 (100)	2 (100)	2 (100)
	1 (10)	0	0	0

Abbreviation: FUS-STN, ultrasound subthalamo

[a] The 2 patients who ha in the off-medication s it after antiparkinsoni intake. In addition, an patients presented wi only after antiparkinso medication intake.

[b] Totals represent numb events at each time po

living, occurring in 1 p

Staged Bilateral MRI-Guided Ultrasound Subthalamotomy for Parkinson Disease

From jamanetwork.com

6 12 2.2K

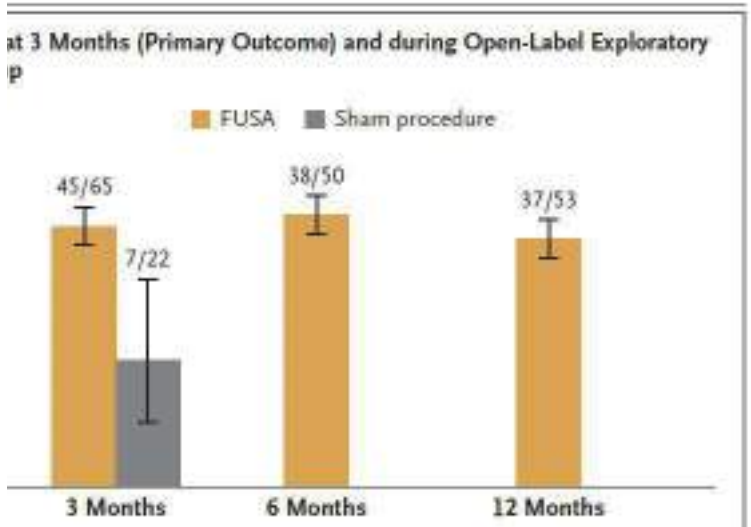
The NEW ENGLAND JOURNAL of MEDICINE

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 followup
- Did not address bilateral lesions



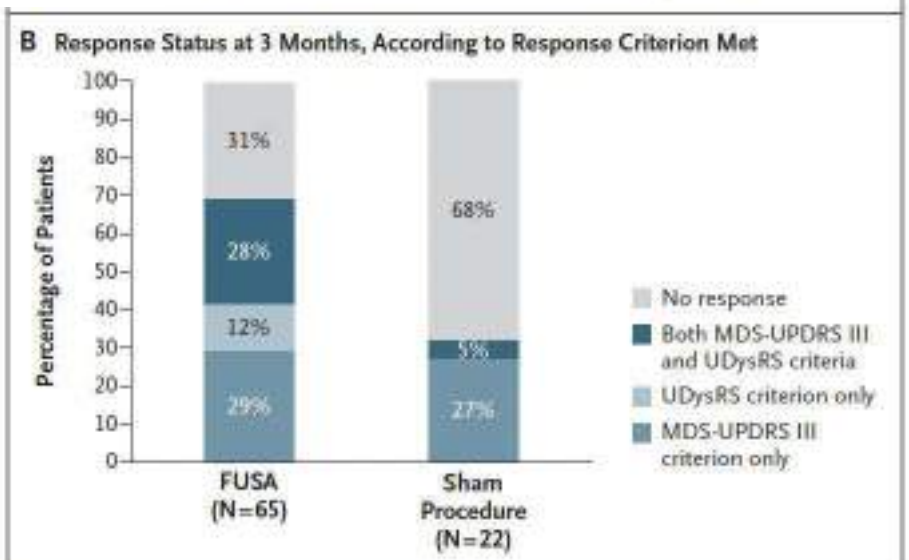
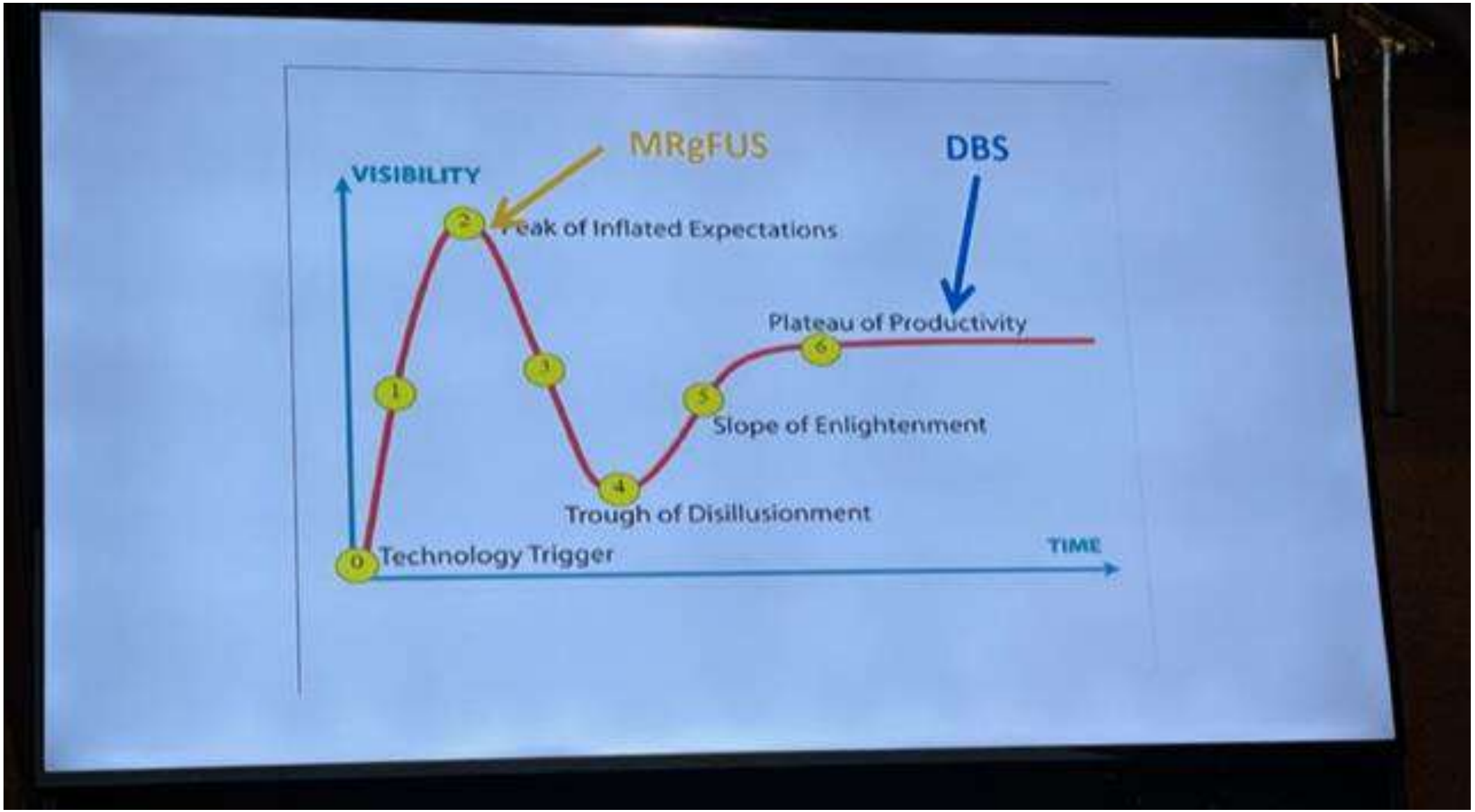
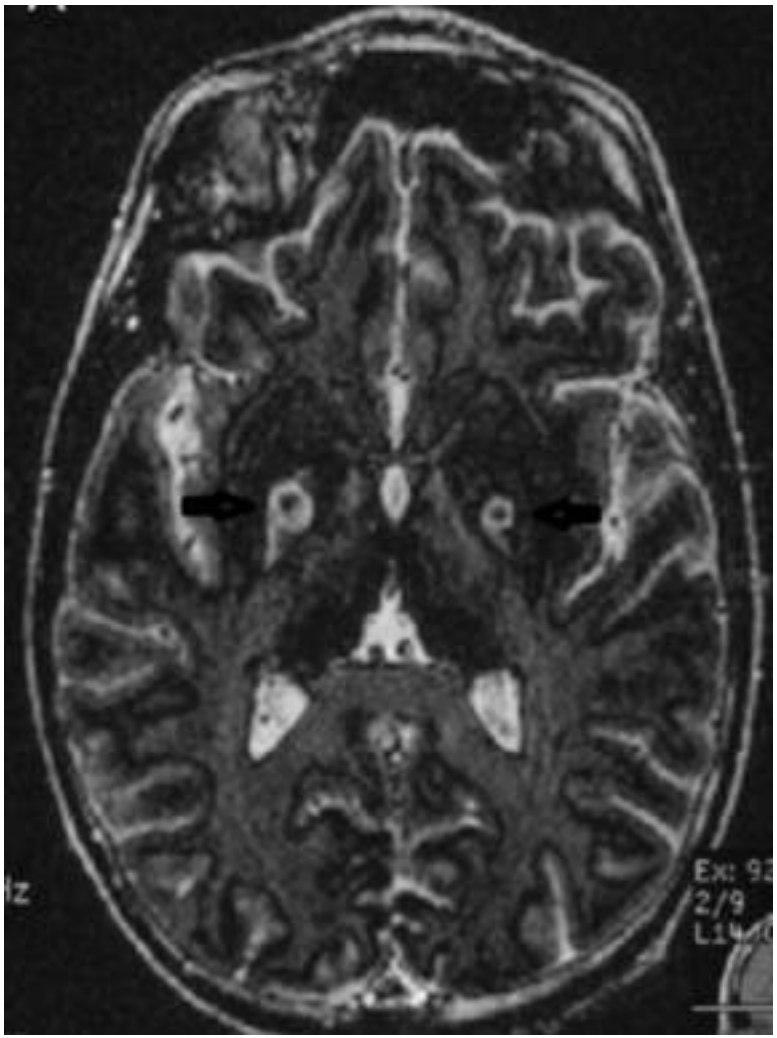


Figure 2. Response Status.

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.



Binit Shah 2023 World Parkinson Congress



Focused Ultrasound Foundation
@FUSFoundation

FDA Expands Use of Focused Ultrasound for Parkinson's

The FDA has approved bilateral focused ultrasound treatment for Parkinson's disease (PD). Patients with advanced PD now have the option to receive focused ultrasound on both sides of their brain in two sessions at least six months apart. This ruling is an important milestone for patients, as PD is a systemic disease with symptoms including rigidity and dyskinesia that can impact the whole body.

The technology was initially cleared by the FDA to treat PD on one side in 2021.
Learn more: fusfoundation.org/posts/fda-appr...



Gamma Knife

ORIGINAL CONTRIBUTION

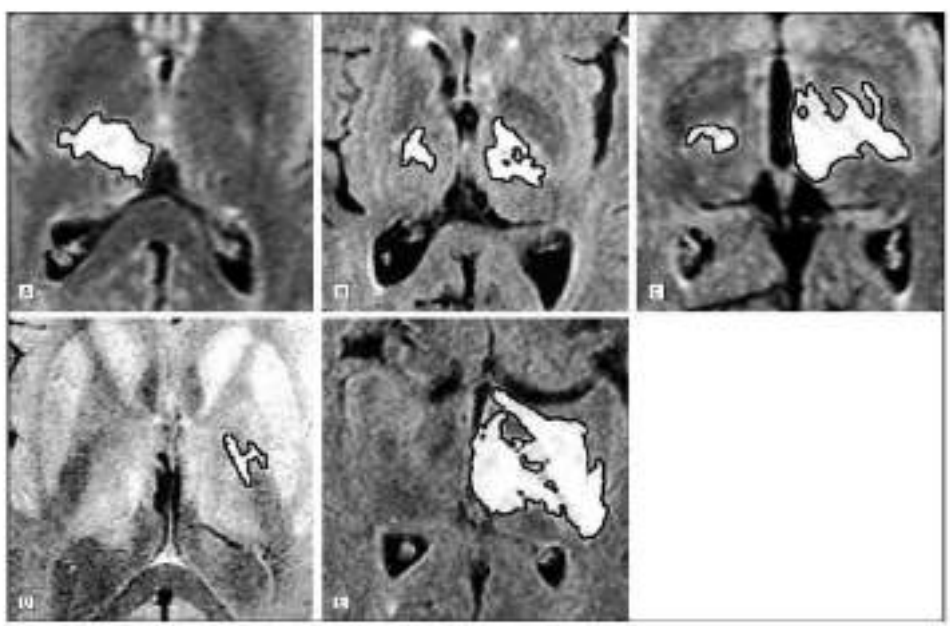
Complications of Gamma Knife Surgery for Parkinson Disease

Michael S. Okun, MD; Natividad P. Stover, MD; Thyagarajan Subramanian, MD; Marla Gearing, PhD; Bruce H. Wainer, MD, PhD; Chad A. Holder, MD; Ray L. Watts, MD; Jorge L. Juncos, MD; Alan Freeman, MD; Marian L. Evatt, MD; Stephan U. Schuele, MD; Jerrold L. Vitek, MD, PhD; Mahlon R. DeLong, MD

Table 1. Reported Complications of GK Surgery for PD*

Source, n	Pallidotomy†	Thalamotomy†	Complications
Lindquist et al,[14] 1997‡	0	2	Transient hemiparesis (n = 1)
Rand et al,[5] 1999	0	7	None reported
Pan et al,[7] 1999	0	6	Limb weakness (n = 1)
O'Dye et al,[6] 1999	0	6	None reported (all patients underwent previous mapping)
Friehs et al,[15] 1999	4	0	Dementia and psychosis (n = 1)
Bowen et al,[16] 1997	1	0	Visual field problem (n = 1)
Young et al,[17] 1998	33	27	Visual field problem (n = 1) and hypophonia and aged problem (n = 1)
Duma et al,[18] 1999	18	42	Visual field problems (n = 4), speech/swallowing problems (n = 3), gait problems (n = 3), dysarthria (n = 1), and numbness (n = 1)
Friehs et al,[19] 1999	2	16	Slow finger movements (n = 2); action tremor (n = 1); hemiparesis (unrelated infarct) (n = 1); hypophonia/dysphagia (n = 1); severe symptomatic edema (n = 4); and dysarthria, sickness, and weakness (n = 1)

*GK indicates gamma knife; PD, Parkinson disease.
†Data are given as total number of patients undergoing surgery, as reported in each article.
‡Observations were made in 1996.



Gamma Knife Thalamotomy for Disabling Tremor

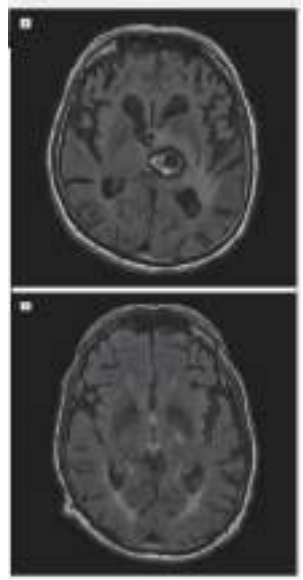
A Blinded Evaluation FREE

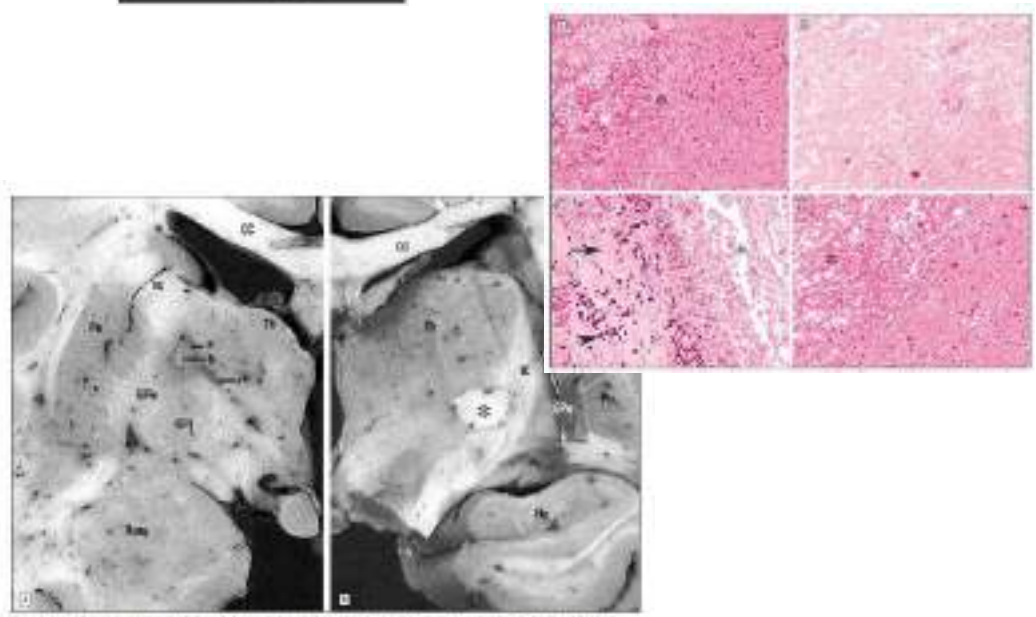
Shen-Yang Lim, MBBS, MD, FRACP; Mojgan Hodaie, MD, MSc, FRCSC; Melanie Fallis, RN; Yu-Yan Poon, RN; Filomena Mazzella, RN; Elena Moro, MD, PhD

[+] Author Affiliations

Arch Neurol. 2010;67(5):584-588. doi:10.1001/archneurol.2010.69.

Text Size: A A A





Spinal Cord Stimulation

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

Letters: New Observations | Full Access

Spinal Cord Stimulation for Very Advanced Parkinson's Disease: A 1-Year Prospective Trial

Sreeram Prasad MD, David H. Aguirre-Padilla MD, Yu-Yan Poon RN, Sukhwinder Kalsi-Ryan PhD, MSc, BScPT, Andres M. Lozano MD, PhD, Alfonso Fasano MD, PhD

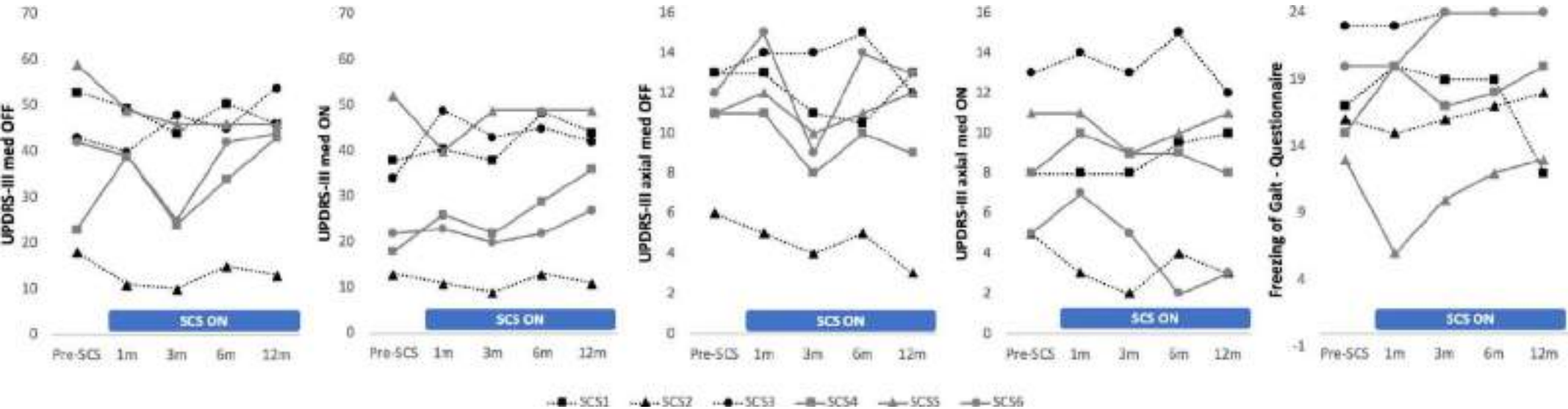
First published: 20 April 2020 | https://doi.org/10.1002/mds.28065

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

Research Article | Full Access

Spinal Cord Stimulation Therapy for Gait Dysfunctio Advanced Parkinson's Disease Patients

Olivia Samotus MSc, Andrew Parrent, Mandar Jog MD



Article

Walking naturally after spinal cord injury using a brain–spine interface

https://doi.org/10.1038/s41586-023-06094-5

Received: 1 August 2022

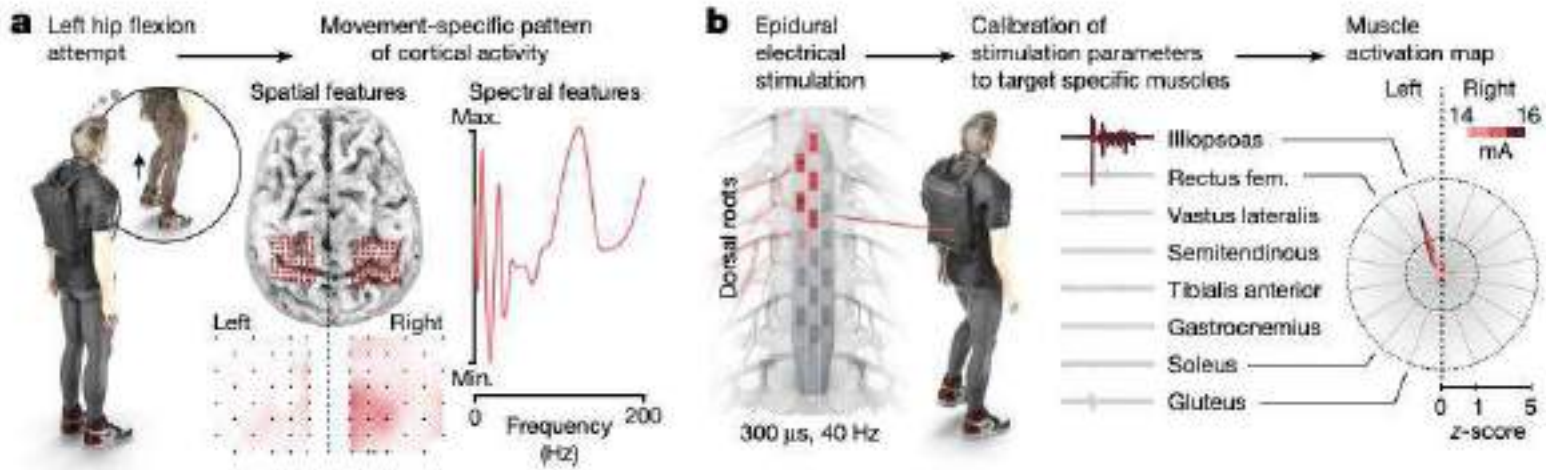
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Henri Lorach[1,2,3,10], Andrea Galvez[1,2,3,10], Valeria Spagnolo[1,2,3], Felix Martel[4], Serpil Karakas[4], Nadine Intering[1,2,3], Molywan Vat[1,2,3], Olivier Faivre[4], Cathal Harte[1,2,3], Salif Komi[1,2,3], Jimmy Ravier[1,2,3], Thibault Collin[1,2,3], Laure Coquoz[1,2,3], Icare Sakr[1,2,3], Edeny Baaklini[1,2,3], Sergio Daniel Hernandez-Charpak[1,2,3], Gregory Dumont[1,2,3], Rik Buschman[5], Nicholas Buse[5], Tim Denison[5,6], Ilse van Nes[7], Leonie Asboth[1,2,3], Anne Watrin[8], Lucas Struber[4], Fabien Sauter-Starace[4], Lilia Langar[9], Vincent Auboiroux[4], Stefano Carda[2], Stephan Chabardes[4,9], Tetiana Aksenova[4], Robin Demesmaeker[1,2,3], Guillaume Charvet[4,11] ✉, Jocelyne Bloch[1,2,3,11] ✉ & Grégoire Courtine[1,2,3,11] ✉





NOVEMBER 9, 2023 | 3 MIN READ

Man with Parkinson's Walks Smoothly thanks to an Experimental Spinal Implant

Electrical stimulation to the lower spine has improved the mobility of a man with Parkinson's disease for the past two years, but researchers say larger clinical trials are needed to assess the device

BY EMILY WALTZ & NATURE MAGAZINE

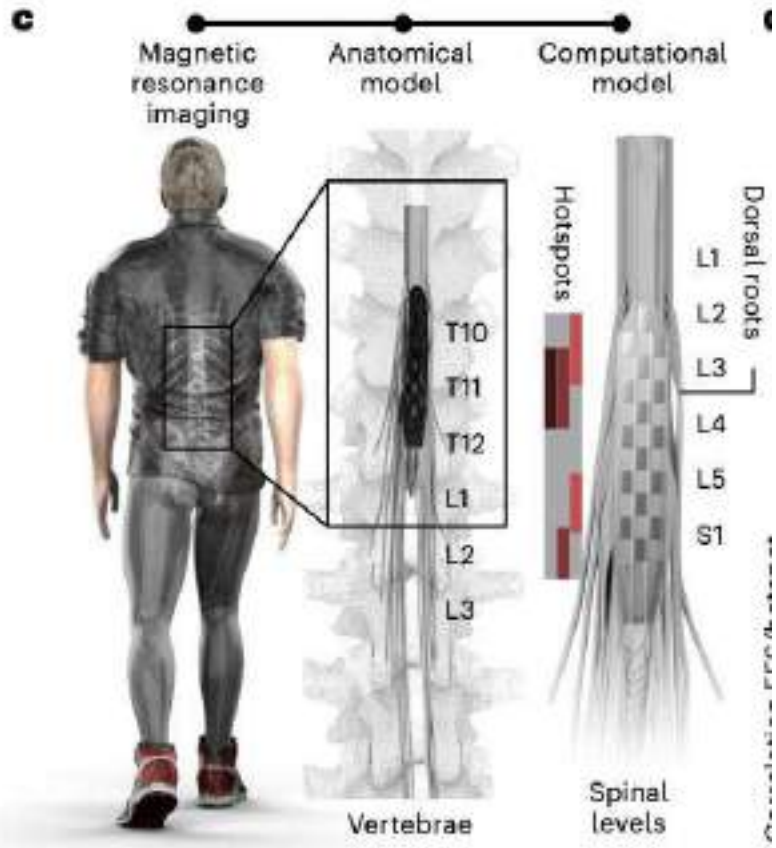


nature medicine

Article

https://doi.org/10.1038/s41591-023-02584-1

A spinal cord neuroprosthesis for locomotor deficits due to Parkinson's disease





Surgical Treatment of Parkinson's Disease (DBS)

- Why Apply Electricity to the Brain?
- How Does DBS Work?
- Patient Selection
- Differences in Surgical Approach
- Programming and Medications
- Measuring Outcomes
- Evolving Technologies

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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



‘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”

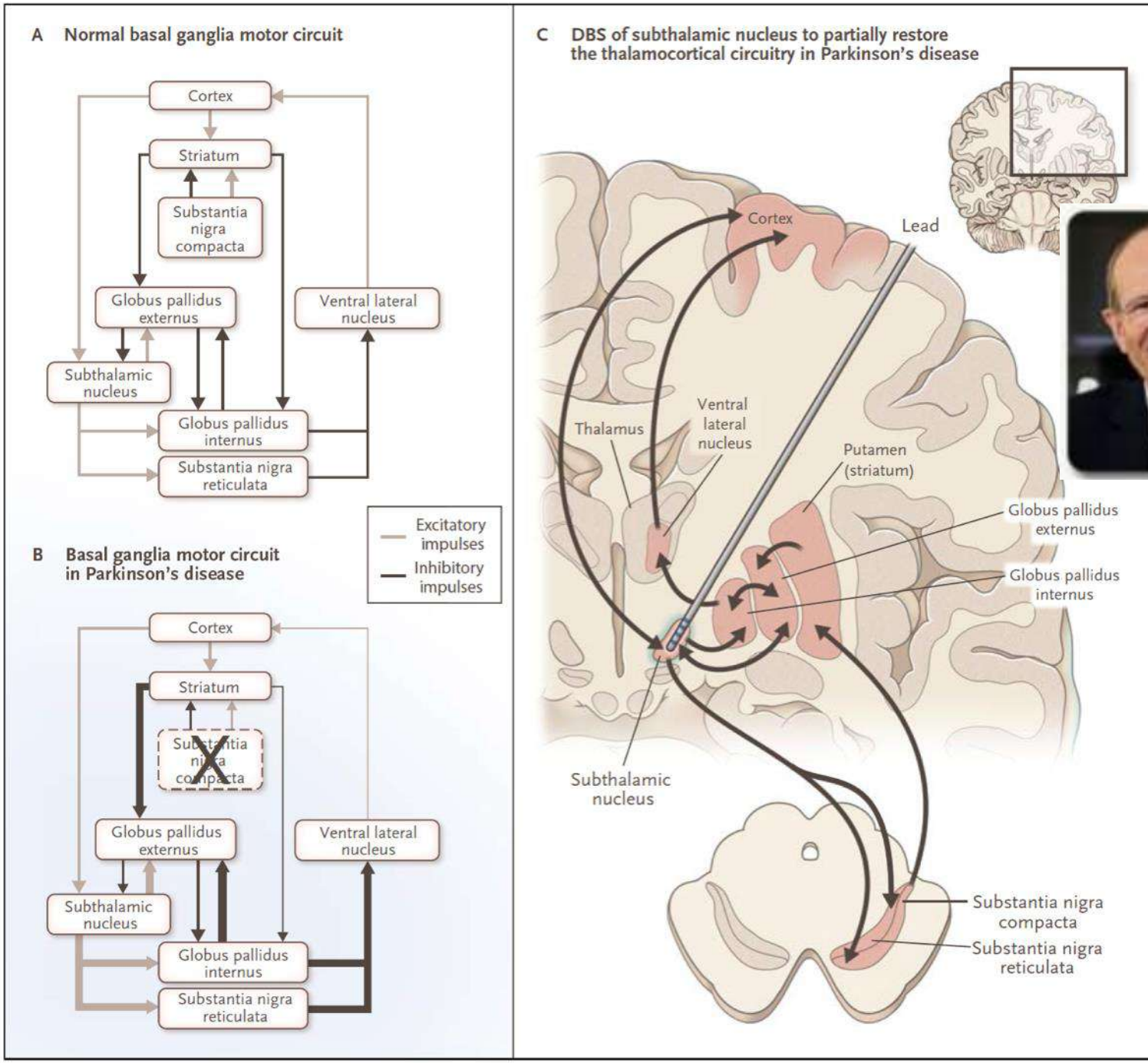


Figure 1. The DeLong "Box" Models of Basal Ganglia Circuitry and Their Use in Guiding Deep-Brain Stimulation (DBS).

YouTube

Browse | Movie

TEDxUF - Michael Okun and Kelly Foote - We Control Your Brain

TEDx Subscribe 14,785 videos



Your brain controls everything

We can control your brain

Ethical Guiding Principle (DBS)

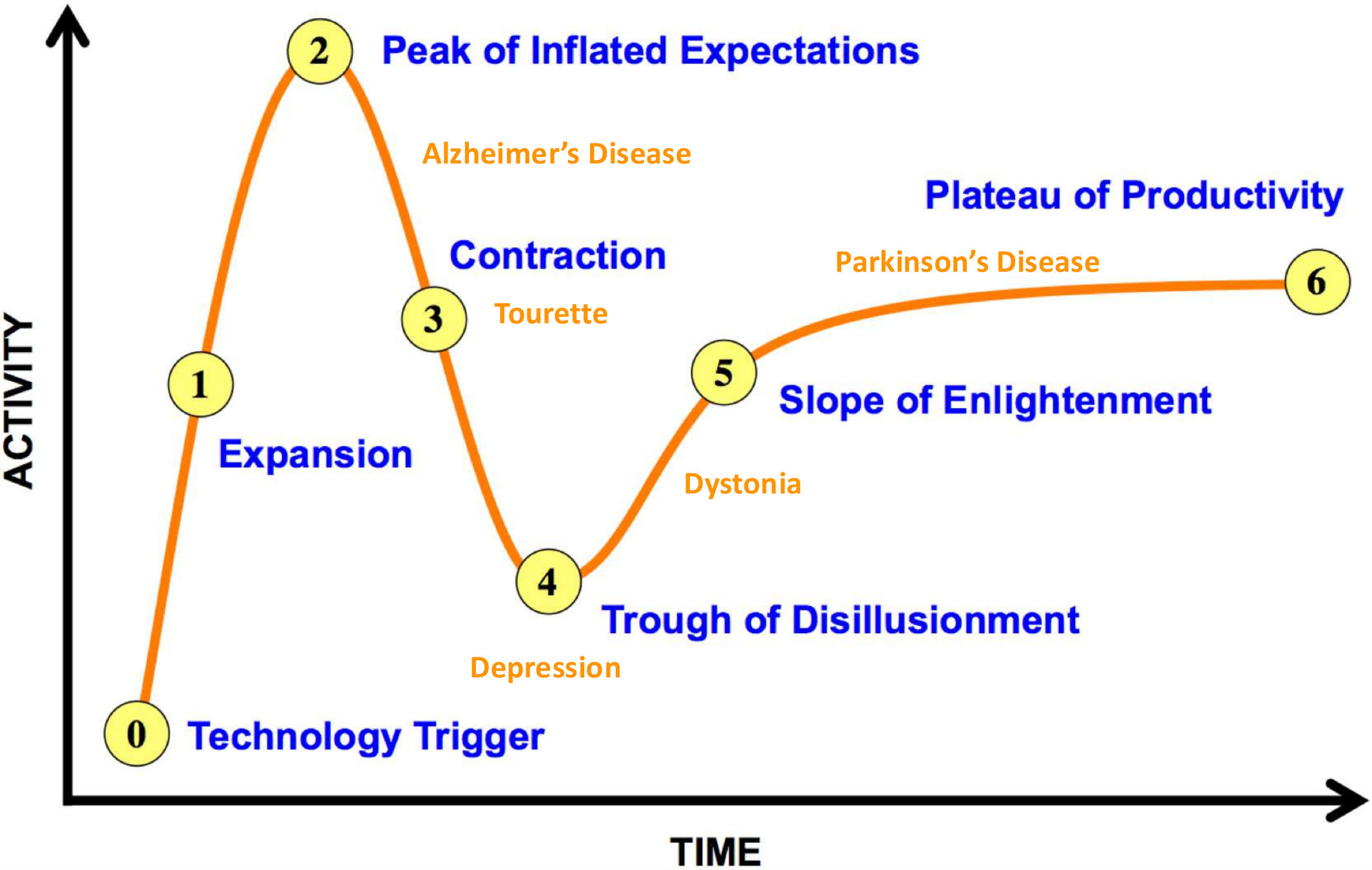











ACTIVITY
TIME
0
Technology Trigger
1
Expansion
2
Peak of Inflated Expectations
Alzheimer's Disease
3
Contraction
Tourette
4
Trough of Disillusionment
Depression
5
Slope of Enlightenment
Dystonia
6
Plateau of Productivity
Parkinson's Disease

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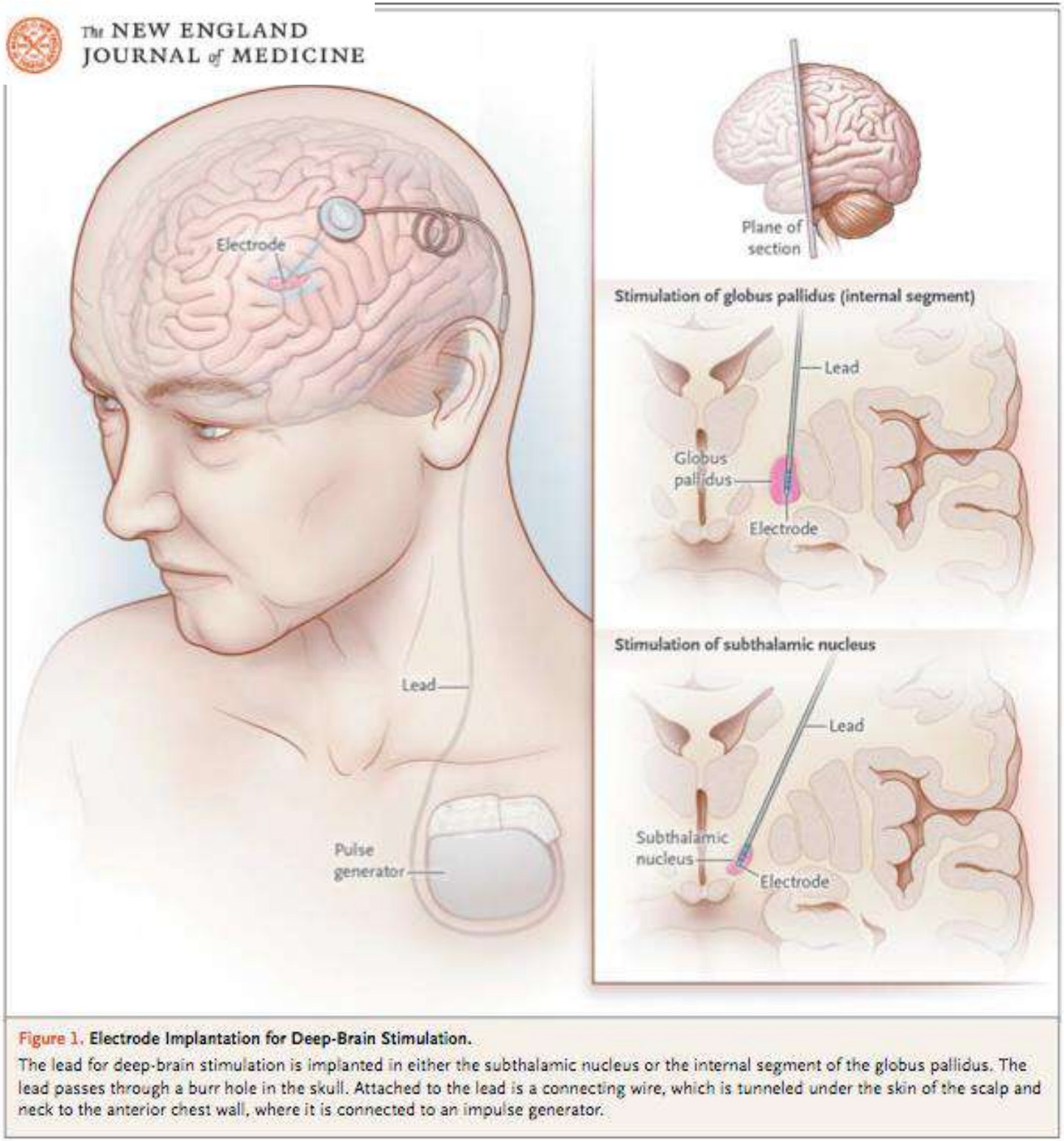


Figure 1. **Electrode Implantation for Deep-Brain Stimulation.**

The lead for deep-brain stimulation is implanted in either the subthalamic nucleus or the internal segment of the globus pallidus. The lead passes through a burr hole in the skull. Attached to the lead is a connecting wire, which is tunneled under the skin of the scalp and neck to the anterior chest wall, where it is connected to an impulse generator.

Neural-Network Modulation

Tiny Current
Big Effect

Grey Matter
White Matter
Interfaces

There is a knowledge gap:



Don’t confuse physiological and biological changes with the actual mechanism of action

Neurophysiologic

Neurochemical

Neurovascular

Neurogenic

Neuro-oscillations

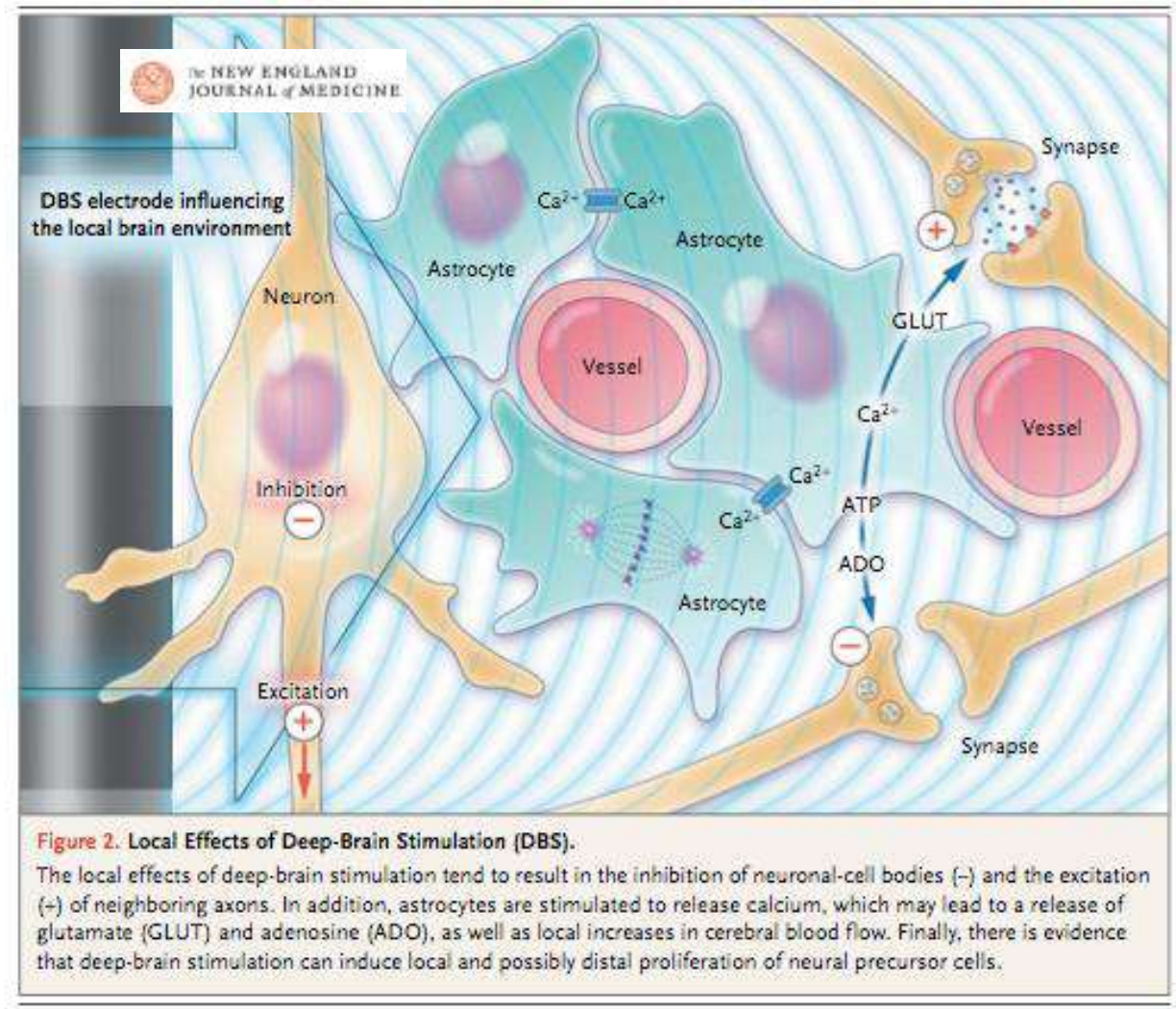


Figure 2. **Local Effects of Deep-Brain Stimulation (DBS).**
The local effects of deep-brain stimulation tend to result in the inhibition of neuronal-cell bodies (–) and the excitation (+) of neighboring axons. In addition, astrocytes are stimulated to release calcium, which may lead to a release of glutamate (GLUT) and adenosine (ADO), as well as local increases in cerebral blood flow. Finally, there is evidence that deep-brain stimulation can induce local and possibly distal proliferation of neural precursor cells.

Okun, M.S. N Engl J Med. 2012 Oct 18;367(16):1529-38

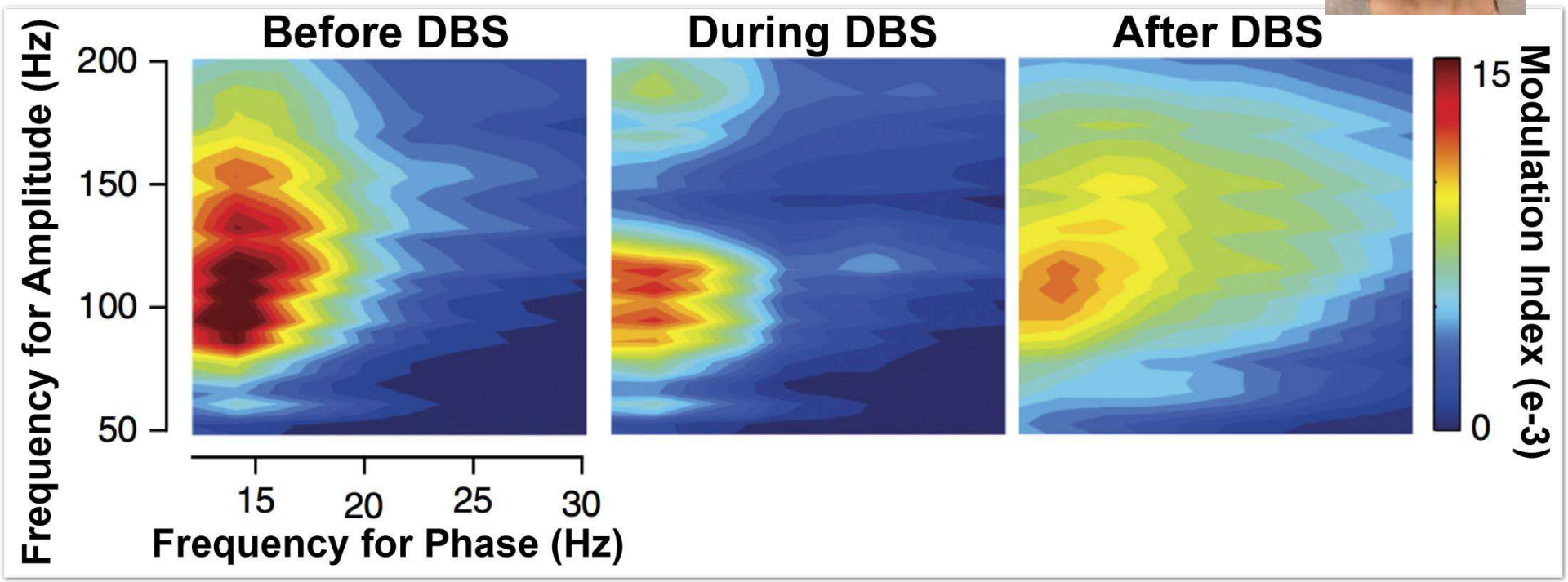
Therapeutic deep brain stimulation reduces cortical phase-amplitude coupling in Parkinson's disease

Coralie de Hemptinne[1], Nicole C Swann[1], Jill L Ostrem[2], Elena S Ryapolova-Webb[1], Marta San Luciano[2], Nicholas B Galifianakis[2] & Philip A Starr[1,3]

Received 31 December 2014; accepted 12 March 2015; published online 13 April 2015; doi:10.1038/nn.3997



NATURE NEUROSCIENCE ADVANCE ONLINE PUBLICATION



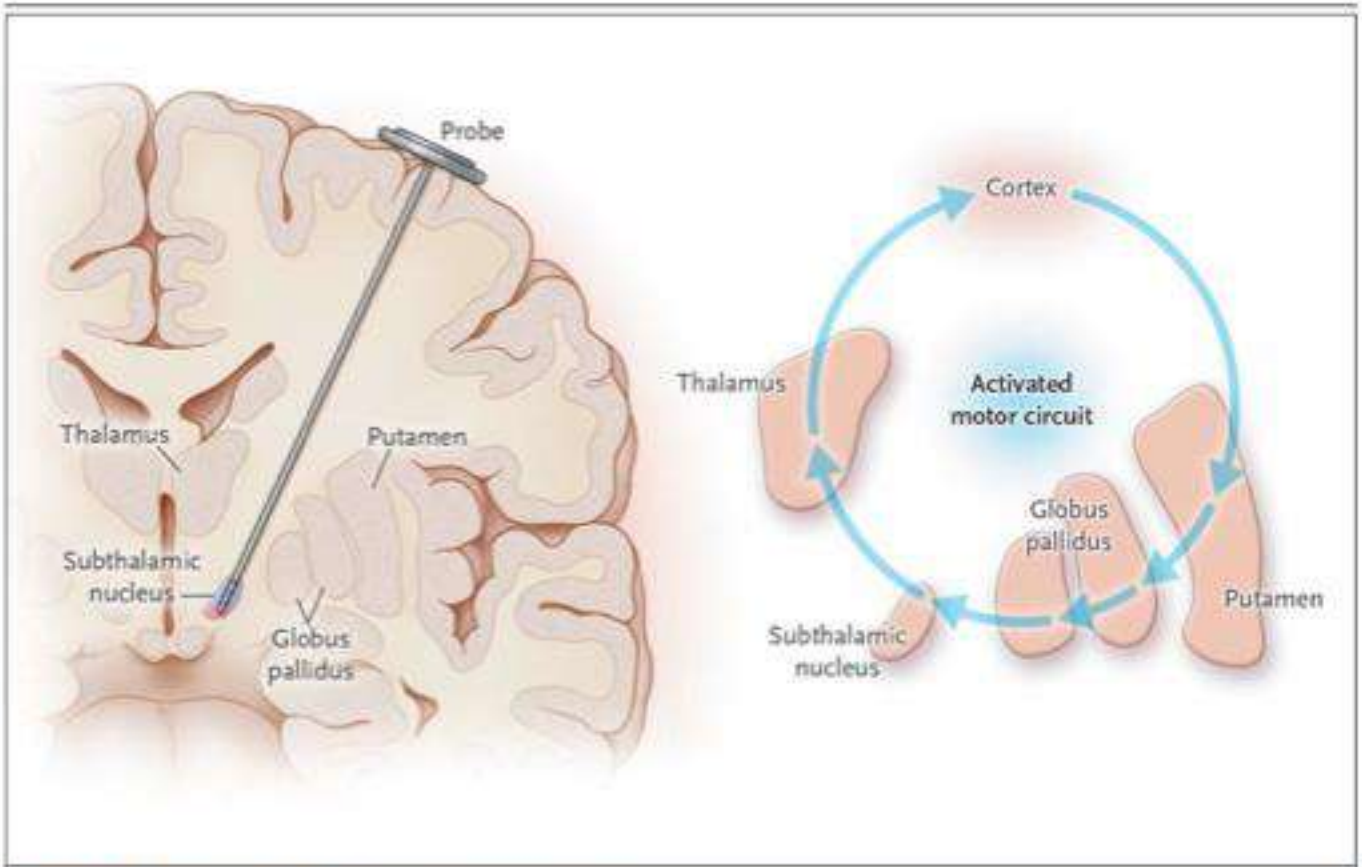


Figure 3. **Network Effects of Deep-Brain Stimulation.**

Deep-brain stimulation has broad effects on neural networks in addition to, or as a consequence of, its local influences. Motor pathways are complex, and their disturbance in Parkinson's disease is likewise far-ranging. Deep-brain stimulation modulates the feedback loops that ultimately determine motor control.

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What operation should be performed?

Brain target(s), unilateral vs. bilateral, simultaneous vs. staged

When to operate?

How early is too early to intervene?

Who should be operated?

Disease duration, age, symptom profiles and the use of the interdisciplinary screening team

Why to operate?

The argument for tailoring

These are Triage Tools not Screening Tools

Development and initial validation of a screening tool for Parkinson disease surgical candidates

M.S. Okun, MD; H.H. Fernandez, MD; O. Pedraza, BS; M. Misra, BS; K.E. Lyons, PhD; R. Pahwa, MD; D. Tarsy, MD; L. Scollins, MSN, RN, ANP; K. Corapi, BS; G.M. Friehs, MD; J. Grace, PhD; J. Romrell, PA; and K.D. Foote, MD

Abstract—As there is currently no standardized assessment tool for evaluating Parkinson disease (PD) patients for deep brain stimulation (DBS), the authors developed the Florida Surgical Questionnaire for Parkinson Disease (FLASQ-PD). Part I of the study was a retrospective analysis of 174 patients presenting for a surgical screening. Part II was a multicenter study to assess the correlation of FLASQ-PD scores. The results of this study suggest that the FLASQ-PD may be a useful triage tool for screening PD patients for DBS surgery.

NEUROLOGY 2004;63:161–163

J Neurol (2009) 256:83–88
DOI 10.1007/s00415-009-0069-1

ORIGINAL COMMUNICATION

A decision tool to support appropriate referral for deep brain stimulation in Parkinson's disease

Elena Moro
Niels Allert
Roberto Eleopra
Jean-Luc Houeto
Tra-Mi Phan
Herman Stoevelaar
International Study Group on Referral Criteria for DBS*

Diagnosis
Absolute Red Flags for Surgery
General Characteristics
Favorable/Unfavorable Characteristics
Adequate Medication Trial* (could





Movement disorders neurologist

History, physical, review scans
UPDRS on/off, TRS, UDRS/BFMDRS, other
Discussion of expectations

Case-specific referral

PT/OT/speech
Social work
Financial counselor

Fast track referral

Neurosurgery

History, physical
Scan review
Comorbidity
Risks/benefits
Expectations

Neuropsychology

Psychological history
Screen mood issues
Neurocognitive profile
Discuss expectations

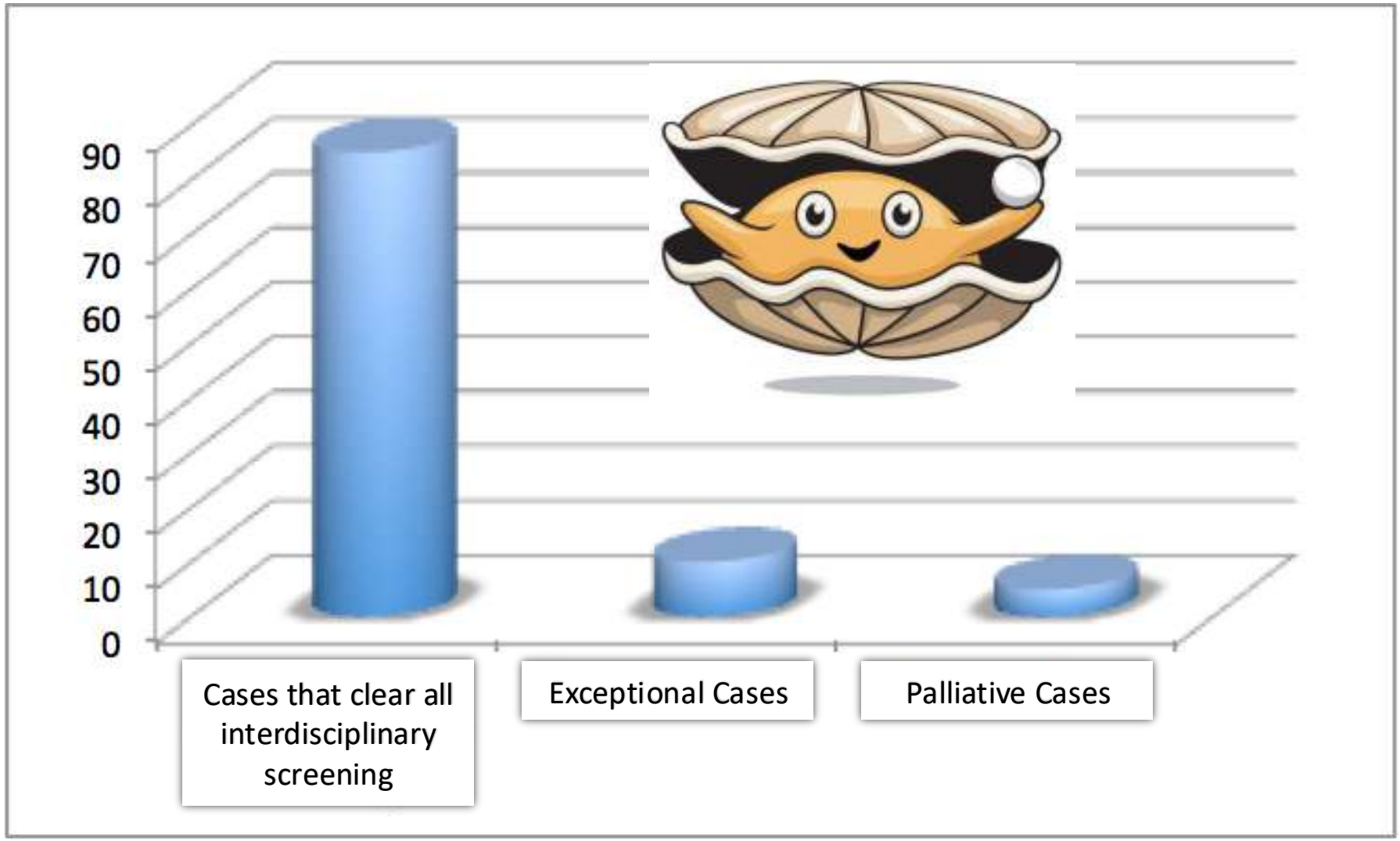
Psychiatry

SCID diagnosis from semi-structured interview
Axis I and II
Treat and stabilize mood
Manage expectations

Interdisciplinary meeting

Discuss motor, mood, cognitive, quality of life, expectation issues
Discuss exceptional cases (refractory tremor, dyskinesia, dystonia etc.)
Discuss targets and staged versus simultaneous (time frame between targets)

Consider Your DBS Candidates in Three Groups



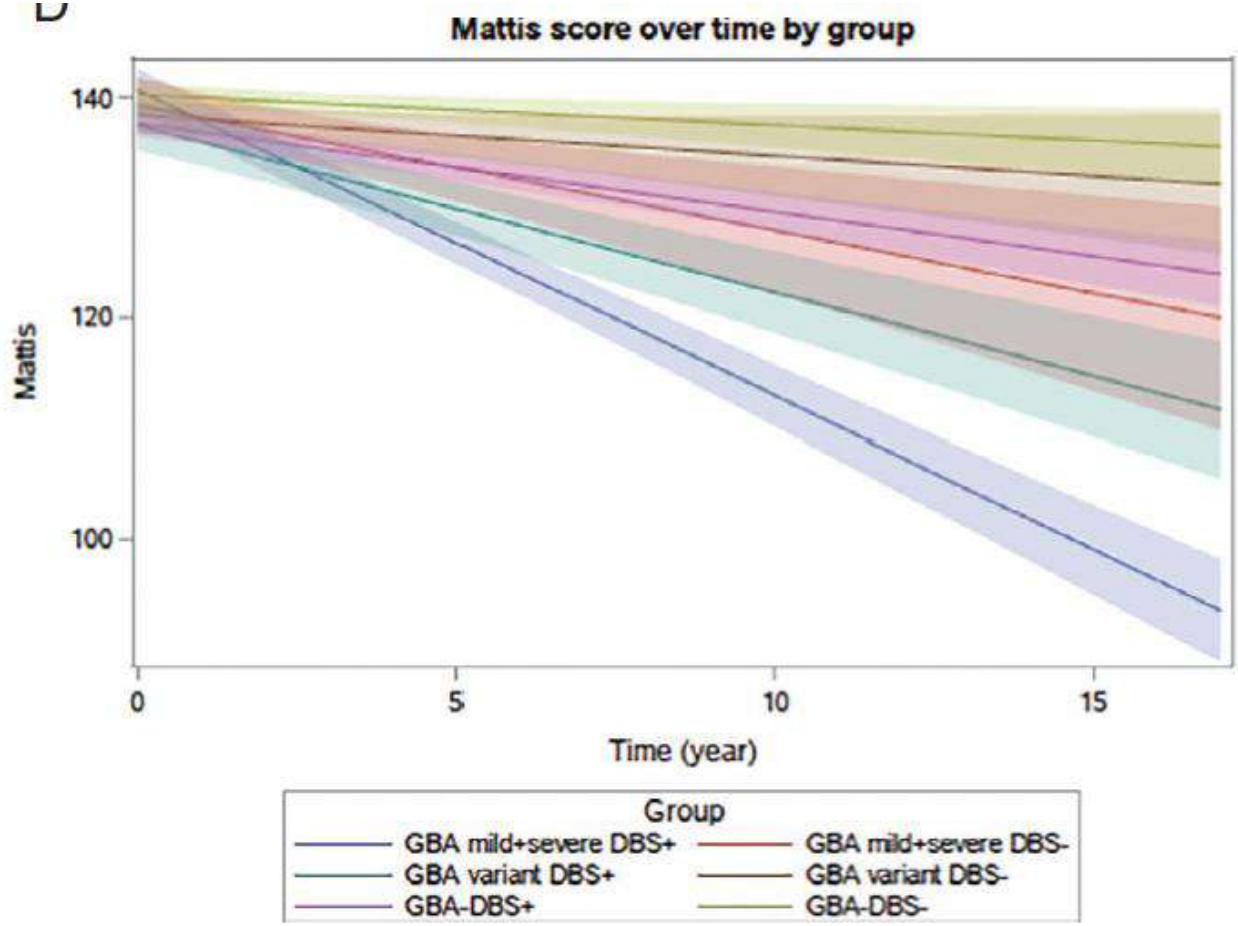
Parkinson Disease and Subthalamic Nucleus Deep Brain Stimulation: Cognitive Effects in *GBA* Mutation Carriers

Gian Pal, MD, MS[1,2] Graziella Mangone, MD



Combined effects of GBA mutations and STN-DBS negatively impact cognition

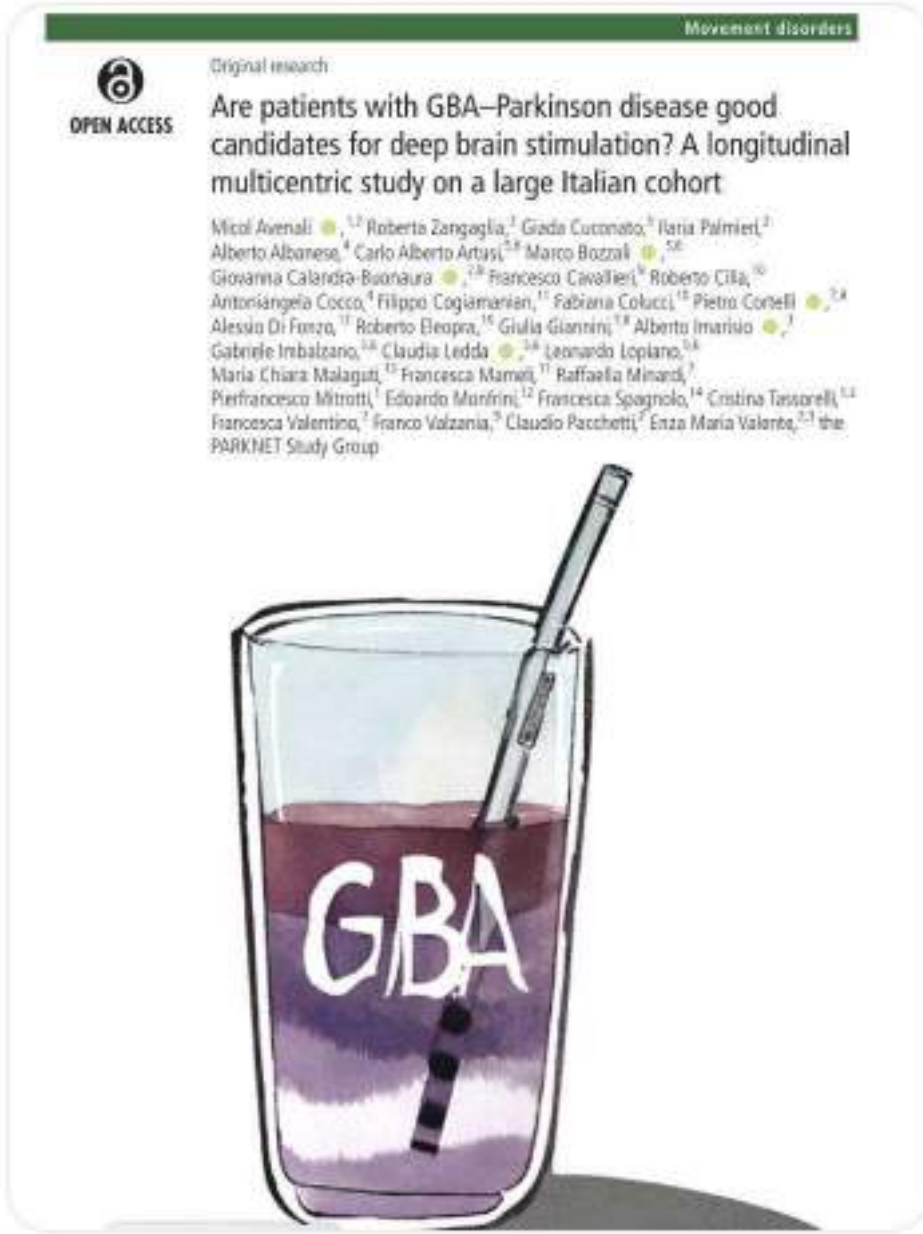
Controversial





Do we need **genetic testing** prior to offering **deep brain stimulation** for Parkinson's? A really important debate has recently broken out over GBA status and STN DBS. An early paper from Pal was followed by many multi-country papers. Now, we have a new Italian paper @bmj_latest and

Show more



Movement disorders

OPEN ACCESS

Original research

Are patients with GBA–Parkinson disease good candidates for deep brain stimulation? A longitudinal multicentric study on a large Italian cohort

Micol Avenali, Roberta Zangaglia, Giada Cuconato, Ilaria Palmieri, Alberto Albanese, Carlo Alberto Artusi, Marco Bozzali, Giovanna Calandra-Buonaura, Francesco Cavallieri, Roberto Cilia, Antoniangela Cocco, Filippo Cogiamanian, Fabiana Colucci, Pietro Cortelli, Alessio Di Fonzo, Roberto Eleopra, Giulia Giannini, Alberto Imarisio, Gabriele Imbalzano, Claudia Ledda, Leonardo Lopiano, Maria Chiara Malaguti, Francesca Mameli, Raffaella Minardi, Pierfrancesco Mitrotti, Edoardo Monfrini, Francesca Spagnolo, Cristina Tassorelli, Francesca Valentino, Franco Valzania, Claudio Pacchetti, Enza Maria Valente, the PARKNET Study Group



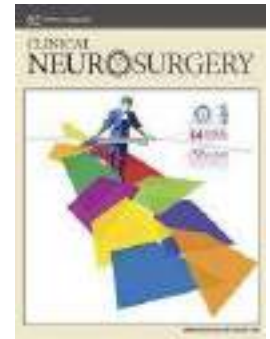
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What is the best approach?

- DBS (staged or simultaneous)
- Lesion Therapy (ablative, gamma knife, ultrasound)
- Frame or frameless
- MER or no MER
- MRI guided (no MER)
- Awake or asleep

- Multiple small studies showing similar results MER vs. MRI guided (power?)
- Asleep: few studies show similar results
- Frame vs. frameless similar results



135

A Comparison of Outcomes Between Deep Brain Stimulation Under General Anesthesia Versus Conscious Sedation With Awake Evaluation

François Alesch, MD; Roshini Jain, MS; Lilly Chen, Thomas Brucke, Fernando Seijo, Esther Suarez San Martin, Claire Haegelen, Marc Verin, Mohammed Maarouf, Michael T. Barbe, Steven Gill, FRCS, MS; Alan Whone, MBChB, MRCS, PhD; Mauro Porta, Domenico Servello, Lars Timmermann

Journal of Neurosurgery

Clinical outcomes using ClearPoint interventional MRI for deep brain stimulation lead placement in Parkinson's disease

NEUROSURGERY

Clinical Motor Outcome of Bilateral Subthalamic Nucleus Deep-Brain Stimulation for Parkinson's Disease Using Image-Guided Frameless Stereotaxy



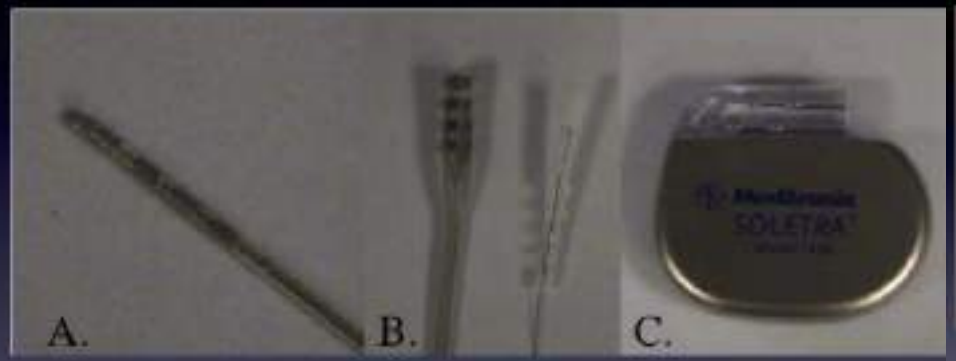


- Become expert at your technique
- Employ quality control pre- and post- placement and outcomes

Surgical Treatment of Parkinson's Disease

- Why Apply Electricity to the Brain?
- How Does DBS Work?
- Patient Selection
- Differences in Surgical Approach
- Programming and Medications
- Measuring Outcomes
- Evolving Technologies

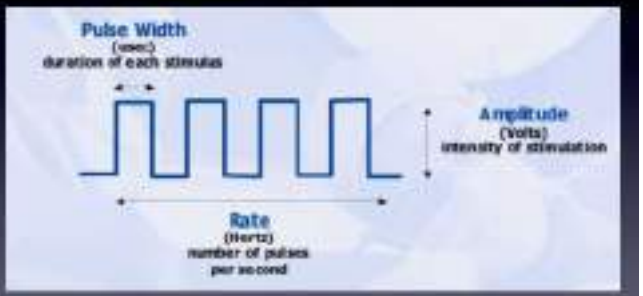
Devices



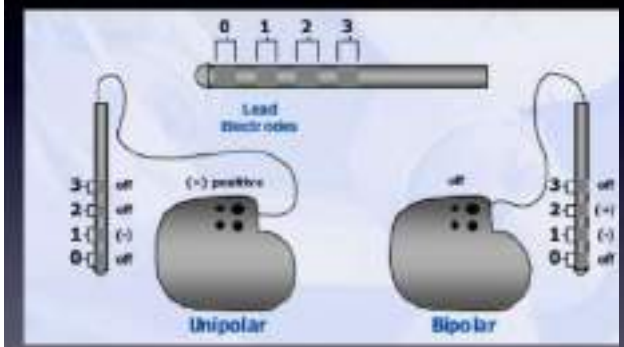


DBS Programmer

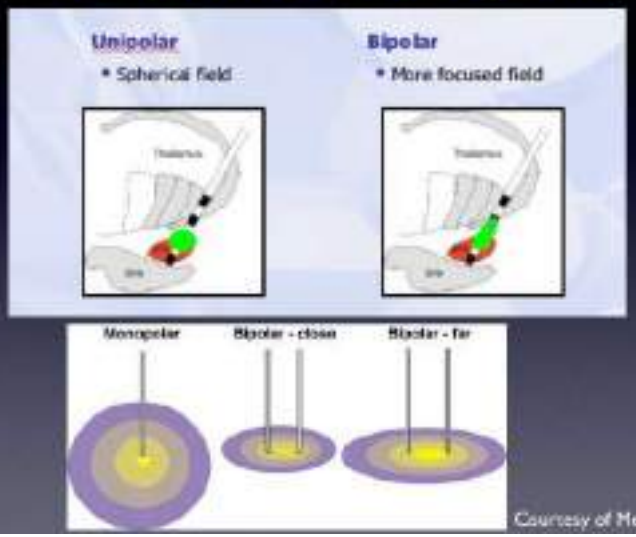
Three Stimulation Parameters



DBS Leads



Unipolar versus Bipolar



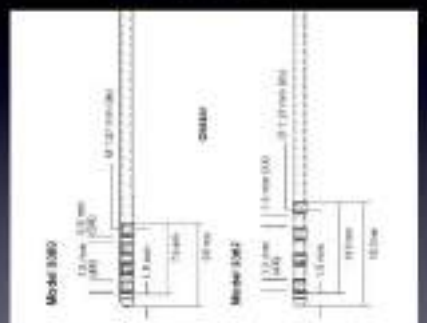
Courtesy of Medtronic, 2005

Common Stimulation Parameters

Parameter	STN	GPi
Amplitude	2.0 – 3.6 V	2.5 – 3.6 V
Pulse Width	60 – 90 µsec	90 – 120 µsec
Rate	135 – 185 Hz	135 – 185 Hz
Electrode Configuration	**Unipolar:** single electrode or 2 adjacent electrodes **Bipolar:** two adjacent electrodes	**Unipolar:** single electrode or 2 adjacent electrodes **Bipolar:** two adjacent electrodes

Thousands of setting combinations
- 12,964 combinations of V, PW and F
- 65 contact configurations

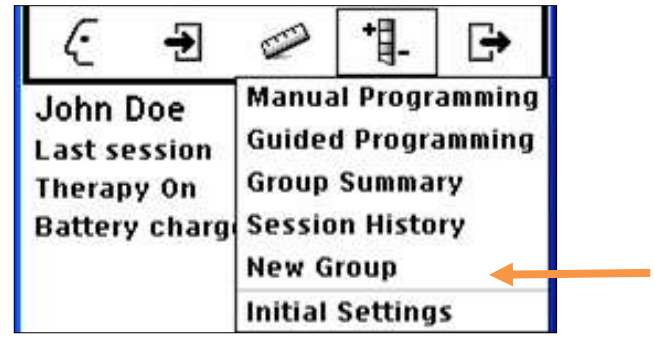
DBS Leads

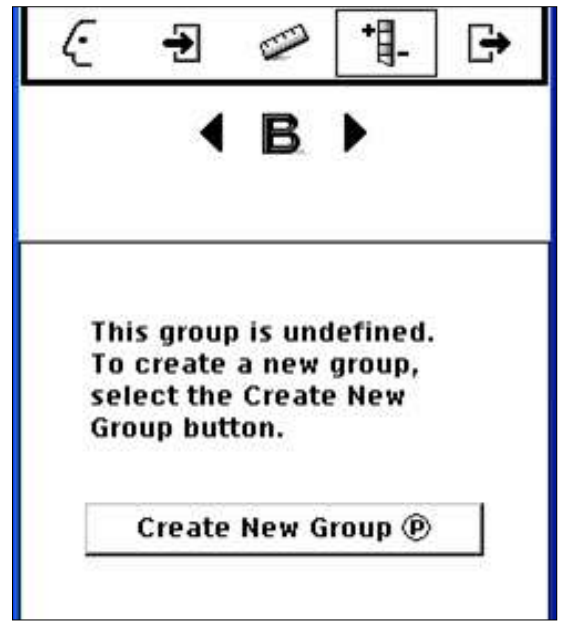


- Single and dual channels devices
- Different lead types/sizes
- Rechargeables
- Thousands programming combinations

Newer Neurostimulator Features: Multiple “Groups”

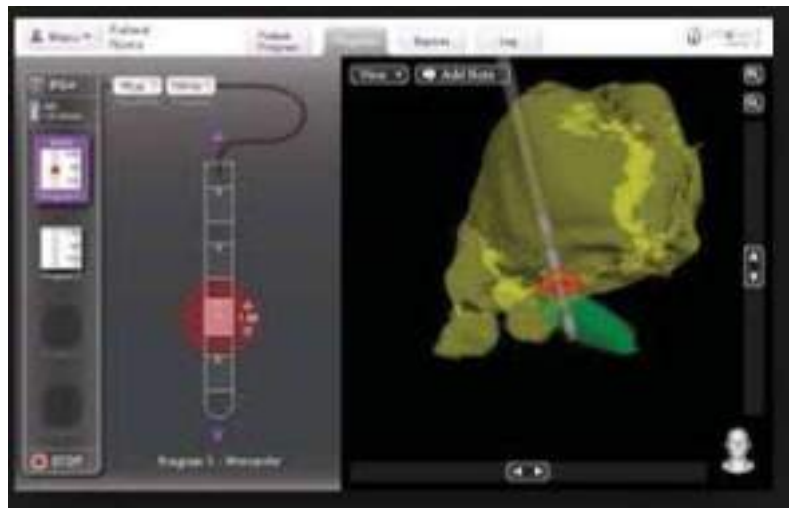
- Groups are different programmed parameters
- Allows pt to choose/test up to four different programmed setting(s)
- Ex: Pts can change setting made in clinic and toggle back to a previous setting





New Interfaces for Programming







Parkinsonism and Related Disorders 31 (2016) 156–158

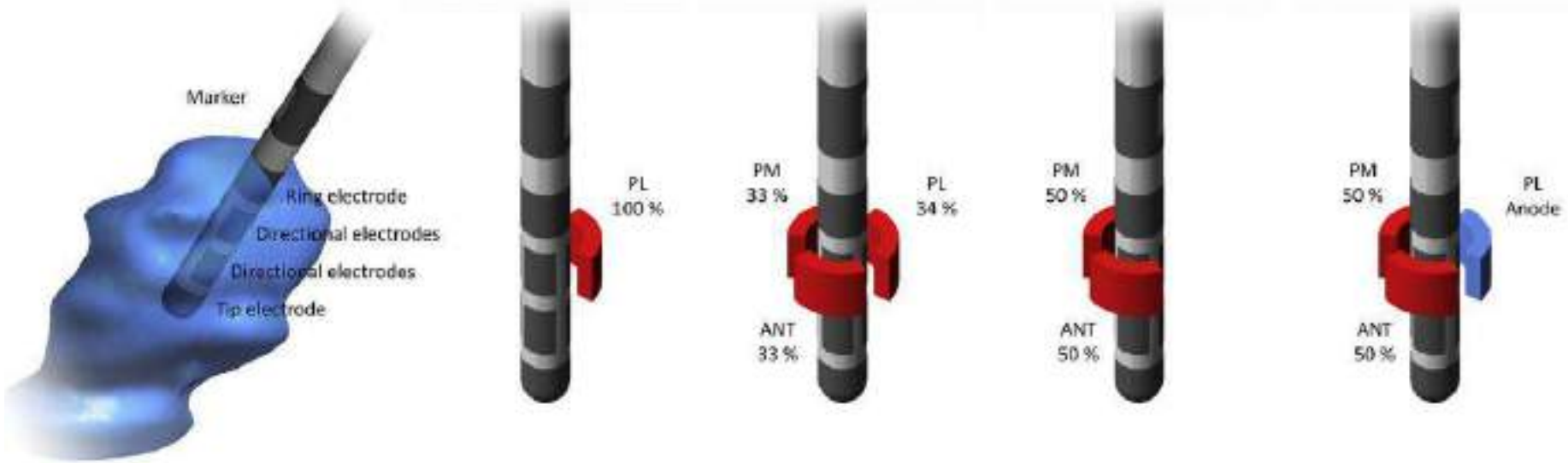
Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

Lead location and stimulation conditions

Reker P, et al



Condition	postero-lateral	circular	anterior + postero-medial	bipolar directional steering
Dysarthria threshold	2.9 mA	3.6 mA	3.9 mA	> 5.0 mA
Rigidity	not resolved	resolved	resolved	resolved
Bradykinesia	moderate	moderate	slight	minimal

Fig. 1. *Lead location and stimulation conditions.* On the left, the patient's individual left STN/substantia nigra with the final lead position is shown. The stereotactic coordinates of the examined row of directional electrodes were 12.8 mm lateral, 1.4 mm posterior and 4 mm ventral to the mid commissural point. The lead features two conventional ring electrodes (most ventral and most dorsal level) and two tripartite electrodes in a 1-3-3-1 design. Each electrode can be differentially activated with an independent current source. Visualization of stimulation direction is schematic and does not represent actual activation volume. Percentages represent fraction of total current distributed through each electrode. PL – posterolateral, ANT – anterior, PM – postero-medial.

Courtesy Jill Ostrem, U



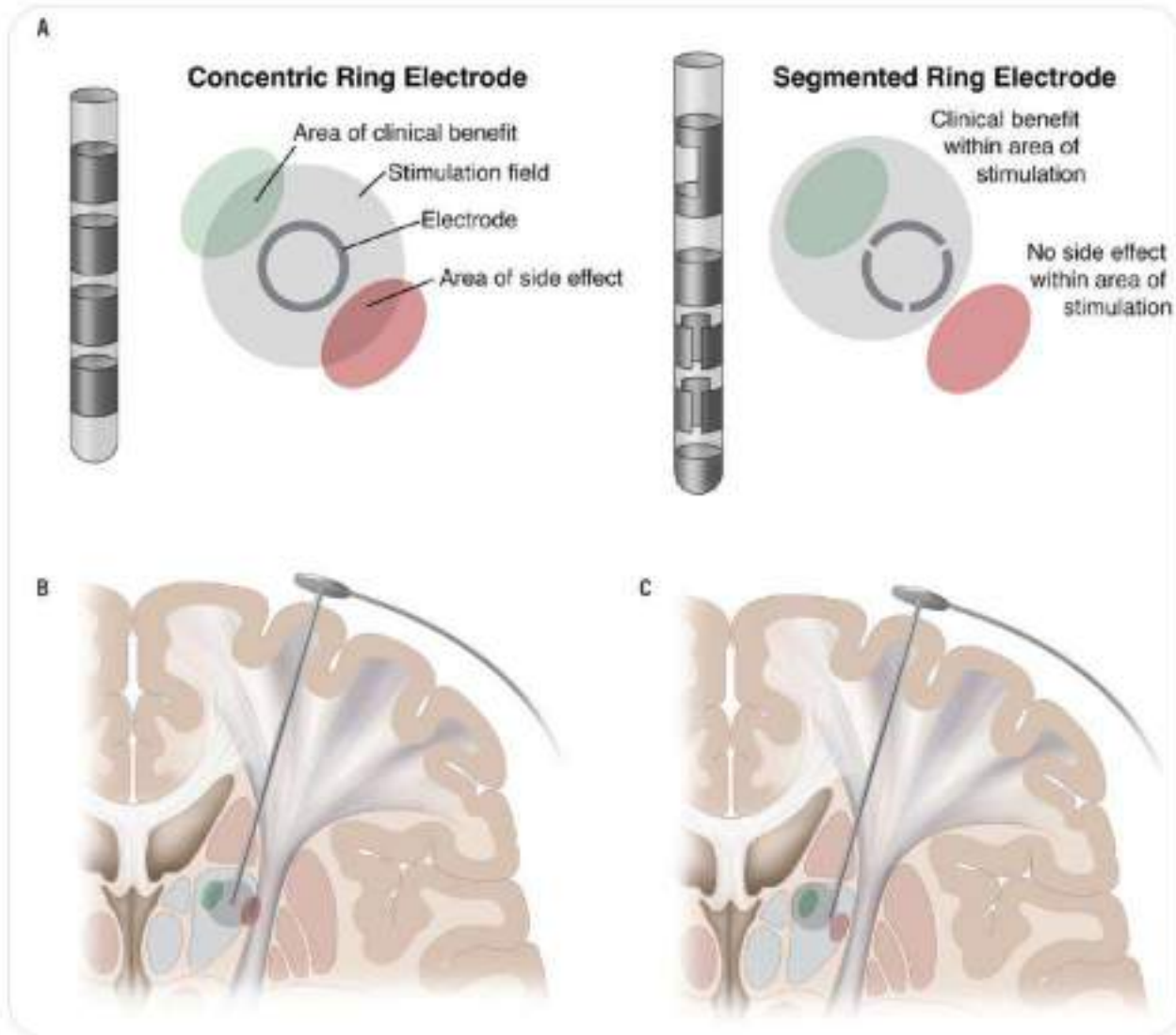
Michael Okun @MichaelOkun · Jun 11

Is **directional deep brain stimulation** programming the **bee's knees**? Is the segment clearly identifiable and stable over time? Spoiler alert: Nope. Karl, Verhagen and colleagues have a terrific new paper @MDCP_Journal.

Key Points:

- The authors noticed that when they programmed

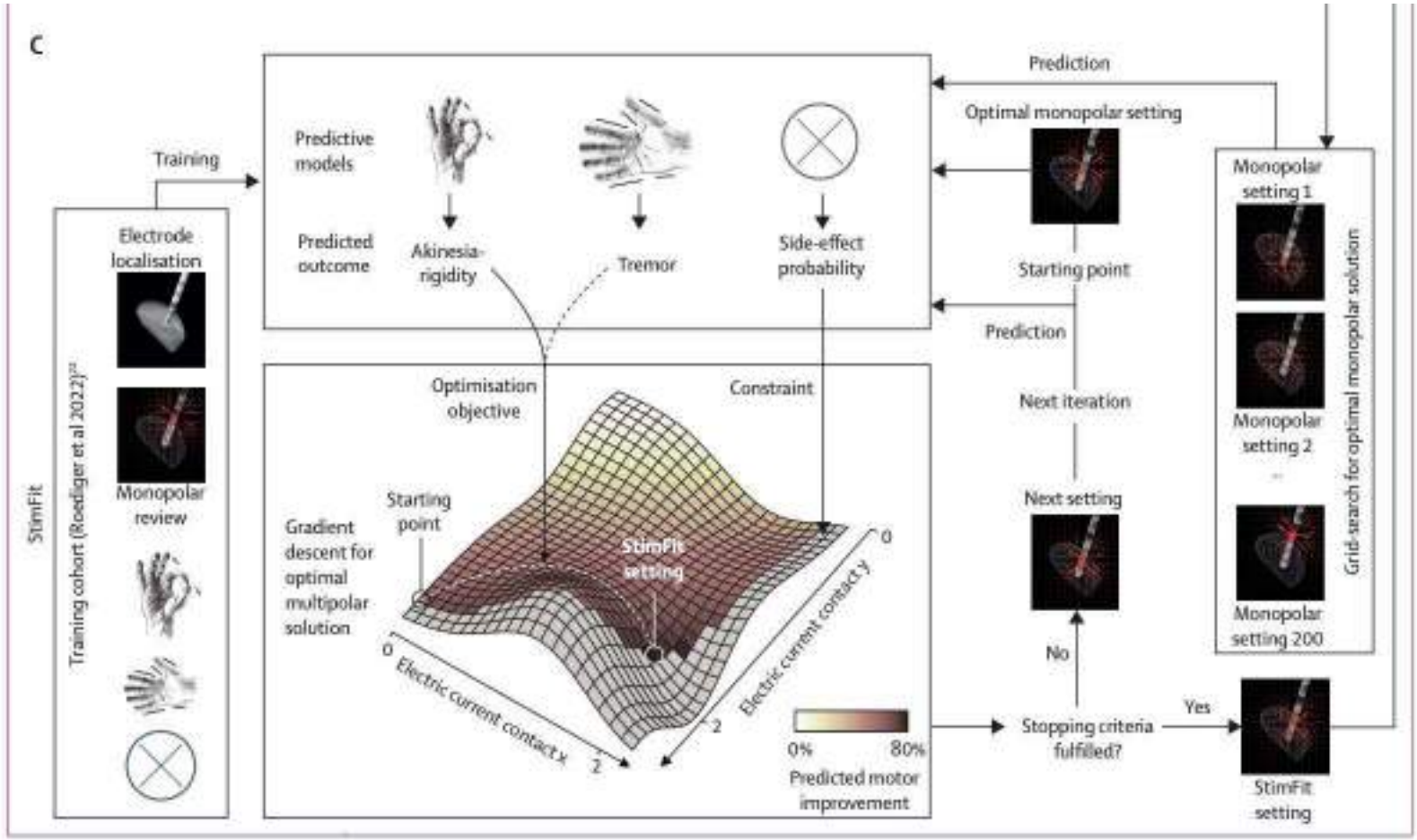
Show more



1 31 93 10K

Automated deep brain stimulation programming based on electrode location: a randomised, crossover trial using a data-driven algorithm

Jan Roediger, Till A. Dembek, Johannes Achtzehn, Johannes L. Busch, Anna-Pauline Krämer, Katharina Faust, Gerd-Helge Schneider, Patricia Krause, Andreas Horn, Andrea A. Kühn



‘No amount of expert programming can make up for a ‘suboptimally’ placed lead.’

Do not depend on segmentation, multiple current sources and other technologies to bail you out.



Brain Stimulation 16 (2023) 1249–1251

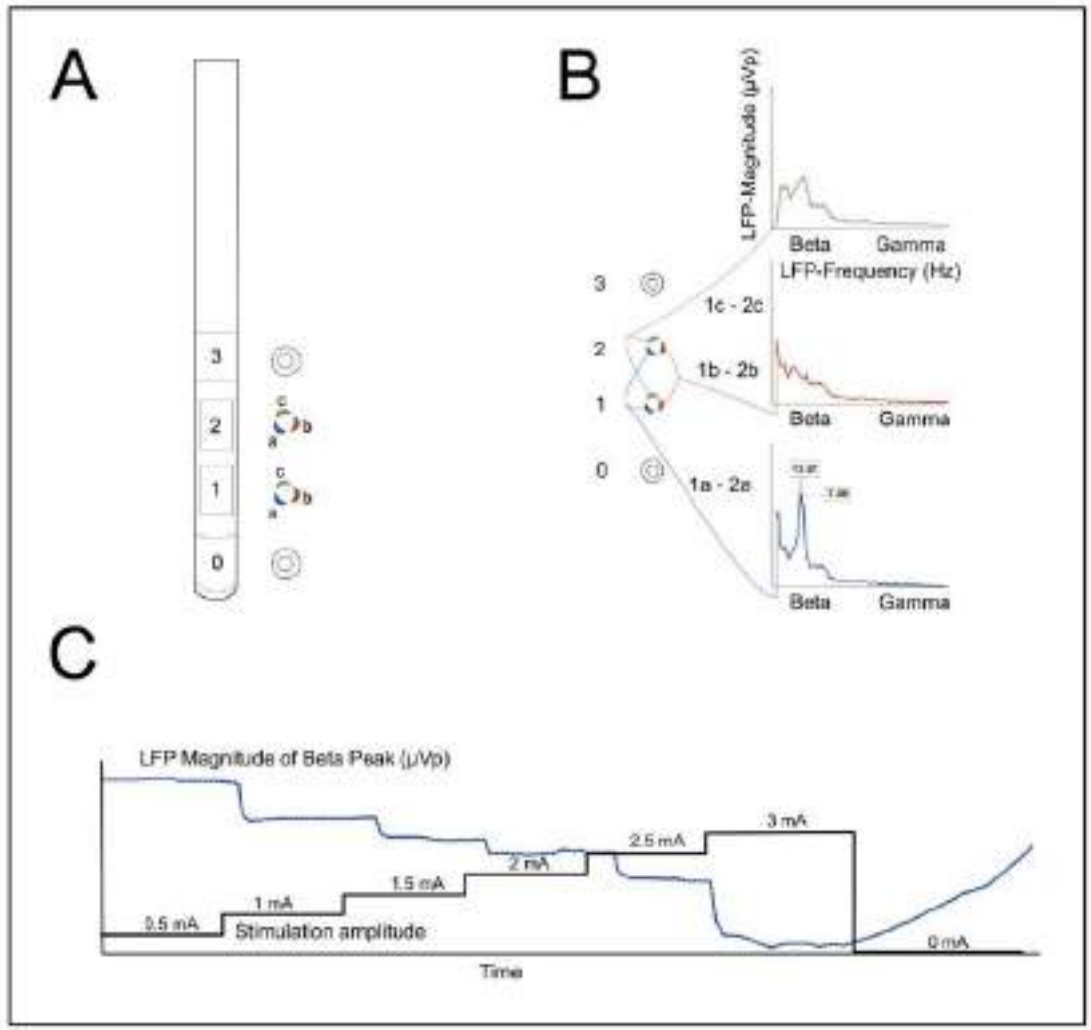
Contents lists available at ScienceDirect

Brain Stimulation

journal homepage: www.journals.elsevier.com/brain-stimulation

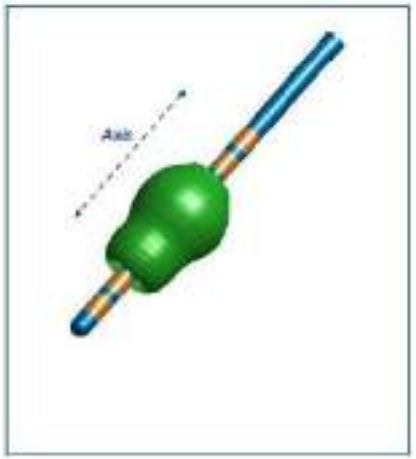
Feasibility of local field potential-guided programming for deep brain stimulation in Parkinson's disease: A comparison with clinical and neuro-imaging guided approaches in a randomized, controlled pilot trial

Tobias Binder [a,1], Florian Lange [a,*,1], Nicolò Pozzi [a], Thomas Musacchio [a], Christine Daniels [a], Thorsten Odorfer [a], Patrick Fricke [b], Cordula Matthies [b], Jens Volkmann [a], Philipp Capetian [a]



Novel Mode of DBS Stimulation

Current Shaping



Multiple-source current steering in subthalamic nucleus deep brain stimulation for Parkinson's disease (the VANTAGE study): a non-randomised, prospective, multicentre, open-label study

(Lancet Neurology, 2015)

Lars Timmermann, Roshini Jain, Lilly Chen, Mohamed Maarouf, Michael T Barbe, Niels Allert, Thomas Brücke, Iris Kaiser, Sebastian Beirer, Fernando Sejio, Esther Suarez, Beatriz Lazano, Claire Haegelen, Marc Vérin, Mauro Porta, Domenico Servello, Steven Gill, Alan Whone, Nic Van Dyck, Francois Alesch

- Vantage Study (N=40) (Boston Scientific device)
- 8 independently powered contact constant-current electrodes
- Fractioned constant current stimulation over multiple electrodes
- Separate frequencies per lead possible
- 64% UPDRS III improvement

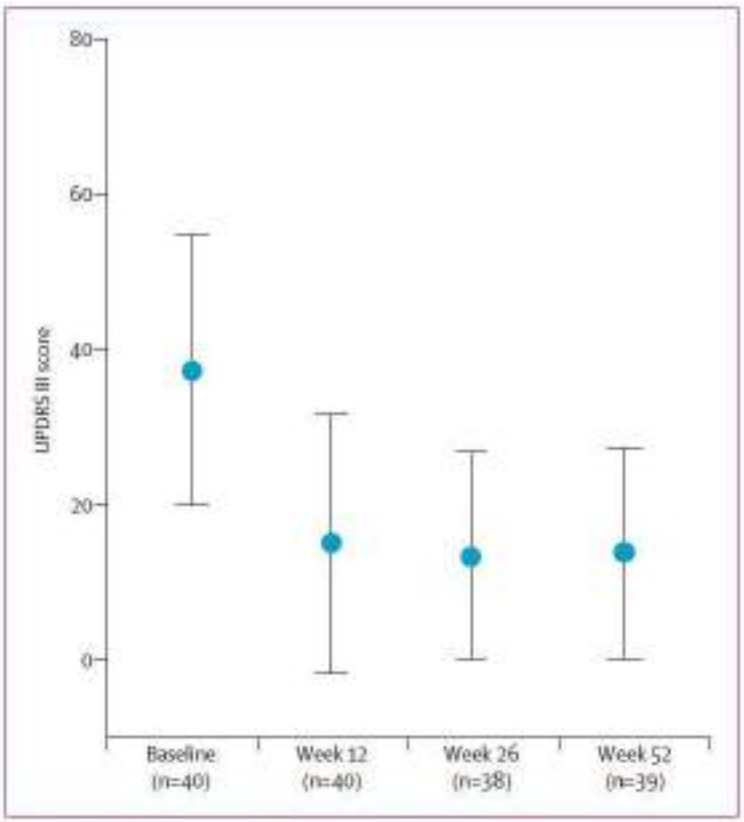
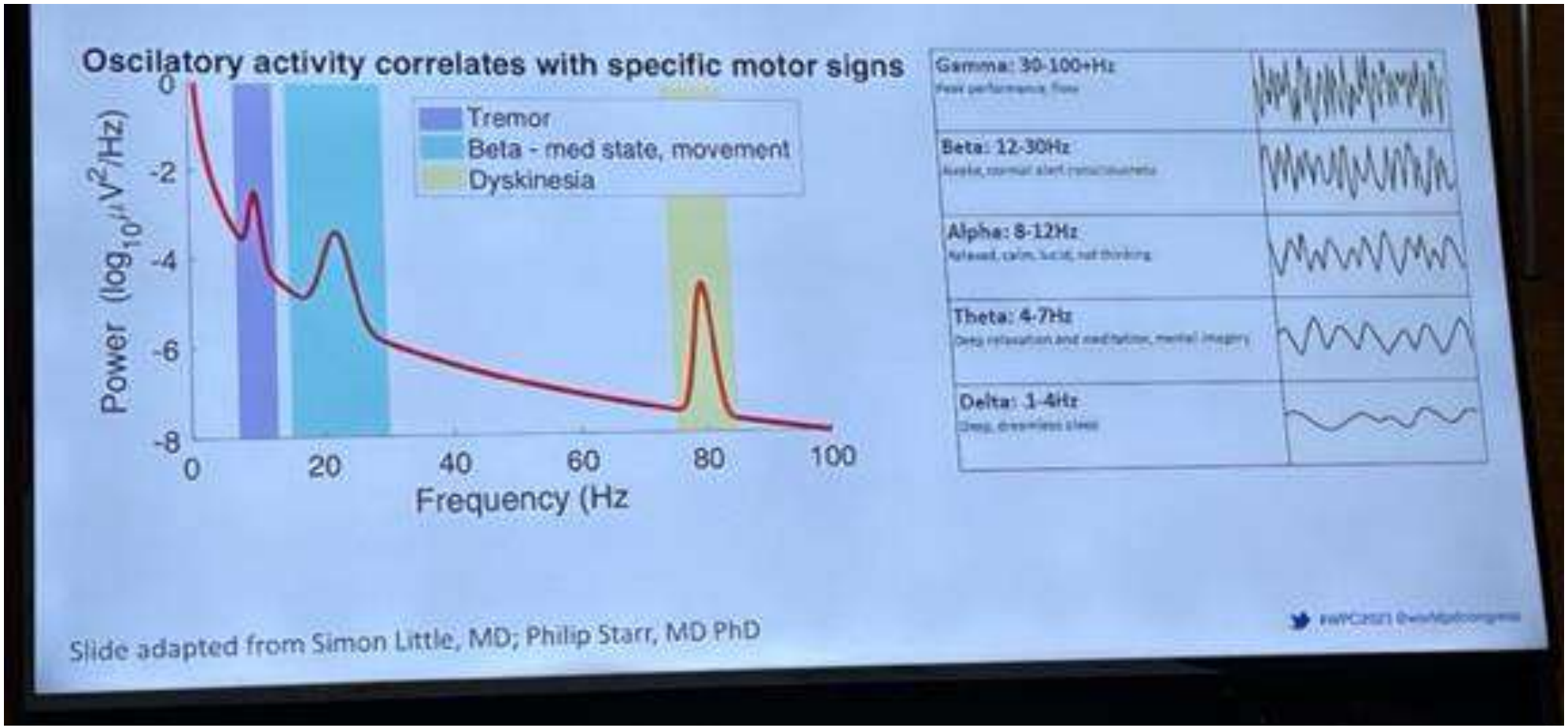


Figure 2: UPDRS III scores at baseline and 12, 26 (primary outcome), and 52 weeks after lead placement
UPDRS III scores range from 0 to 108; low scores represent better results. Dots represent mean scores, error bars represent SD.

Also with three year follow-up data now presented in abstract (Neurosurgery 2016 supplement)

Courtesy Jill Ostrem, U

Physiology based programming (for some)



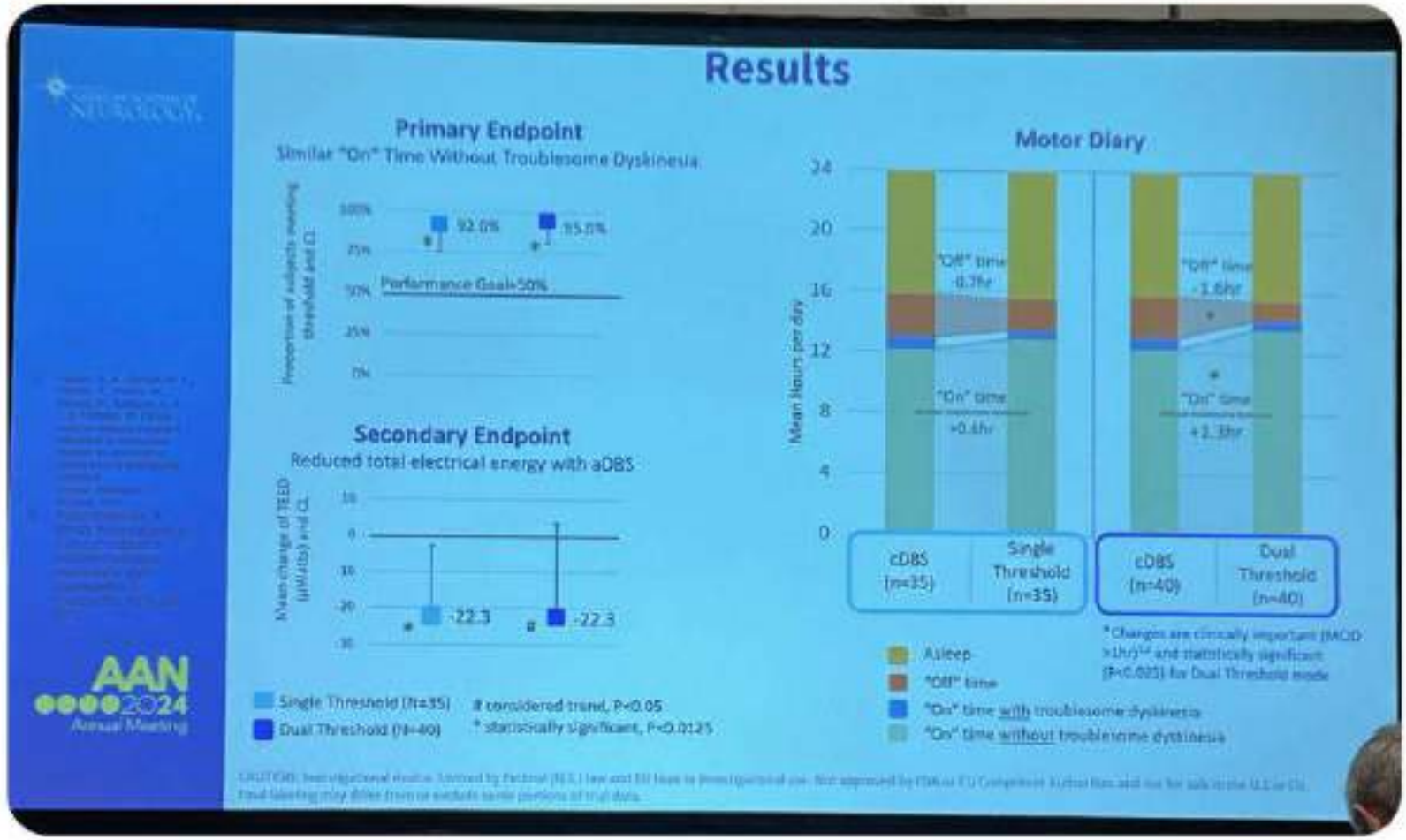
Jill Ostrem 2023 World Parkinson Congress



Michael Okun @MichaelOkun · Apr 14

ADAPT DBS closed loop Parkinson trial results announced today by presentation @AANmember by Helen Brontë-Stewart. It was a positive t and met pre-specified FDA outcomes. Will it be heading to the clinic soo Next steps will be a full publication and submission to FDA





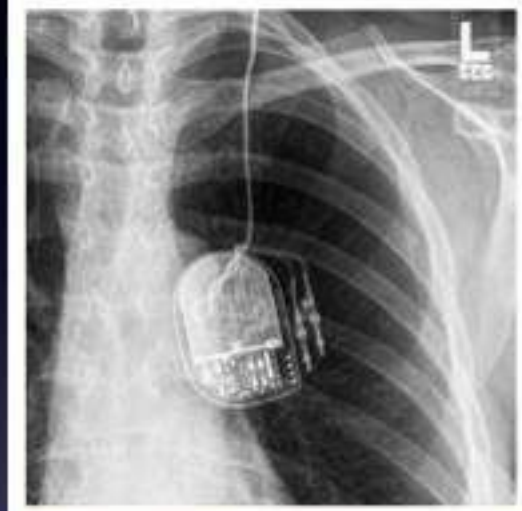
3 19 45 4.5K


FDA Approves First Adaptive DBS System for Parkinson's

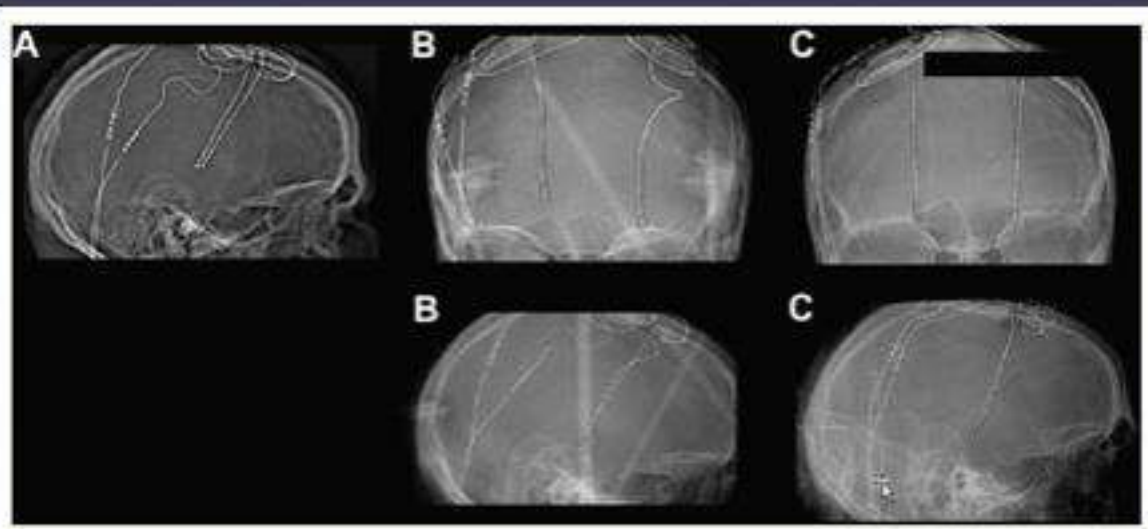


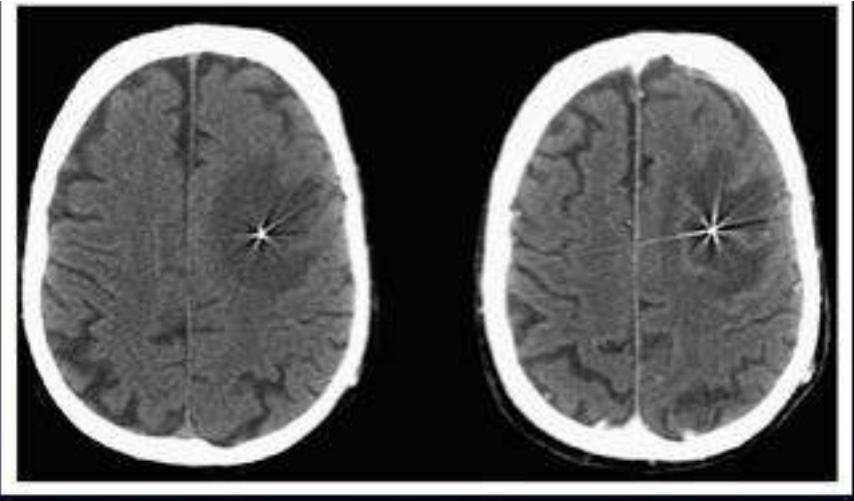
Jill Ostrem 2023 World Parkinson Congress

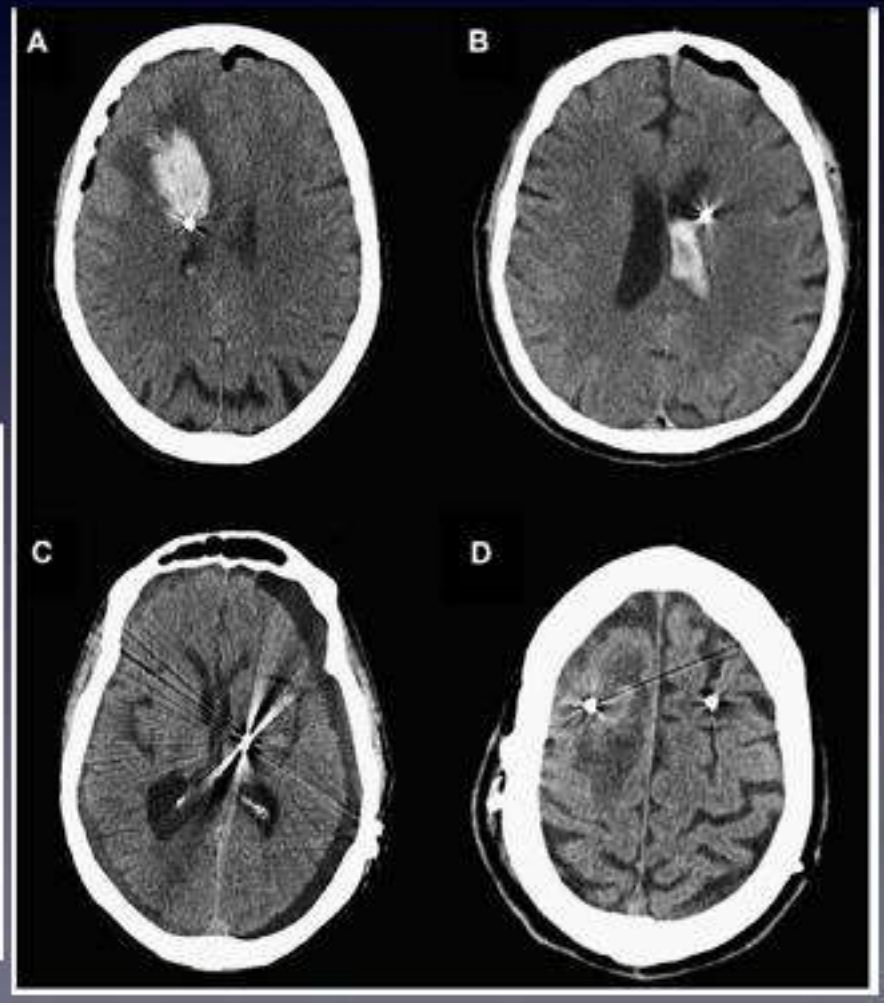
There are Complications Even at the Expert Centers



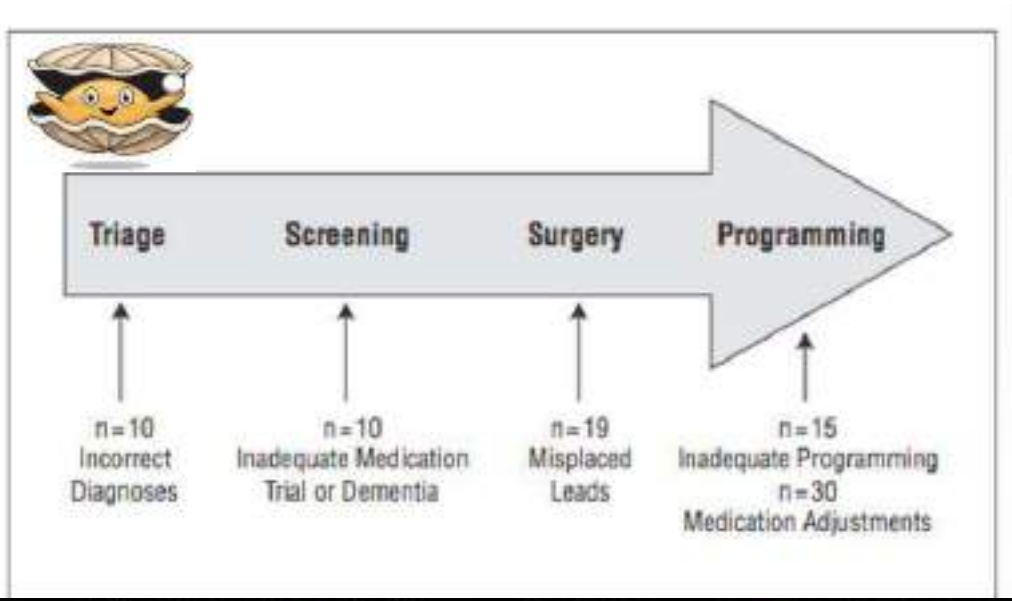


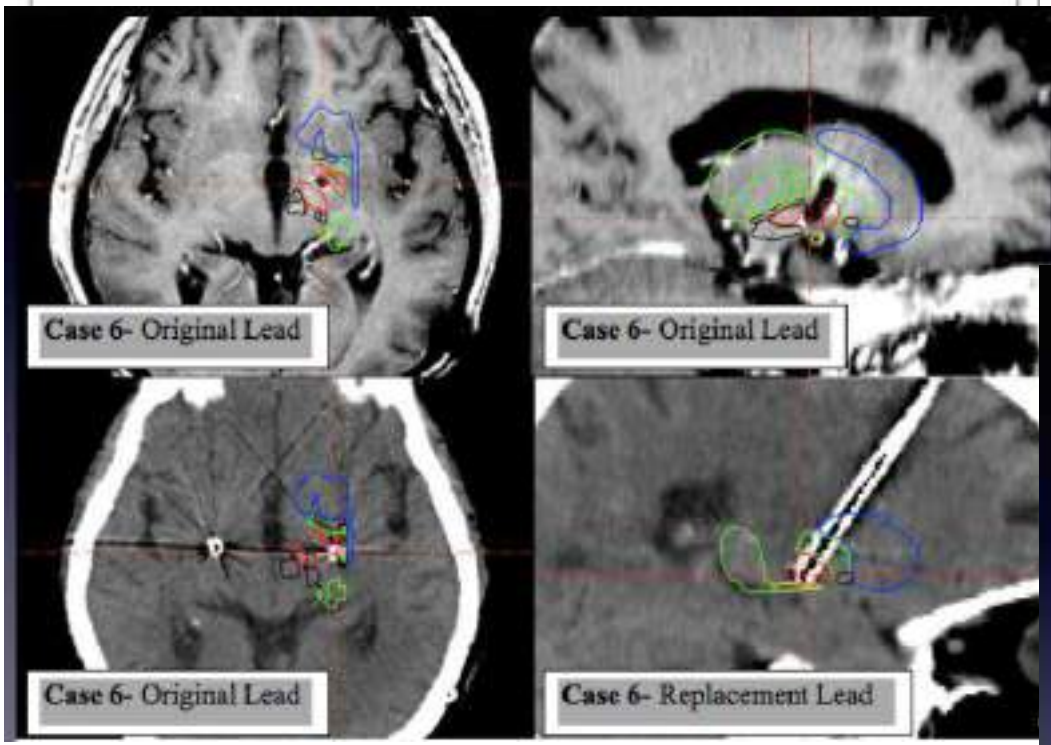






Troubleshoot if Suboptimal Outcome





ORIGINAL CONTRIBUTION

Management of Referred Deep Brain Stimulation Failures

A Retrospective Analysis From 2 Movement Disorders Centers



Even Expert Centers Can Miss- Targets are Very Small



CLINICAL STUDIES

Reoperation for Suboptimal Outcomes after Deep Brain Stimulation Surgery

Limbic, Associative, and Motor Territories Within the Targets for Deep Brain Stimulation: Potential Clinical Implications

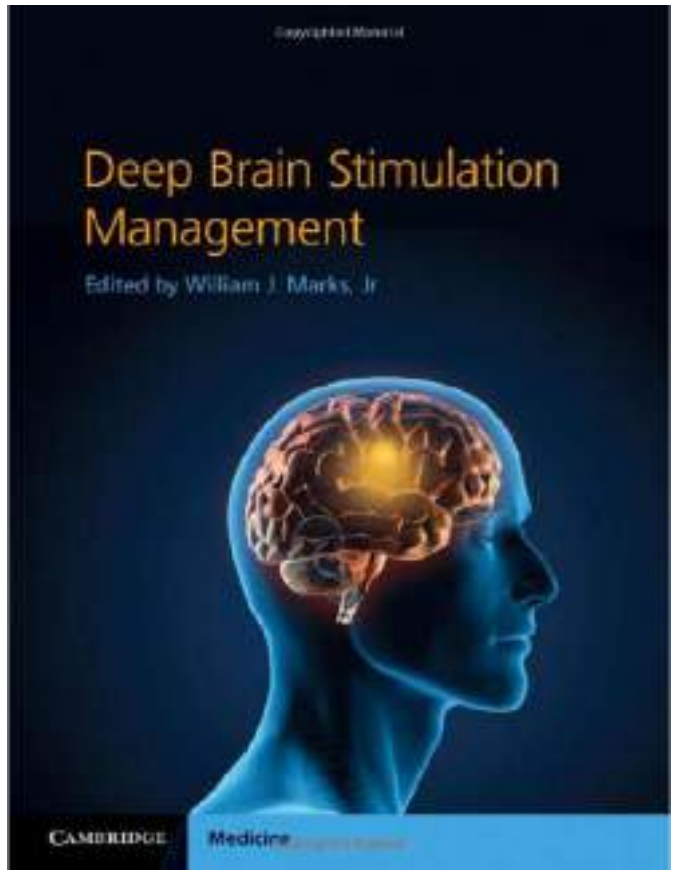
Ashar Sudhyadhom, MS, Frank J. Bova, PhD, Kelly D. Foote, MD, Christian A. Rosado, BS, Lindsey Kirsch-Darrow, MS, and Michael S. Okun, MD



Complications



- Hemorrhage 1-5%
- Infections (immediate/delayed) 3-20%
- Delayed Erosions >5%
- Delayed Venous Infarctions <1%
- Seizure 3%
- Pneumonia <1%
- Air Embolus (cough) 3.2%



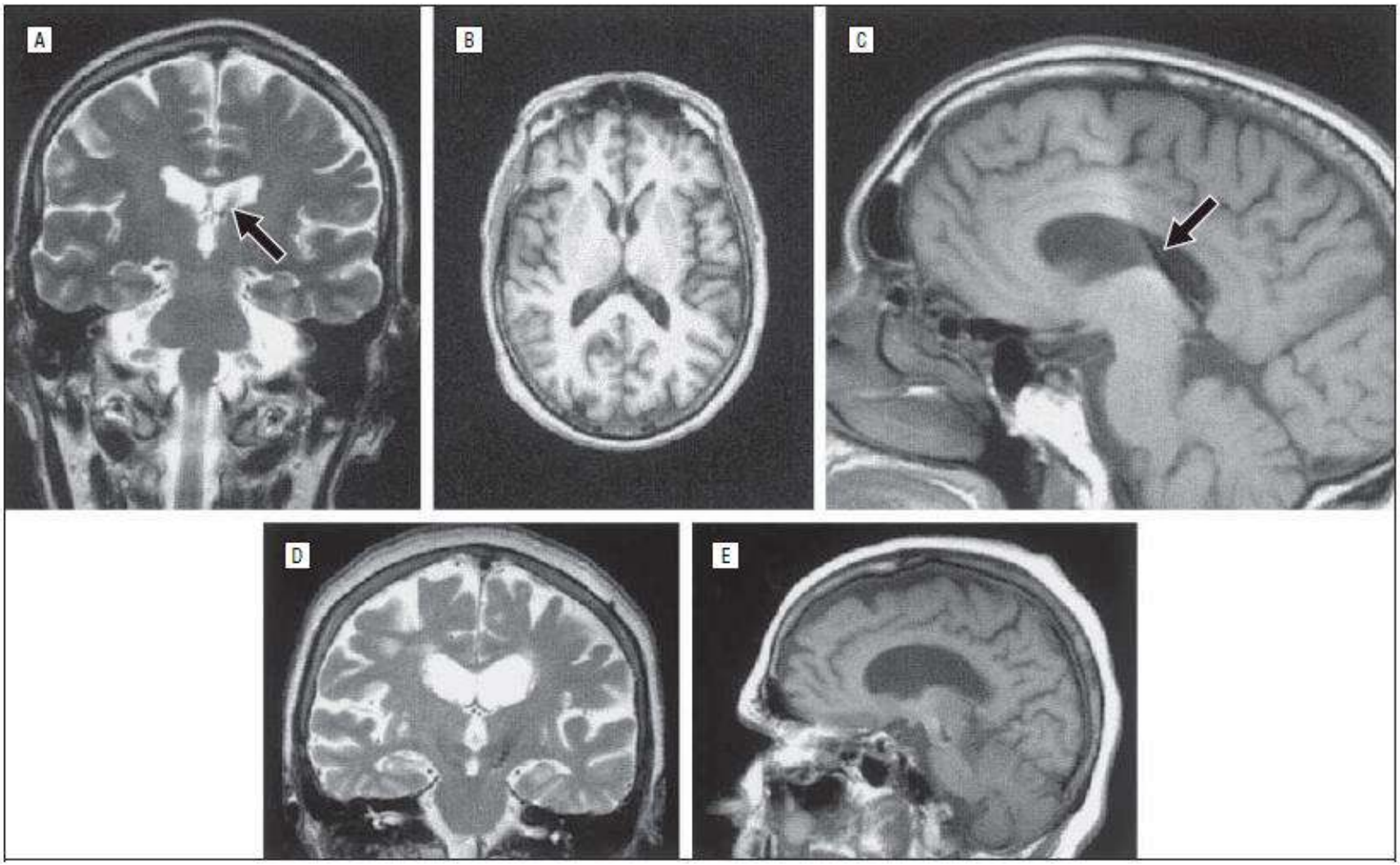
Neuropsychiatric/Neuropsychological/Other Complications
*2 leads >1 rule and “Walking, Talking, Thinking, Feeling”

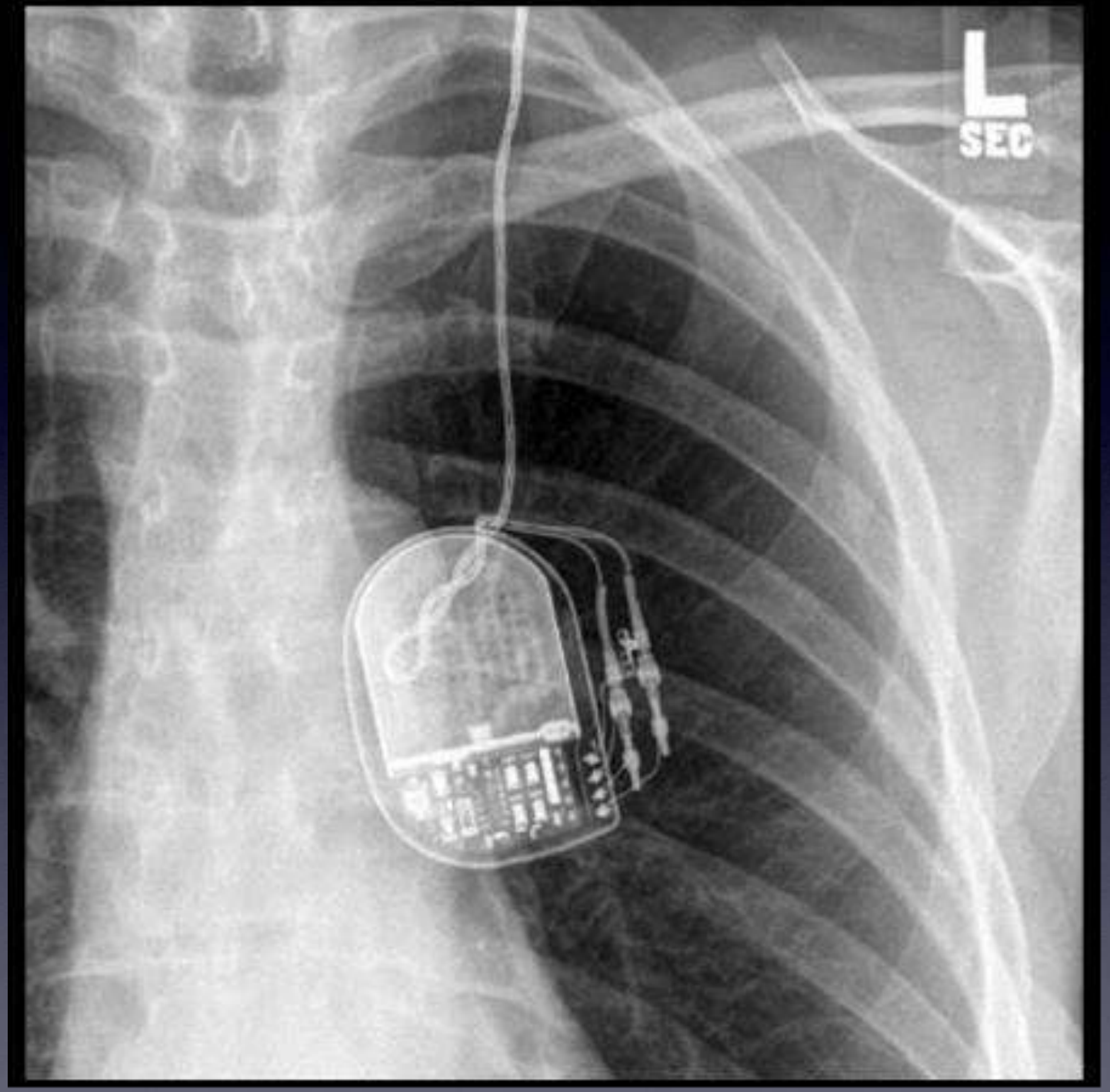
- Depressive symptoms
- Apathy (medication reduction)
- Anger (related penetrations?)
- Suicide attempts/ideation (may be on decline/screening)
- Anxiety/Panic
- Mania (hypomania)
- Pseudobulbar Affect
- Laughter
- Smiling
- ICD





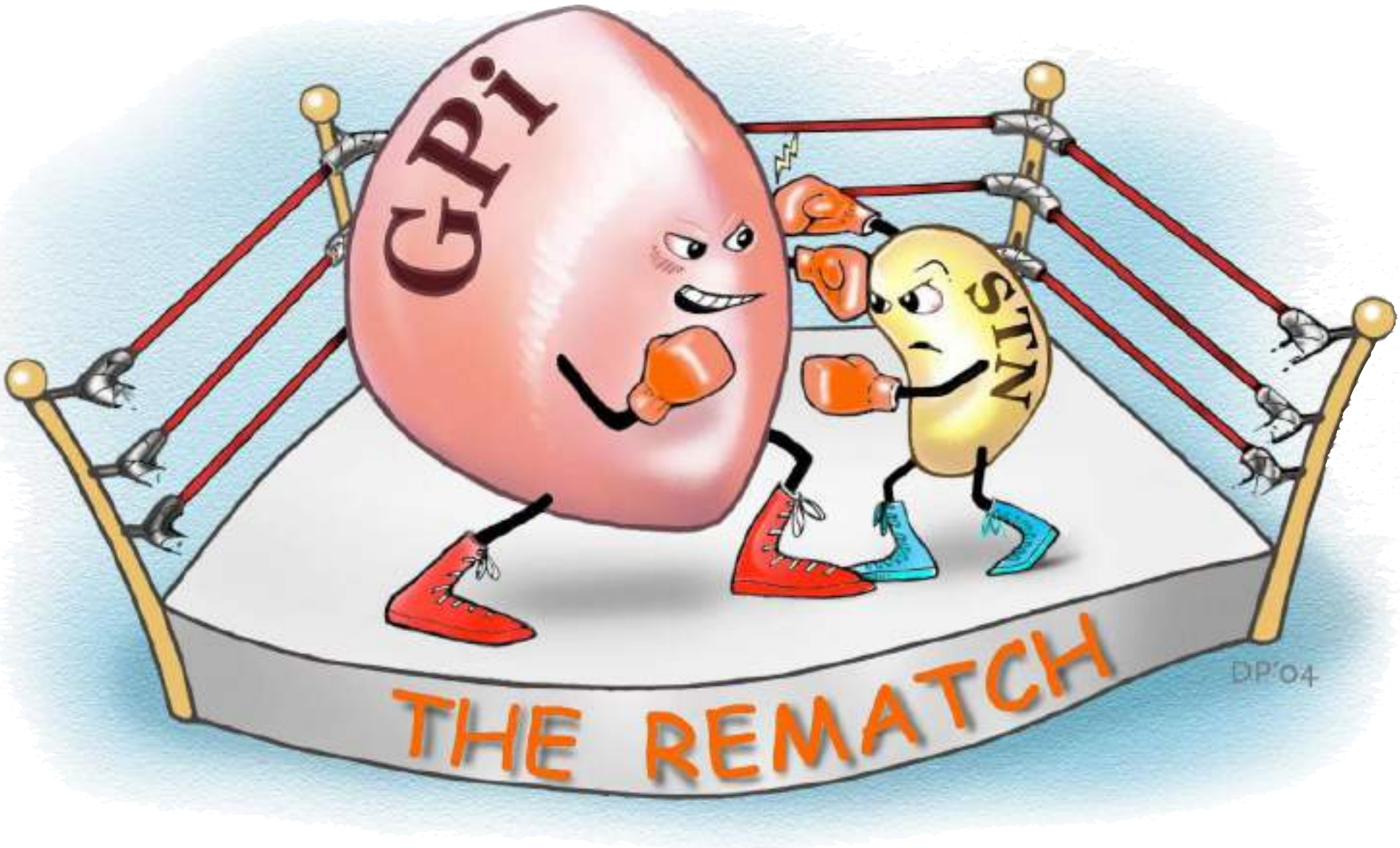
Take a Picture After the Operation




L
SEC

Surgical Treatment of Parkinson's Disease

- Why Apply Electricity to the Brain?
- How Does DBS Work?
- Patient Selection
- Differences in Surgical Approach
- Programming and Medications
- Measuring Outcomes
- Evolving Technologies


GPi
STN
THE REMATCH
DP'04

Randomized Studies
Do they inform us?

Cognition and Mood in Parkinson's Disease in Subthalamic Nucleus versus Globus Pallidus Interna Deep Brain Stimulation: The COMPARE

Michael S. Okun, MD, Hubert H. Fernandez, MD, Samuel S. Wu, Dawn Bowers, PhD, Frank Bova, PhD, Michele Suelter, BS, Charles E. Clifford W. Gordon, Jr., BS, Pam Zeilman, ARNP, Janet Rom Herbert Ward, MD, Ramon L. Rodriguez, MD, and

THE LANCET Neurology

Volume 12, Issue 1, January 2013, Pages 37–44



Articles

Subthalamic nucleus versus globus pallidus bilateral deep brain stimulation for advanced Parkinson's disease (NSTAPS study): a randomised controlled trial

Vincent JJ Odekerken, MD[a], Teus van Laar, MD[d], Michiel J Staal, MD[e], Arne Mosch, MD[f], Carel FE Hoffmann, MD[g], Peter CG Nijssen, MD[h], Guus N Beute, MD[i], Jeroen PP van Vugt, MD[j], Mathieu WPM Lenders, MD[k], M Fiorella Contarino, MD[a], Marieke SJ Mink, MSc[a], Lo J Bour, PhD[a], Pepijn van den Munckhof, MD[b], Prof Ben A Schmand, PhD[a, l], Prof Rob J de Haan, PhD[c], P Richard Schuurman, MD[b], Rob MA de Bie, MD[a]



The NEW ENGLAND JOURNAL of MEDICIN

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ORIGINAL ARTICLE

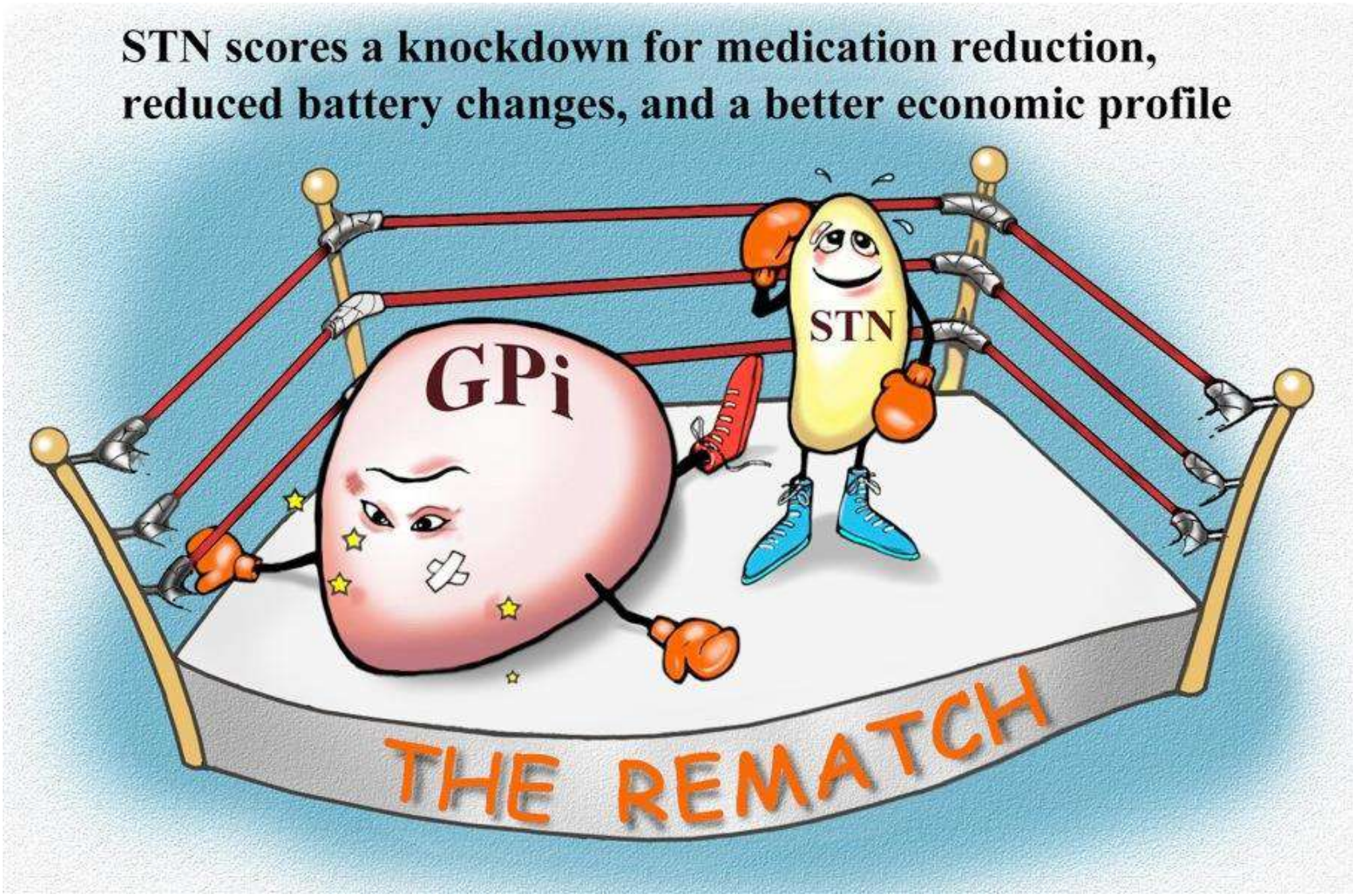
A Correction

Pallidal versus Subthalamic Deep-Brain Stimulation Parkinson's Disease

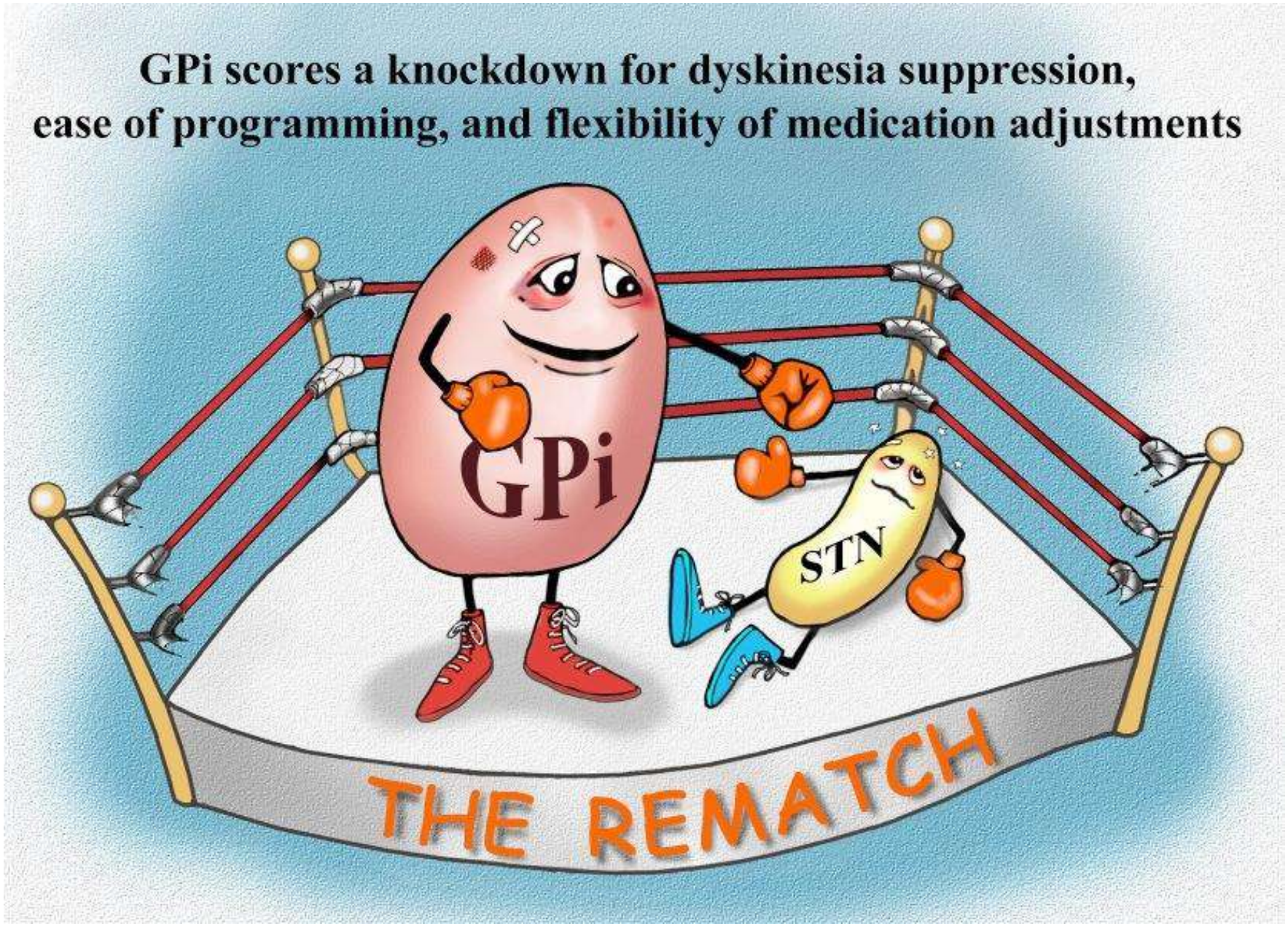
Kenneth A. Follett, M.D., Ph.D., Frances M. Weaver, Ph.D., Matthew Stern, M.D., Kwan Hur, Ph.D., Crystal L. Harris, Pharm.D., Ping Luo, Ph.D., William J. Marks, Jr., M.D., Johannes Rothlind, Ph.D., Oren Sagher, M.D., Claudia Moy, Ph.D., Rajesh Pahwa, M.D., Kim Burchiel, M.D., Penelope Hogarth, M.D., Eugene C. Lai, M.D., Ph.D., John E. Duda, M.D., Kathryn Holloway, M.D., Ali Samii, M.D., Stacy Horn, D.O., Jeff M. Bronstein, M.D., Ph.D., Gatana Stoner, R.N., C.C.R.C., Philip A. Starr, M.D., Ph.D., Richard Simpson, M.D., Ph.D., Gordon Baltuch, M.D., Ph.D., Antonio De Salles, M.D., Ph.D., Grant D. Huang, Ph.D., and Domenic J. Reda, Ph.D. for the CSP 468 Study Group

N Engl J Med 2010; 362:2077-2091 | June 3, 2010 | DOI: 10.1056/NEJMoa0907083

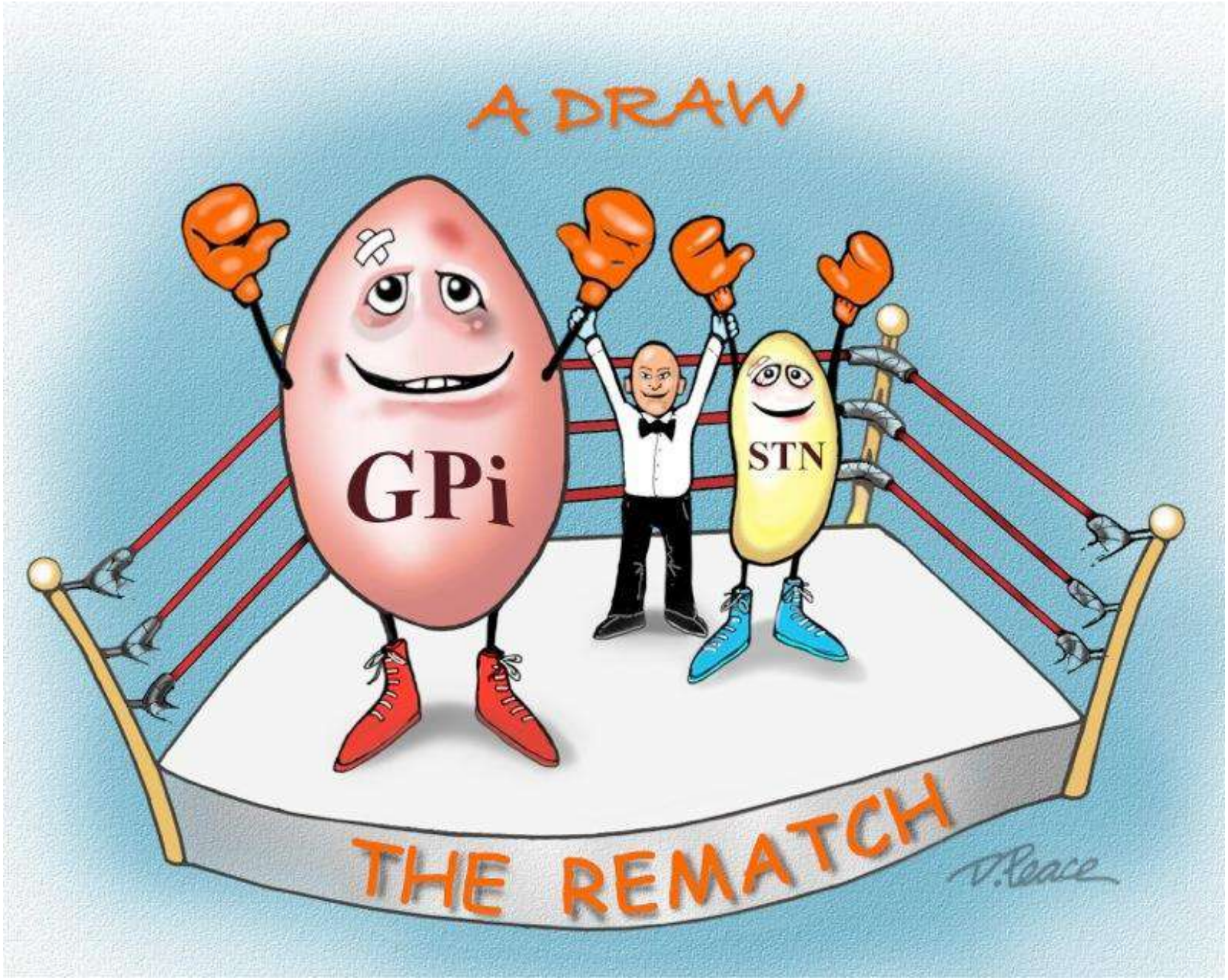
Movement Disorders
CLINICAL PRACTICE



Movement Disorders
CLINICAL PRACTICE



Movement Disorders
CLINICAL PRACTICE



Movement Disorders
CLINICAL PRACTICE

Table 2: 2013 Summary Scorecard for the STN vs. GPi Rematch

	Bilateral GPi	Unilateral GPi	Bilateral STN	Unilateral STN
Mood/Behavior	+	+		
Off-Period Motor Symptoms	+	+	+	+



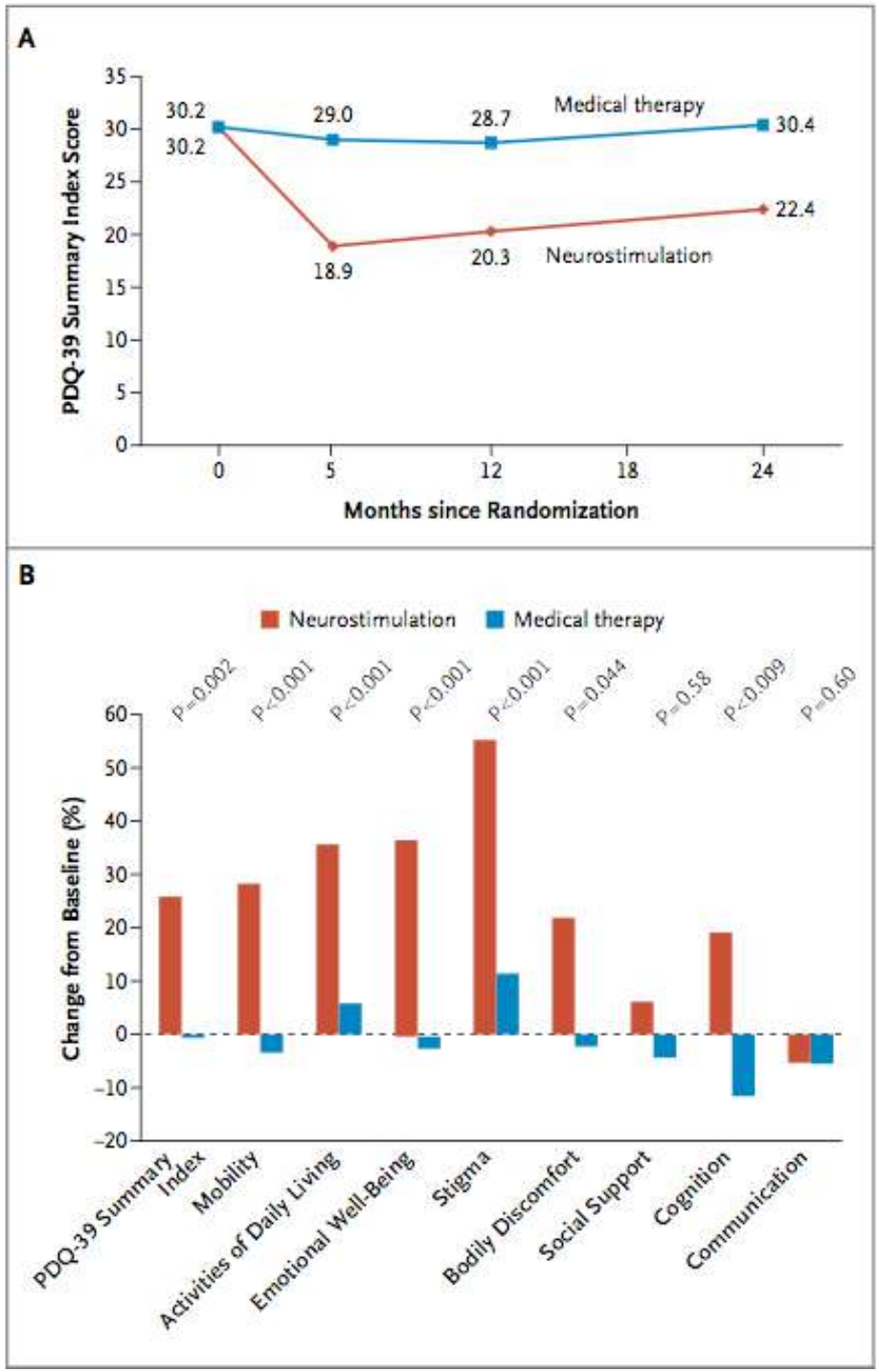
Legend: + slight or possible advantage; ++ definite advantage

Will the future mean earlier?

ORIGINAL ARTICLE

Neurostimulation for Parkinson's Disease with Early Motor Complications

W.M.M. Schuepbach, J. Rau, K. Knudsen, J. Volkmann, P. Krack, L. Timmermann, T.D. Hälbig, H. Hesekamp, S.M. Navarro, N. Meier, D. Falk, M. Mehdorn, S. Paschen, M. Maarouf, M.T. Barbe, G.R. Fink, A. Kupsch, D. Gruber, G.-H. Schneider, E. Seigneuret, A. Kistner, P. Chaynes, F. Ory-Magne, C. Brefel Courbon, J. Vesper, A. Schnitzler, L. Wojtecki, J.-L. Houeto, B. Bataille, D. Maltête, P. Damier, S. Raoul, F. Sixel-Doering, D. Hellwig, A. Gharabaghi, R. Krüger, M.O. Pinsker, F. Amtage, J.-M. Régis, T. Witjas, S. Thobois, P. Mertens, M. Kloss, A. Hartmann, W.H. Oertel, B. Post, H. Speelman, Y. Agid, C. Schade-Brittinger, and G. Deuschl, for the EARLYSTIM Study Group*


A
PDQ-39 Summary Index Score
Months since Randomization
Medical therapy
Neurostimulation
30.2
30.2
29.0
28.7
30.4
18.9
20.3
22.4
B
Neurostimulation
Medical therapy
Change from Baseline (%)
P=0.002
P<0.001
P<0.001
P<0.001
P<0.001
P=0.044
P=0.58
P<0.009
P=0.60
PDQ-39 Summary Index
Mobility
Activities of Daily Living
Emotional Well-Being
Stigma
Bodily Discomfort
Social Support
Cognition
Communication

Parkinsonism and Related Disorders 96 (2022) 13–17

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

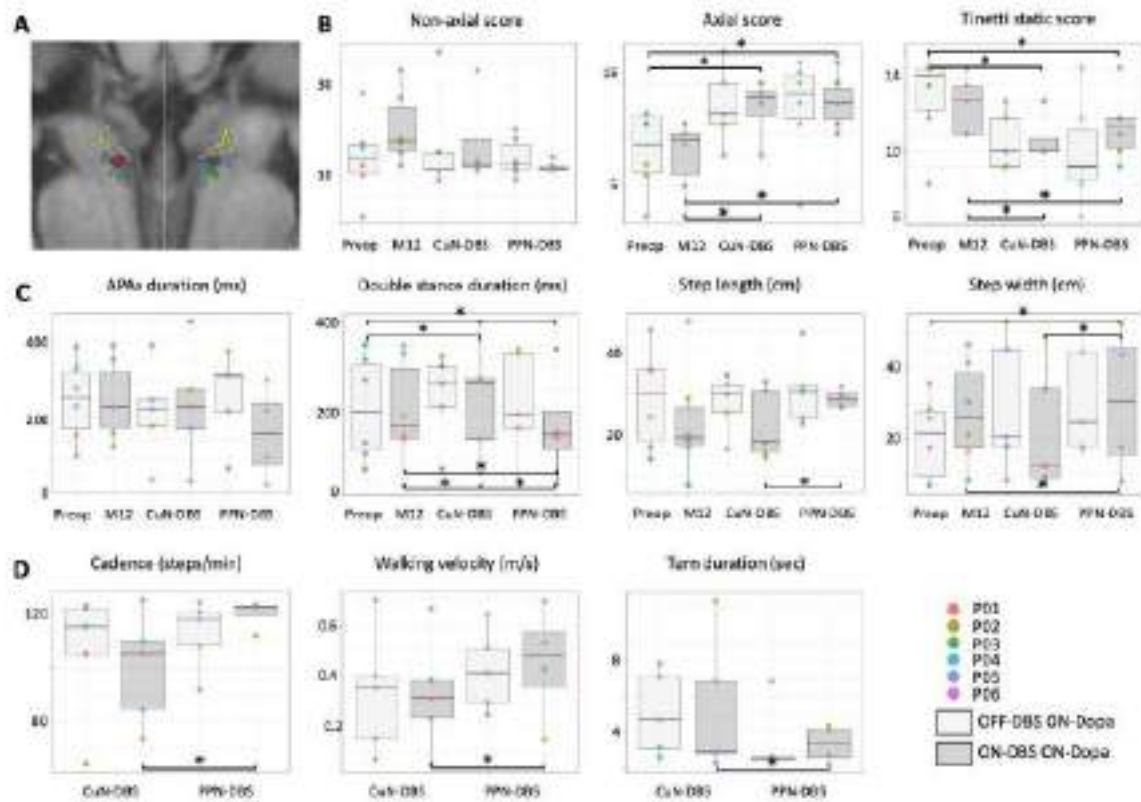
journal homepage: www.elsevier.com/locate/parkreldis

Short communication

Stimulation of the pedunculopontine and cuneiform nuclei for freezing of gait and falls in Parkinson disease: Cross-over single-blinded study and long-term follow-up

Julie Bourilhon [a,b,1], Yannick Mullie [b,1], Claire Olivier [b], Saoussen Cherif [b], Hayat Belaid [c], David Grabli [b], Virginie Czernecki [c], Carine Karachi [b,c], M...

[a] Service de Neurophysiologie Clinique, CHU Rouen, Université de Normandie, F-76000, Rouen, Fra
[b] Institut du Cerveau, INSERM U1127, Pitié-Salpêtrière Hospital, F-75013, Paris, France
[c] Service de Neurochirurgie, Pitié-Salpêtrière Hospital, APHP, F-75013, Paris, France



- Not improve dopa resistant gait and balance disorders

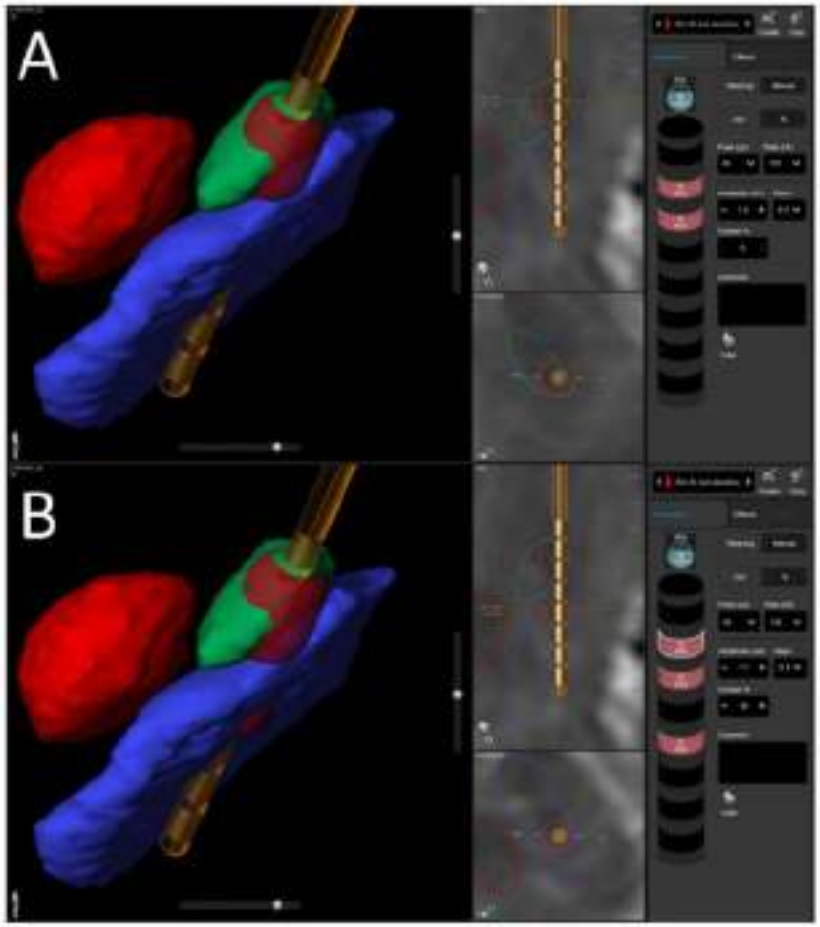
Journal of
Clinical Medicine

MDPI

Article

Combined Stimulation of the Substantia Nigra and the Subthalamic Nucleus for the Treatment of Refractory Gait Disturbances in Parkinson's Disease: A Preliminary Study

Marta Villadóniga [1], Lidia Cabañes-Martínez [1,*], Laura López-Viñas [1], Samira Fanjul [2], Marta del Álamo [3] and Ignacio Regidor [1]



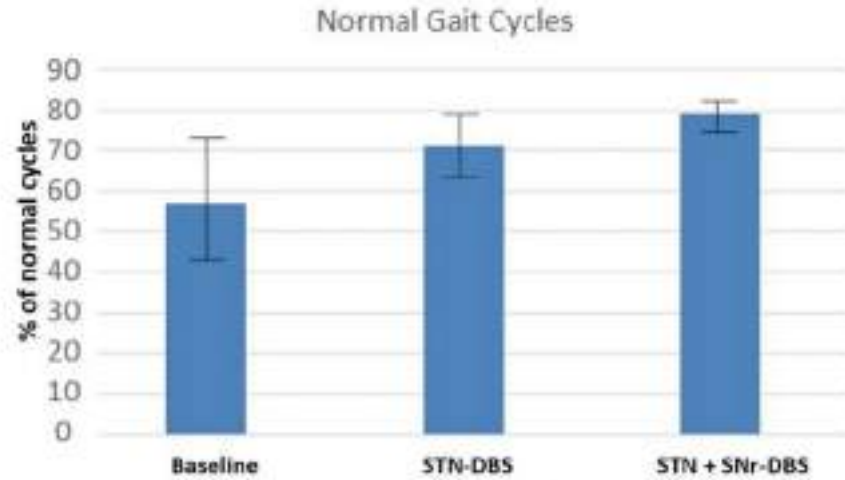


Figure 4. Differences of mean between baseline and the different STN parameters in percentage of cycles with the right sequence (HFPS). STN: Subthalamic nucleus stimulation; STN + SNR: Dual Subthalamic and nigral stimulation.

‘Evolve The Technology to Reach More People’

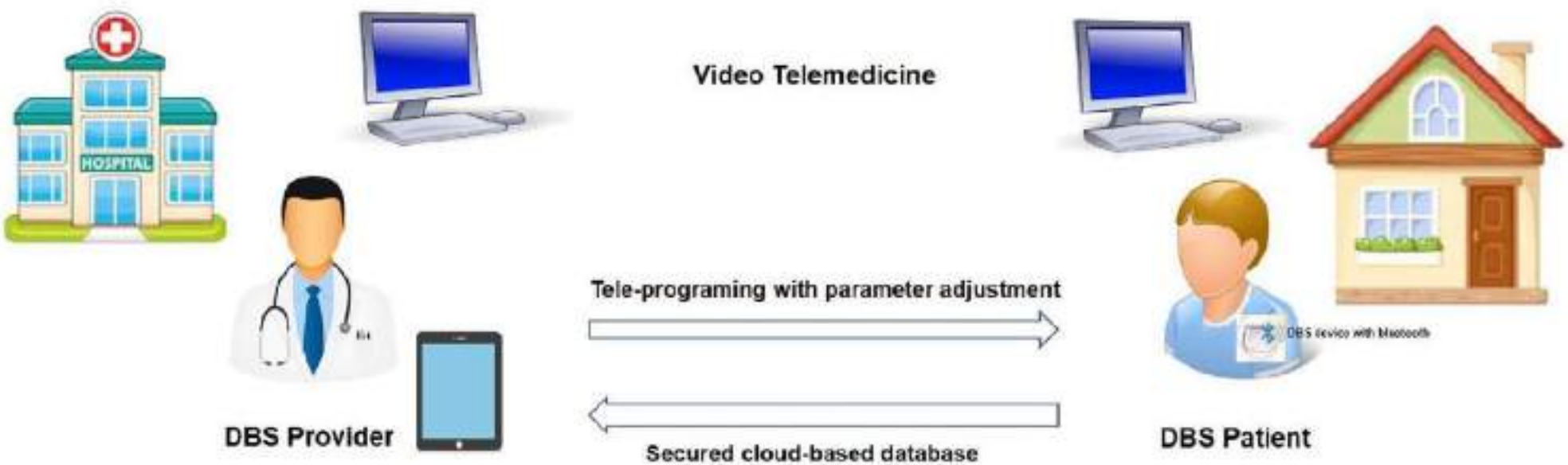
Chronic invasive brain sensing at home.



Implementation of a Novel Bluetooth Technology for Remote Deep Brain Stimulation Programming: The Pre– and Post–COVID-19 Beijing Experience







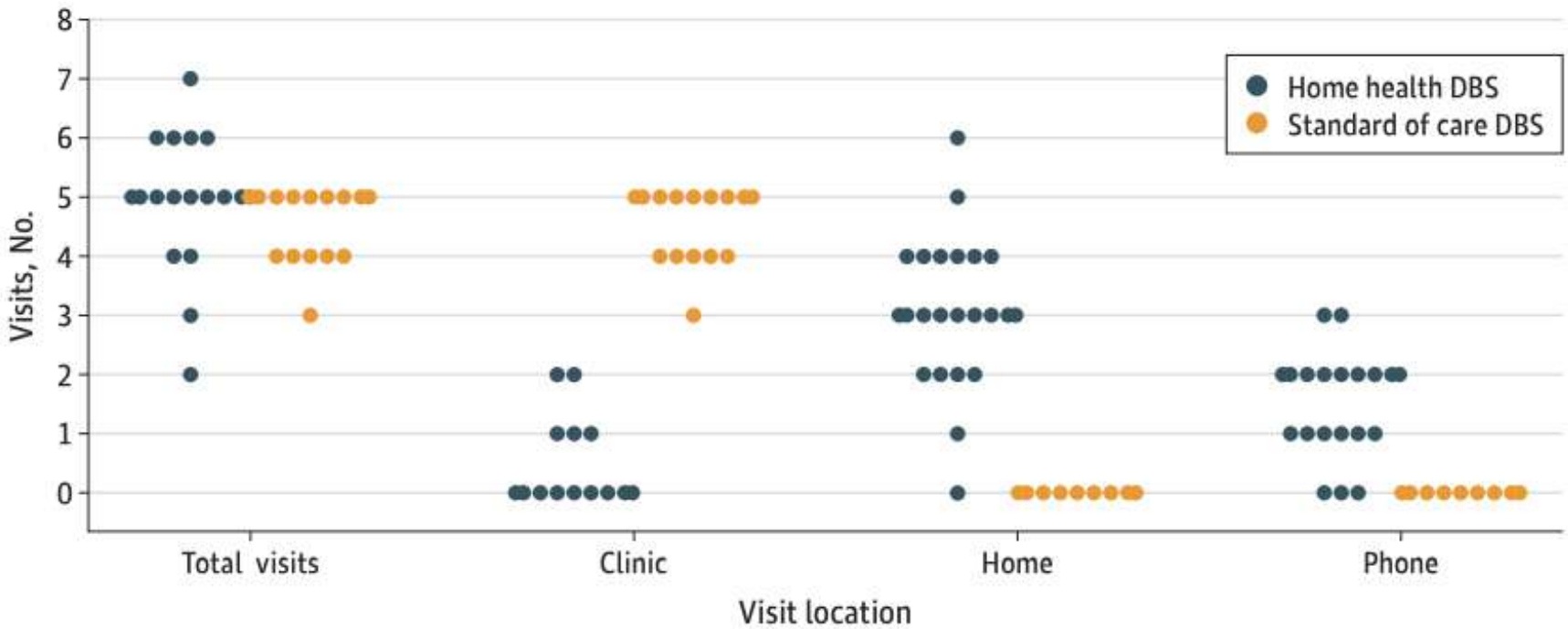
JAMA Neurology | Original Investigation

Home Health Management of Parkinson Disease Deep Brain Stimulation
A Randomized Clinical Trial

Gordon Duffley, PhD; Barbara J. Lutz, PhD; Aniko Szabo, PhD; Adrienne Wright, RN; Christopher W. Hess, MD; Adolfo Ramirez-Zamora, MD; Pamela Zeilman, ARNP; Shannon Chiu, MD; Kelly D. Foote, MD; Michael S. Okun, MD; Christopher R. Butson, PhD



Figure 2. Deep Brain Stimulation (DBS) Postoperative Management Visit Types Grouped by Study Arm

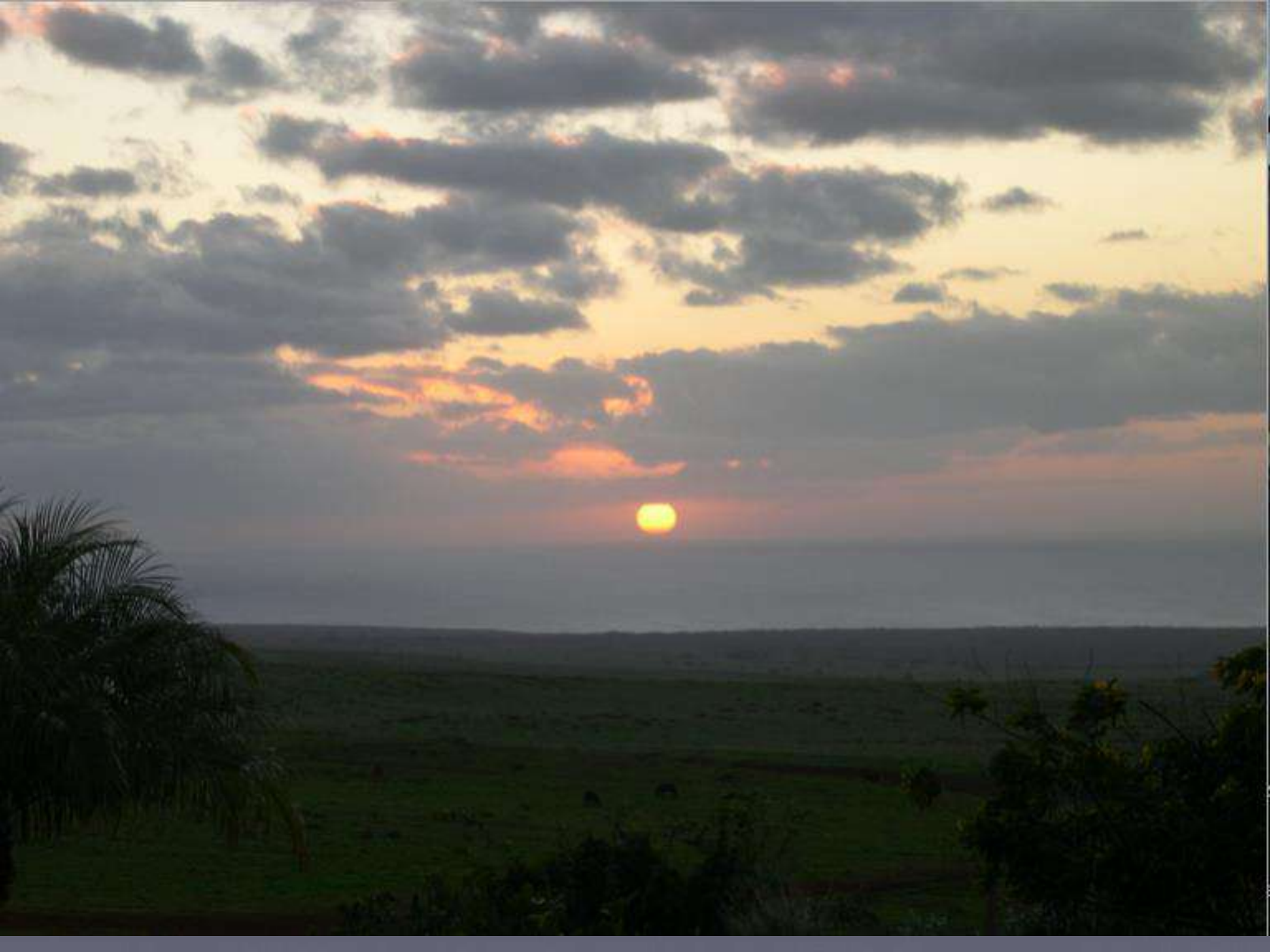




Contact Information:

okun@neurology.ufl.edu





Want to learn more on this topic:

Check out some of the extra slides

What's New?



RESEARCH ARTICLE

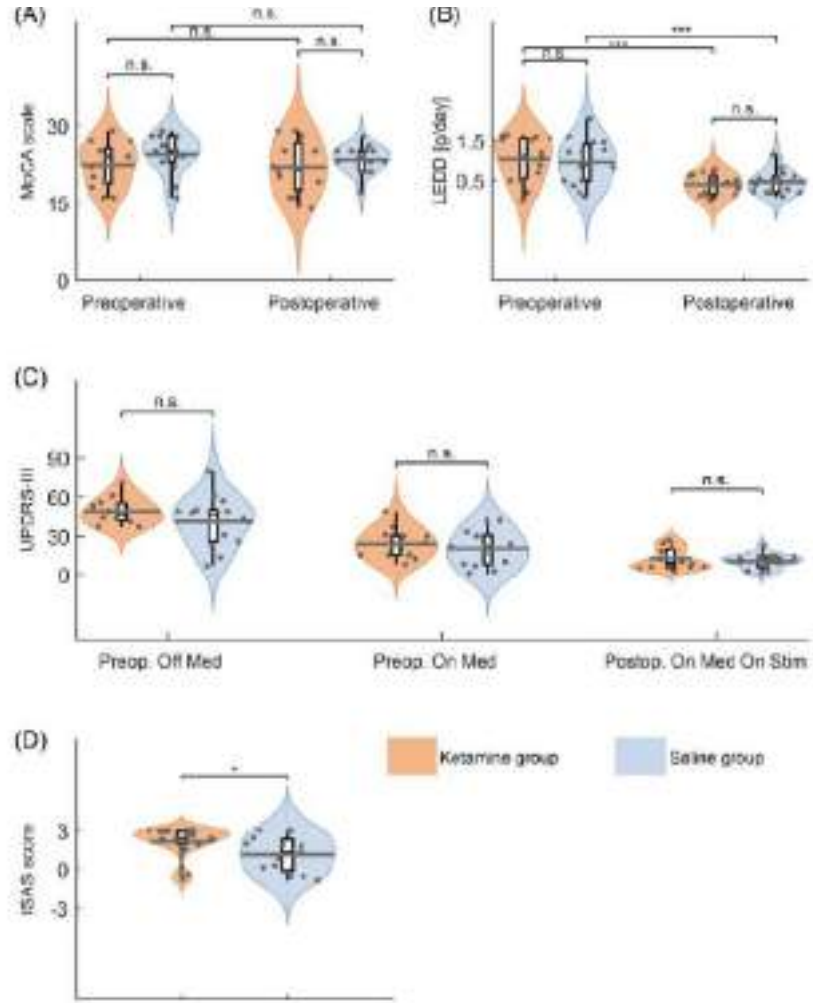
Interleaved Propofol-Ketamine Maintains DBS Physiology and Hemodynamic Stability: A Double-Blind Randomized Controlled Trial

Evgeniya Kornilov, MD,[1,2*] Halen Baker Erdman, MSc,[3] Eilat Kahana, MD, PhD,[1] Shlomo Fireman, MD,[1] Omer Zarchi, PhD,[4] Michal Israelashvili, PhD,[2] Johnathan Reiner, MD,[5] Amir Glik, MD,[5,6,7] Penina Weiss, PhD,[8] Rony Paz, PhD,[2] Hagai Bergman, MD, PhD,[3,9,10] and Idit Tamir, MD, PhD[11]

Ketamine-induced conscious sedation: high quality MER

Superior patient satisfaction and hemodynamic stability

Similar post-operative outcomes



Brain Stimulation 16 (2023) 1249–1251

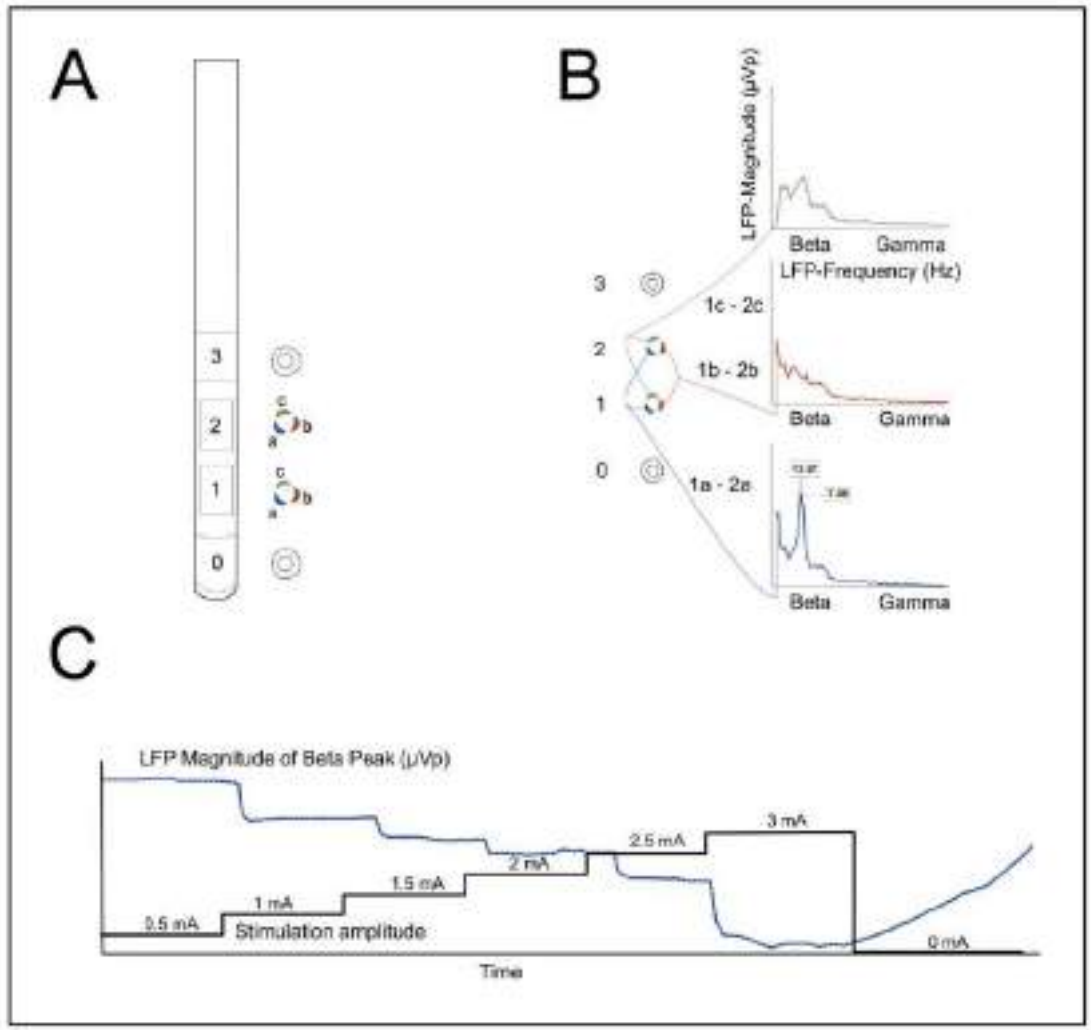
Contents lists available at ScienceDirect

Brain Stimulation

journal homepage: www.journals.elsevier.com/brain-stimulation

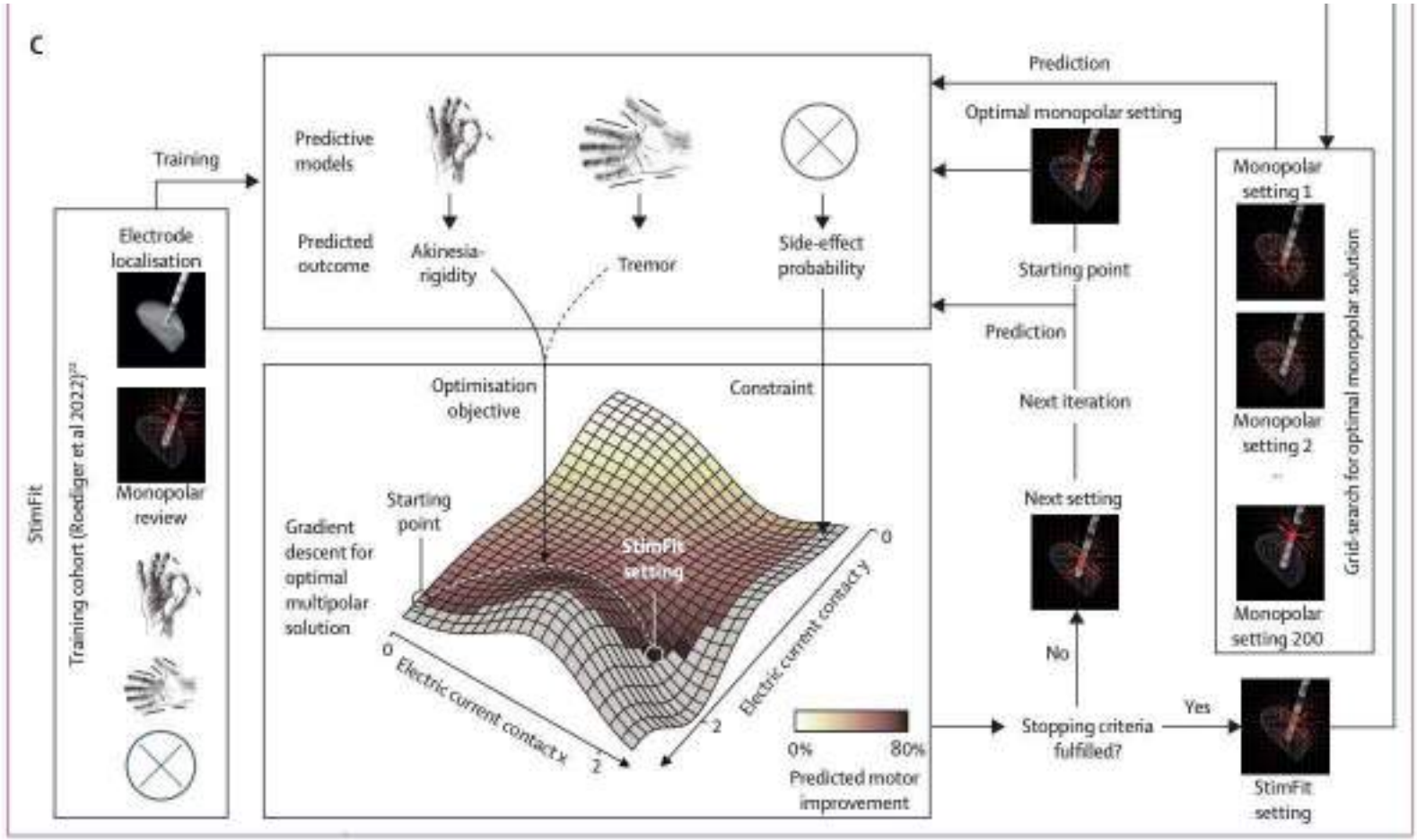
Feasibility of local field potential-guided programming for deep brain stimulation in Parkinson's disease: A comparison with clinical and neuro-imaging guided approaches in a randomized, controlled pilot trial

Tobias Binder [a,1], Florian Lange [a,*,1], Nicolò Pozzi [a], Thomas Musacchio [a], Christine Daniels [a], Thorsten Odorfer [a], Patrick Fricke [b], Cordula Matthies [b], Jens Volkmann [a], Philipp Capetian [a]



Automated deep brain stimulation programming based on electrode location: a randomised, crossover trial using a data-driven algorithm

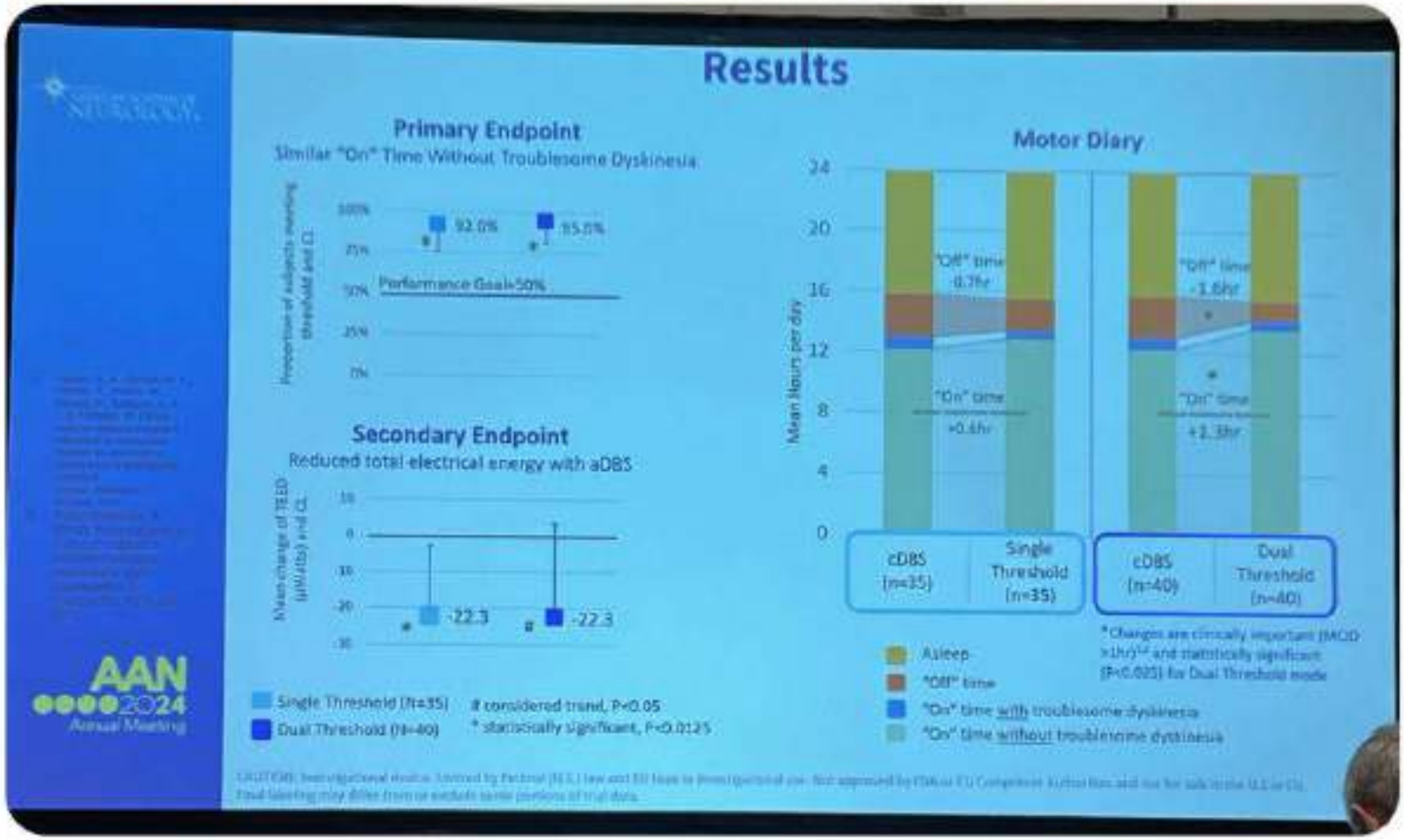
Jan Roediger, Till A. Dembek, Johannes Achtzehn, Johannes L. Busch, Anna-Pauline Krämer, Katharina Faust, Gerd-Helge Schneider, Patricia Krause, Andreas Horn, Andrea A. Kühn





Michael Okun @MichaelOkun · Apr 14

ADAPT DBS closed loop Parkinson trial results announced today by presentation @AANmember by Helen Brontë-Stewart. It was a positive trial and met pre-specified FDA outcomes. Will it be heading to the clinic soon. Next steps will be a full publication and submission to FDA

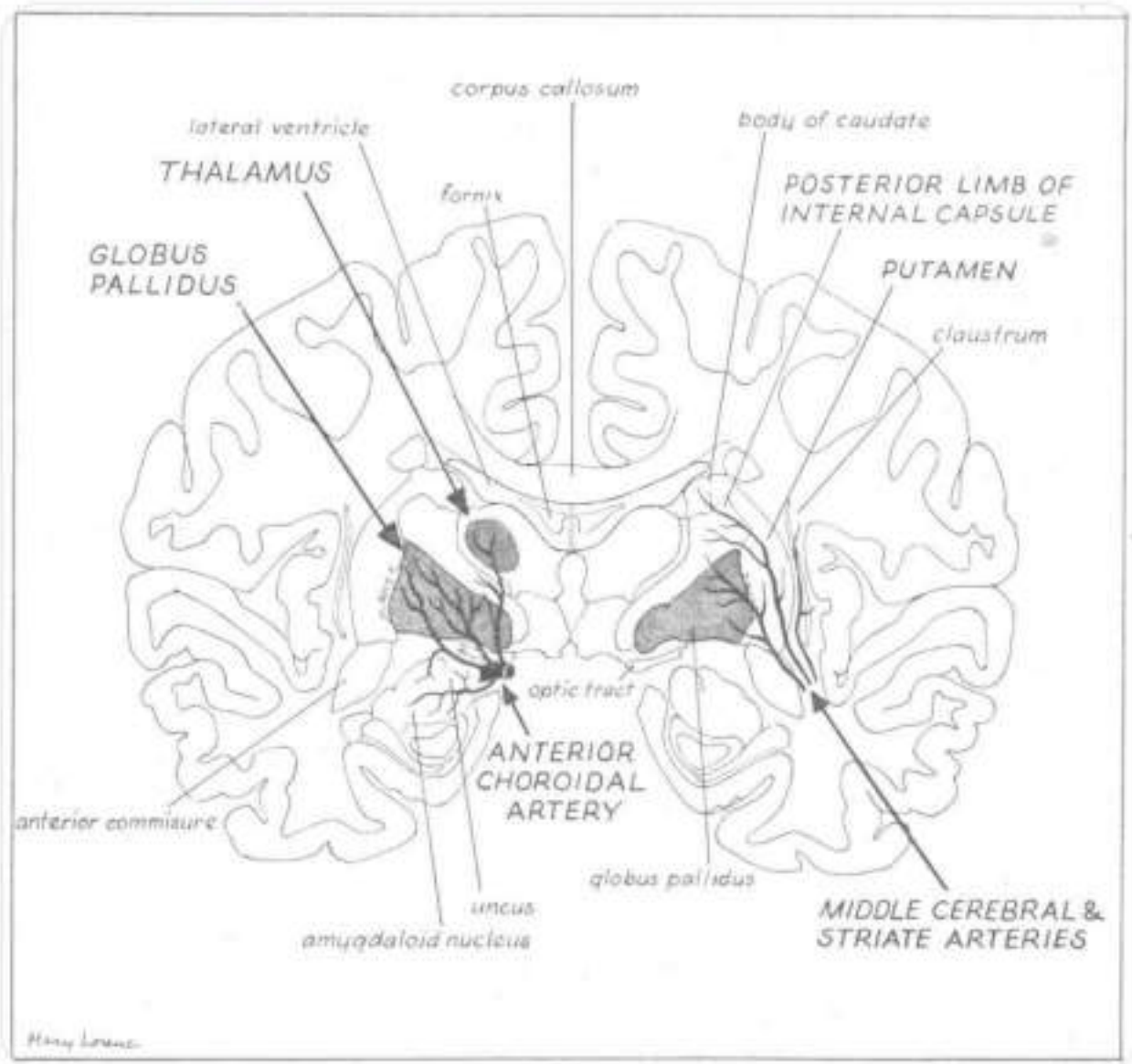


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DBS Think Tank @DBSThinkTank · Jan 18

Throwback Thursday to 1958 when Irving Cooper described his experience of accidentally sacrificing the AChA during pedunculotomy and observed resolution of tremor and parkinsonism. This led to AChA ligation and eventually pallidectomy

ncbi.nlm.nih.gov/pmc/articles/P...



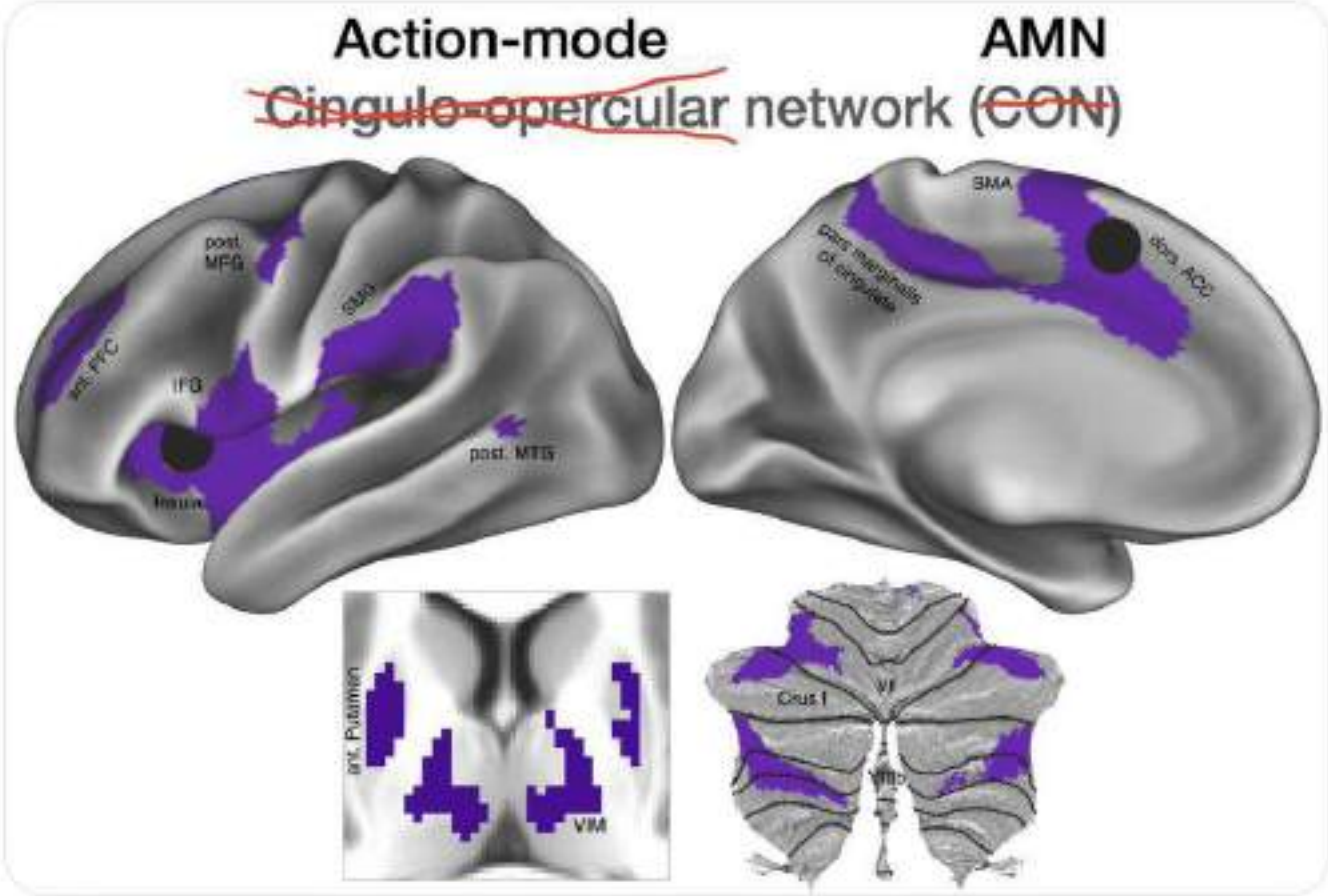
You reposted



Nico Dosenbach @ndosenbach · Feb 1

Introducing the Action-Mode Network – AMN. Better late than never! 17 years ago, we clumsily called this the Cingulo-opercular Network (CON) based on its anatomy (we weren't exactly sure what it does). Now we've finally got the evidence to give it the functional name it deserves:

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Evan Gordon and DosenbachLab

15 295 898 171K

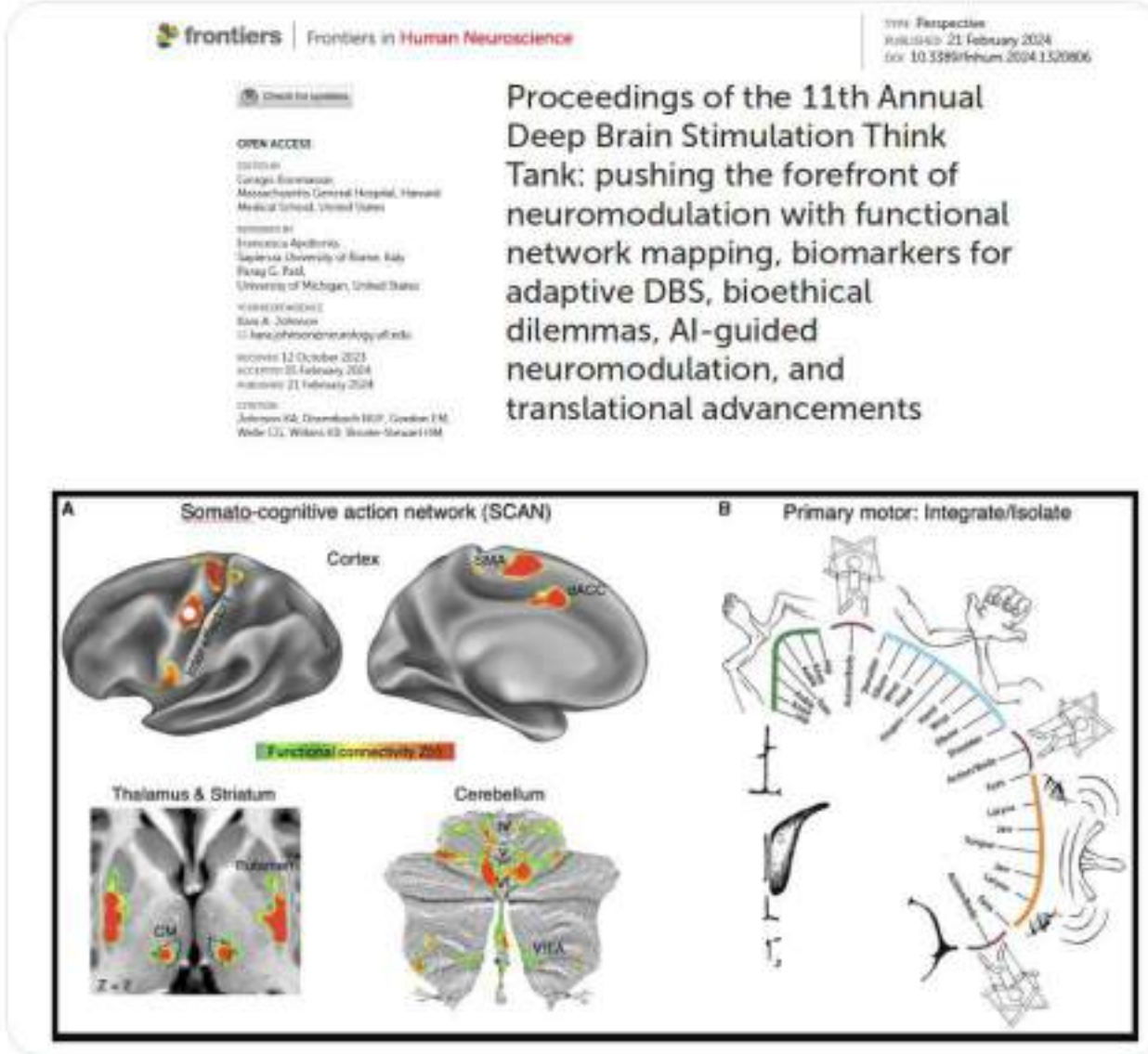
You reposted



Michael Okun @MichaelOkun · Feb 21

The **Deep Brain Stimulation (DBS) Think Tank XI** proceedings is published! “Pushing the Forefront of Neuromodulation,” the updates, paper and meeting were highlighted by @ndosenbach who presented research recently published in @Nature w/Evan Gordon to identify and characterize the

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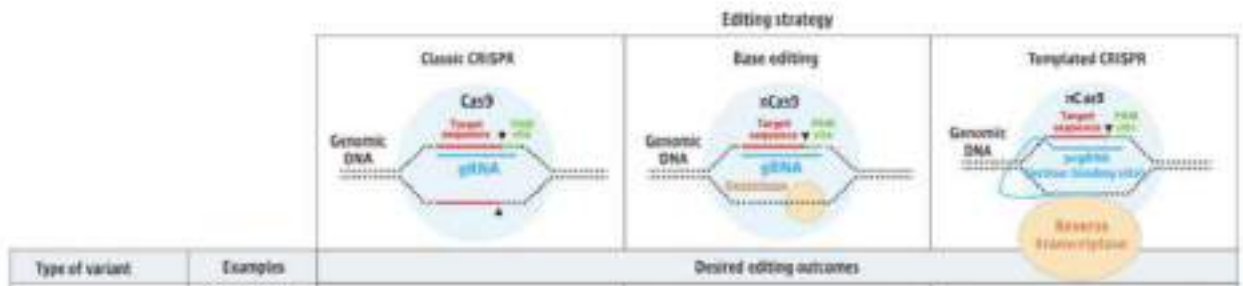
Michael Okun @MichaelOkun · Feb 4

Can you name **3 'gene editing' strategies** which may use **CRISPR** technology to **target neurological diseases**? How about classic cutting, base editing or templated repair? Gene editing using clustered regularly interspaced short palindromic repeats (CRISPR) has arrived and we will all Show more

JAMA Neurology | Review

Building CRISPR Gene Therapies for the Central Nervous System
A Review

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



Type of variant	Examples	Desired editing outcomes		
Recessive	Frataxin (FA) CLN (BD) Parkin (PD) CSTB (EPM1)	1. Double-stranded break Deletion of 1 to millions of bp 2. With optional donor DNA repair template Insertion of new sequence	From C to T Precise single-base conversion	1. Precise deletion of 1 to millions of bp 2. Insertion of new sequence 3. A T Precise single-base conversion
Dominant loss of function	SMN1 (SMA) GRN (FTD) TARDBP (ALS) HTT (HD)			
Dominant gain of function	MAPT (FTD) TARDBP (ALS) HTT (HD)			
Limitation and notes		NHEJ: high risk of unintended edits (insertions and/or deletions) HDR: low integration efficiency in postmitotic cells like neurons HITI: low integration efficiency	Limited to specific bases: C to T, T to C, G to A, or A to G	PE: cannot make large insertions or deletions (≤40-bp insertions and ≤80-bp deletions) TwinPE and PASTE: can make large insertions but are not optimized for in vivo delivery

1 14 34 4.2K



Michael Okun @MichaelOkun · Feb 7

How will **DBS** go if you have a **genetic form of Parkinson's disease**? Great new study on the
motor and non-motor DBS outcomes using a multi-scale meta-analysis by Asimakidou and colleagues @MDCP_Journal.
Key points:
- The authors point out we have **high-throughput sequencing**
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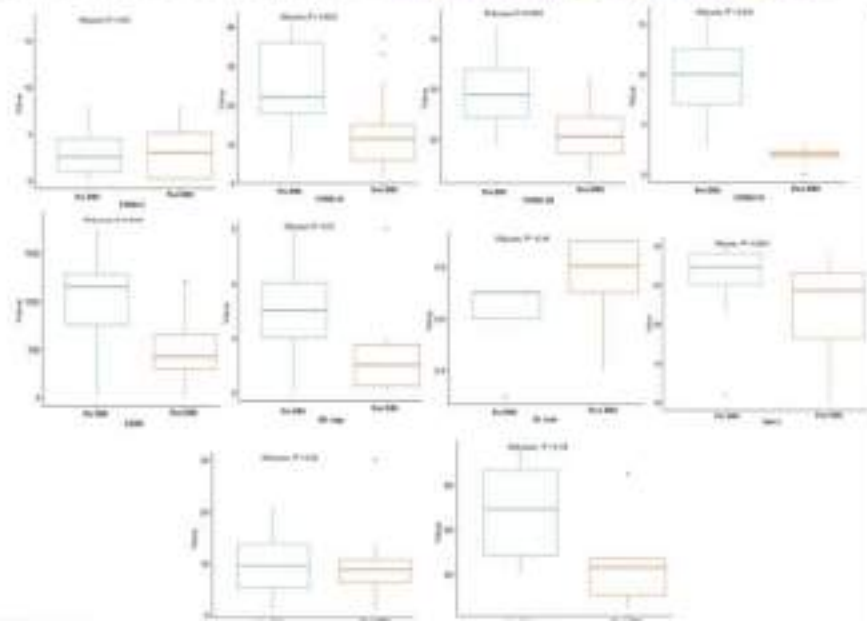
Movement Disorders CLINICAL PRACTICE

REVIEW | Full Access

Motor and Non-motor Outcomes of Deep Brain Stimulation across the Genetic Panorama of Parkinson's Disease: A Multi-Scale Meta-Analysis

Evridiki Asimakidou MD, MSc, Georgia Xiromerisiou MD, PhD, Christos Sidiropoulos MD, PhD

First published: 06 February 2024 | https://doi.org/10.1002/mdc3.13994

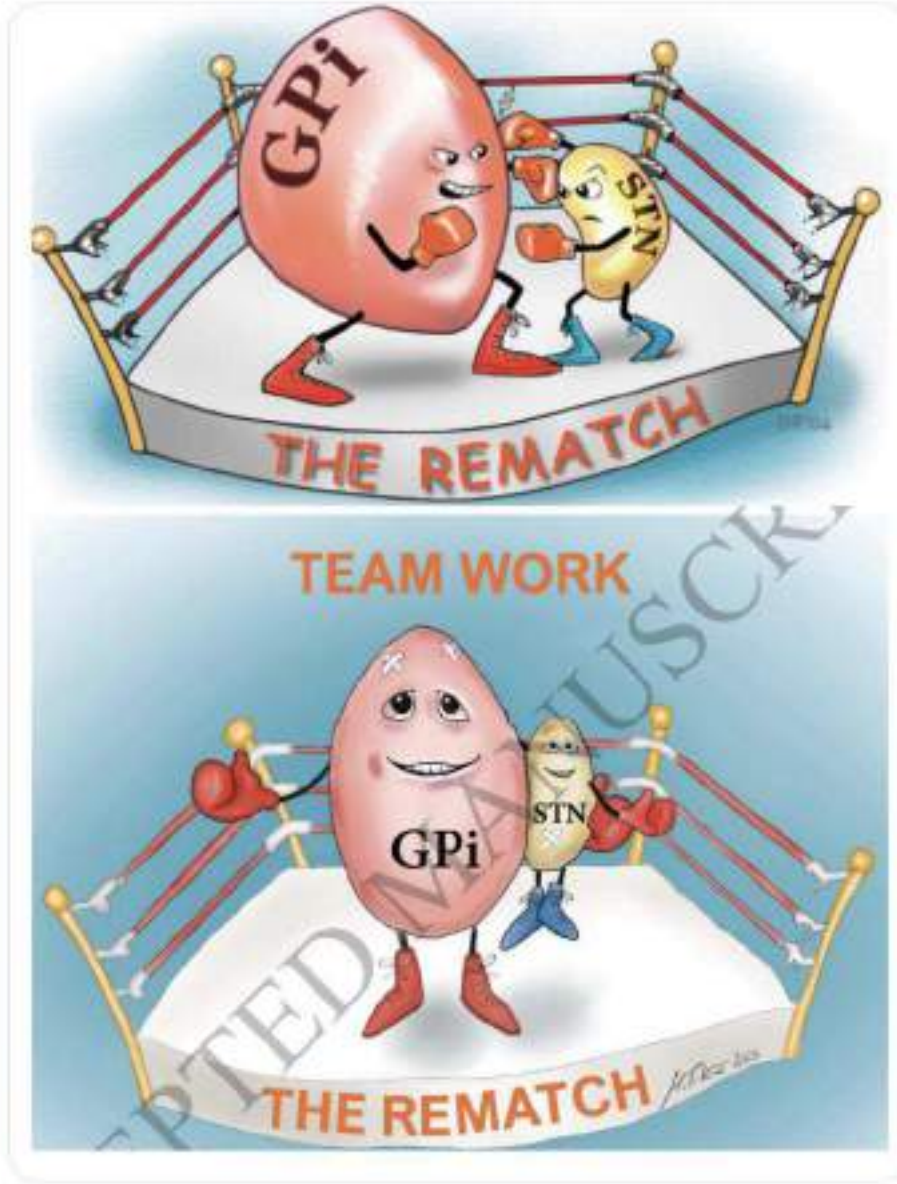




Michael Okun @MichaelOkun · Feb 16

Should we be thinking about the **synergy** of using **STN and GPi DBS together**? Zrinzo explores in a new @Brain1878 editorial which examines the recent **adaptive/closed loop dual target DBS trial** from @DukeU and Dennis Turner's group. Zrinzo cleverly redrew the original 2005 cartoon

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Michael Okun @MichaelOkun · Feb 19

Remote DBS programming by telemedicine? Has it arrived? Fung and Fasano have a fresh article @MDCP_Journal out about their experience in **Canada**. News flash for those who don't know: In Canada travel to an experienced center can cover long distances, have lots of burden and can be

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Movement Disorders

CLINICAL PRACTICE

LETTER: NEUROMODULATION

Remote Deep Brain Stimulation Programming in Canada

Wilson K.W. Fung, MBBCA,[1] Maria Belen Jusoh, MD,[1] Michelle Hamani, MSc,[1] Renato P. Munhoz, MD, PhD,[1,2] Suneil K. Kalia, MD, PhD,[3,4] Andres M. Lozano, MD, PhD,[3,4] and Alfonso Fasano, MD, PhD, FAAN[1,2,3,4]*

TABLE 1 Clinical summary of five IV DBS patients programmed remotely from Toronto Western Hospital, Ontario

No.	Sex	Age	Location	Distance (km)	Travel time (min)*	Diagnosis	Disease duration (Y)	DBS targets	Most bothersome symptom(s)	Patient reported outcome	Type of visit (total N of remote sessions)	Challenges faced during programming and stimulation change made	Configuration of DBS settings
1	M	69	Mt Pearl, NFL, CA	3944 k	369 (flight)	PD	17	Bilateral STN	Tremor, balance, peak dose dyskinesia	Moderately improved	F/U (1)	None Changes made: none, program higher frequency	R STN: C + 2—0 mA/ 60 ms/160 Hz L STN: C + 11—12.75 mA/ 60 ms/130 Hz
2	M	64	Utopia, ON, CA	1513	93	PD	9	Bilateral STN	Tremor, peak dose dyskinesia, motor fluctuations	Mild-moderately improved	F/U (1)	Stimulation-induced dysarthria Changes made: none	R STN: C + 1—0.9 mA/ 60 ms/130 Hz L STN: C + 5—5.5 mA/ 60 ms/130 Hz
3	F	74	Vernon, BC, CA	3917	299 (flight)	GD	40	Left VIM	Dystonic tremor	Moderately-greatly improved	F/U (1)	Stimulation-induced dizziness and nausea (transient). Changes made: higher amplitude	L VIM: C + 10B—5.20 mA/ 90 ms/130 Hz
4	F	71	Trinidad and Tobago	4695	595 (flight)	PD	8	Bilateral GPi	Rigidity, peak dose dyskinesia, motor fluctuations	Mild-moderately improved	F/U (5)	Freezing of gait, balance issues, increased risk of falling. Changes made: none, program monitoring	R GPi: C + 1—1.25 mA/ 90 ms/90 Hz R GPi: C + 1—1.0 mA/60 ms/ 90 Hz L GPi: C + 11—1.25 mA/90 ms/ 90 Hz L GPi: C + 11—2.75 mA/90 ms/ 90 Hz
5	F	66	Cavagnolo, NFL, CA	3476	311 (flight)	PD	7	Bilateral STN	Tremor, rigidity, peak-dose dyskinesia, motor fluctuations	Moderately improved	OP, 4 F/U, 3 (5)	Stimulation-induced dysarthria Changes made: new program-current steering (horizontal), higher amplitude, shorter PW	R STN: C + 2B—2.5 mA/90 ms/ 130 Hz L STN: C + 3/4/5/6C + 11/10C—9.1 mA/90 ms/160 Hz
6	F	64	Fowler Falls, ON, CA	937 k	122	PD	11	Bilateral GPi	Stiffness, rigidity, motor fluctuations	Mild-moderately improved	OP (1)	Stimulation-induced dysarthria and freezing of gait.	R GPi: C + 1—3.0 mA/ 90 ms/ 130 Hz



Michael Okun @MichaelOkun · Feb 23

Denied your device? @DBSThinkTank XI even if treatment-resistant condition improves, health insurance may deny coverage for post-trial maintenance on the basis that a device used for an experimental indication and determine it is not “medically necessary”
cutt.ly/9wBLZ2rq

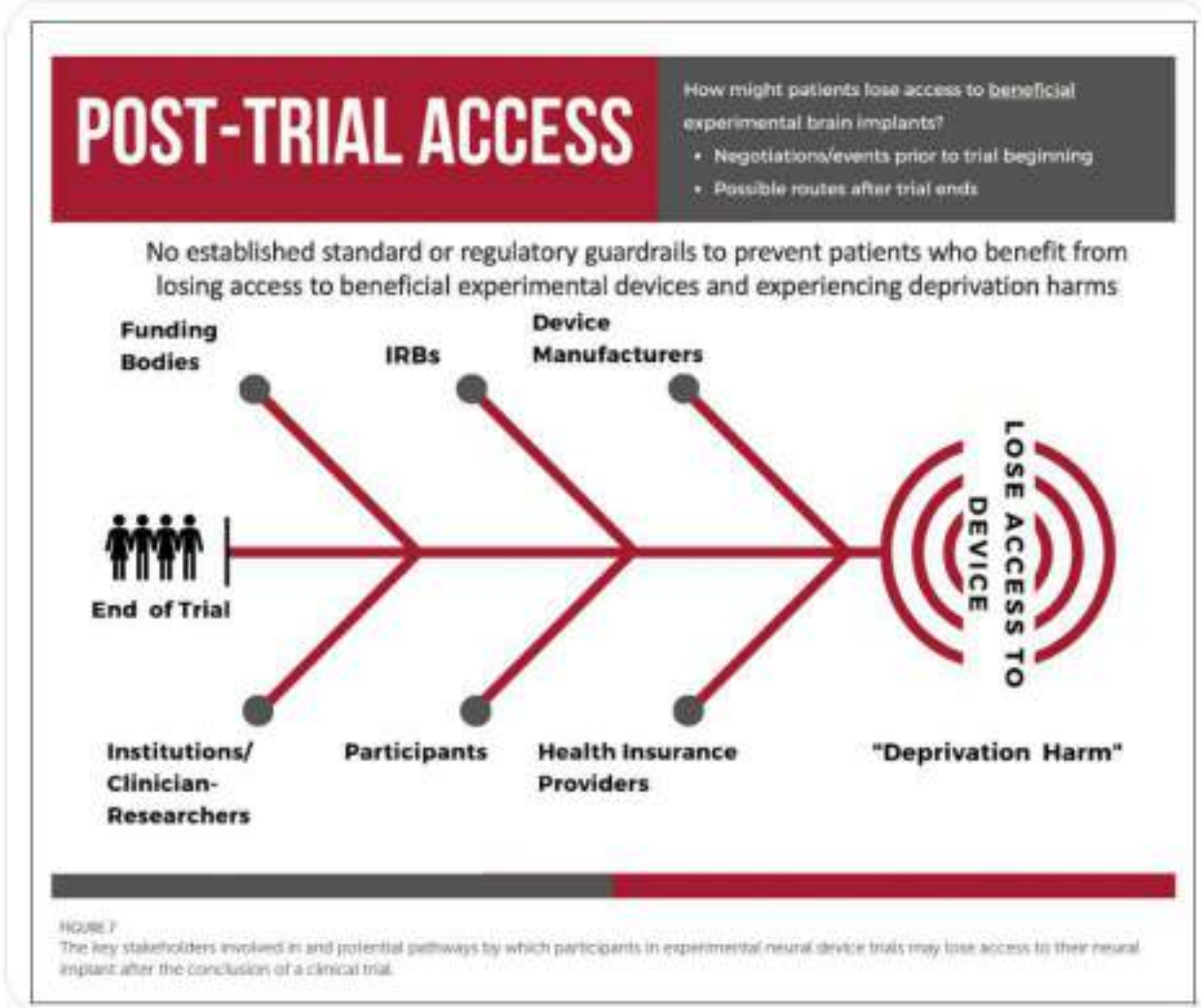


FIGURE 1
The key stakeholders involved in and potential pathways by which participants in experimental neural device trials may lose access to their neural implant after the conclusion of a clinical trial.

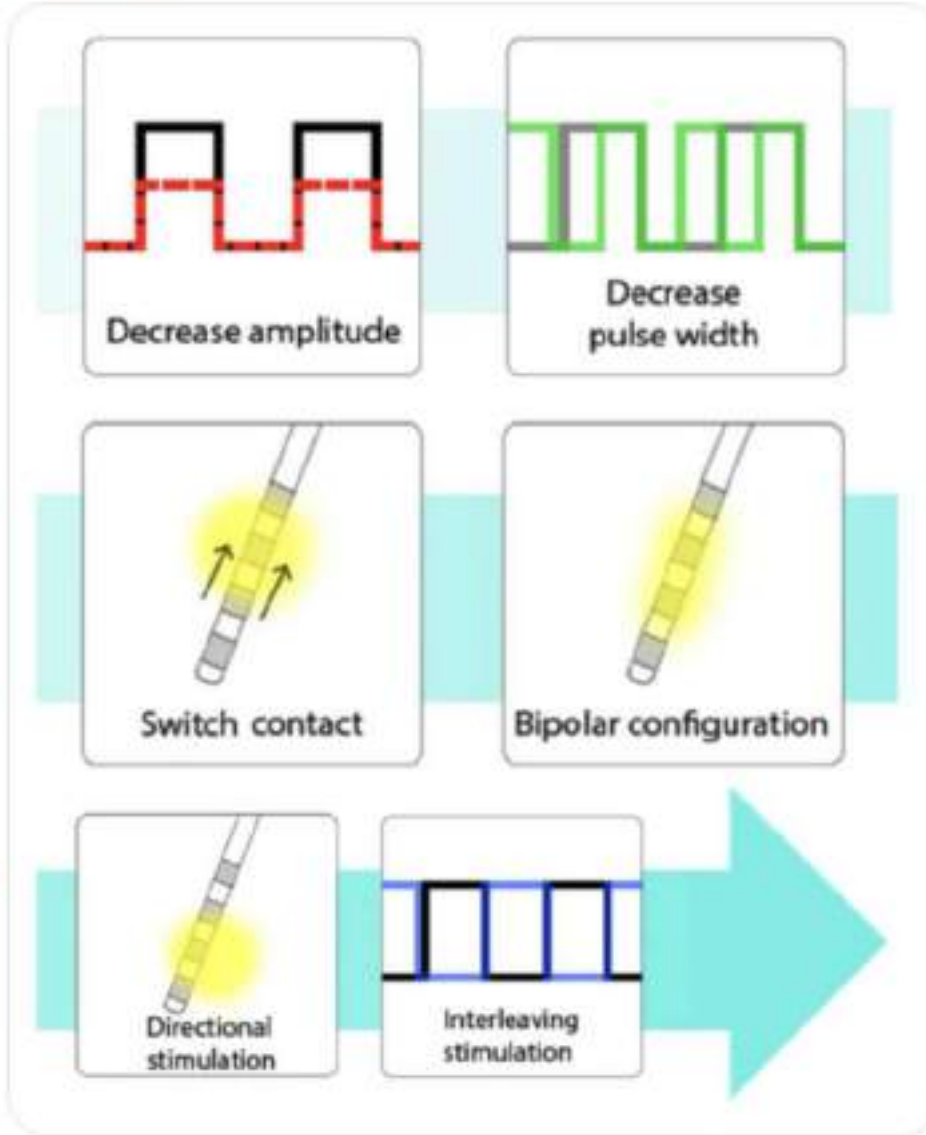
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Michael Okun @MichaelOkun · Feb 26

What is your **DBS programming strategy**? There are hundreds of thousands of possibilities. I love how @JWongggMD @EnriqueZenitram and @filipepsarmento sorted a programming approach in increasing order of complexity. Notice how they *do not* always reflexively increase amplitude

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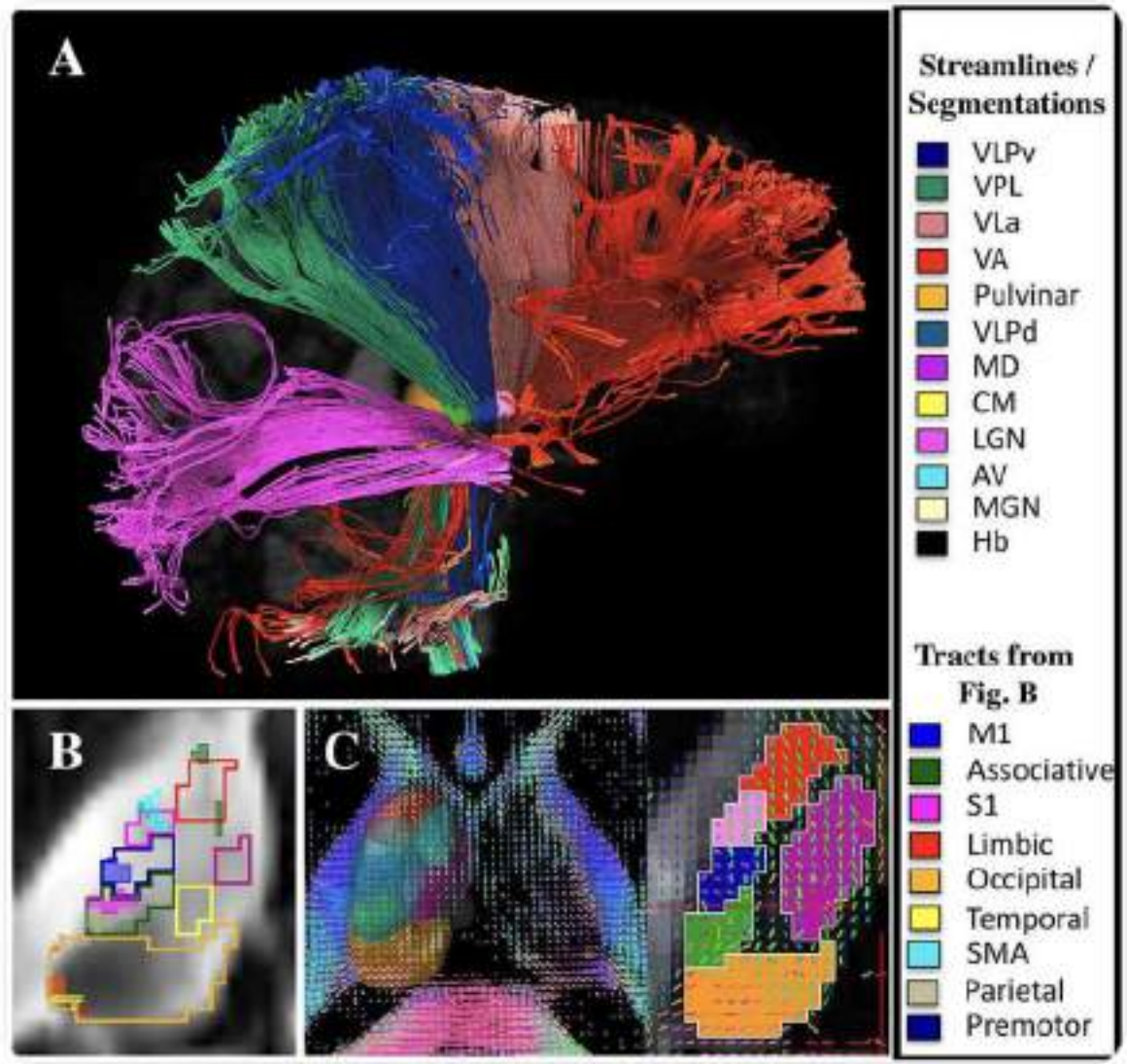


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DBS Think Tank @DBSThinkTank · Feb 26

DiMANI: a new dMRI method to directly visualize thalamic subnuclei for better DBS targeting and optimization. Reproducible, reliable, and clinically relevant. Check out this new paper by Patriat and the Harel lab
#neuroscience #DBS #dMRI

Full details here
frontiersin.org/articles/10.33...

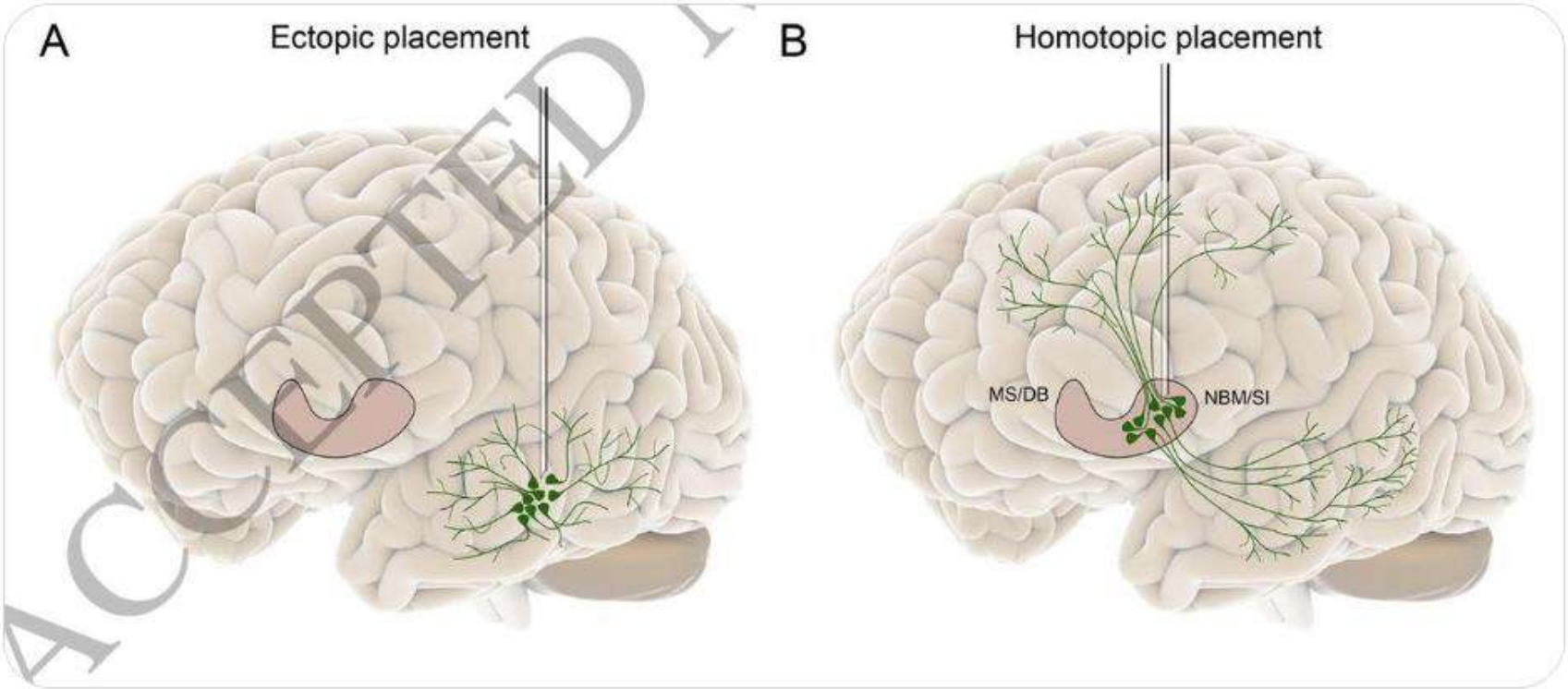




Michael Okun @MichaelOkun · Mar 1

Do you know the two **transplant approaches** being considered for **regenerative medicine** restoration of **memory** and **thinking** in **Parkinson's disease?** Anders Björklund, and Roger Barker @Brain1878 teach us about the basal forebrain cholinergic system as a serious target for **cell**

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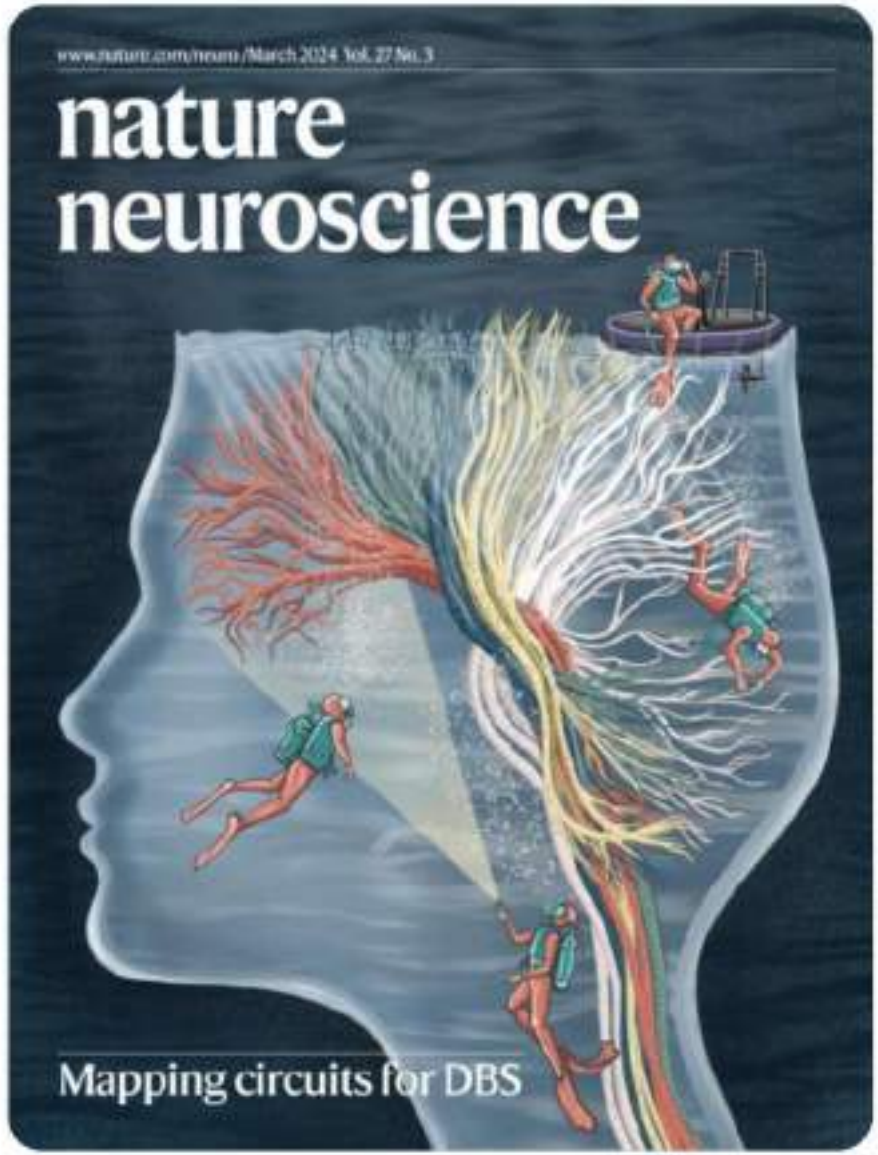
1 12 34 6.5K



Andreas Horn @andreashorn_ · Mar 7

Excited that our article 👇👇 has been featured on the cover of the march issue of @NatureNeuro – even more excited that @b_hollunder, the first-author of the study, hand-drew the cover herself. [🤫 I think she's an artist]

nature.com/neuro/volumes/...





Michael Okun @MichaelOkun · Mar 19

Randomized study data is now published in @TheLancetNeuro the new **pump-patch** continuous 24 hour/day subcutaneous infusion of ND0612 in **Parkinson's disease.** This therapy was compared with oral immediate-release levodopa–carbidopa. @AlbertoEspay and colleagues freshly published.

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Safety and efficacy of continuous subcutaneous levodopa–carbidopa infusion (ND0612) for Parkinson's disease with motor fluctuations (BouNDless): a phase 3, randomised, double-blind, double-dummy, multicentre trial

Alberto J Espay, Fabrizio Stocchi, Rajesh Pahwa, Alberto Albanese, Aaron Ellenbogen, Joaquim J Ferreira, Nir Giladi, Tanya Gurevich, Sharon Hassin-Baer, Jorge Hernandez-Vara, Stuart H Isaacson, Karl Kieburtz, Peter A LeWitt, Lydia Lopez-Manzanares, C Warren Olanow, Werner Poewe, Harini Sarva, Tomi Tanderi, Liat Adar, Laurence Solin, Nelson Lopes, Nissim Sasson, Ryan Case, Olivier Rascol, * on behalf of the BouNDless Study Group†*

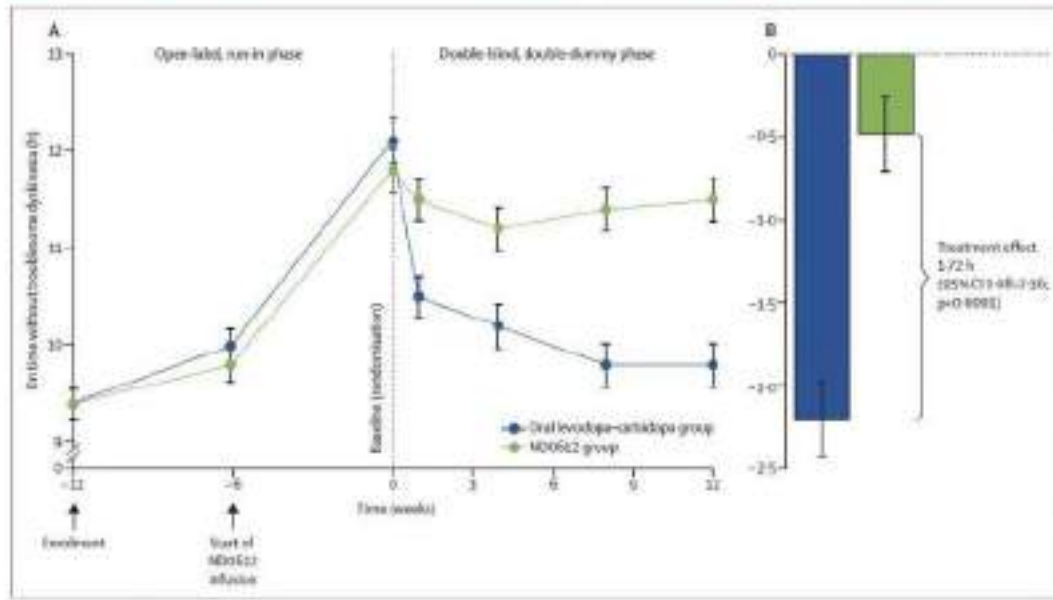


Figure 2: Change in on time without troublesome dyskinesia during the study (primary efficacy endpoint)
(A) Change in least squares mean on time without troublesome dyskinesia from enrolment (−12 weeks) to study endpoint (12 weeks). Error bars are SE. On time was assessed with a 24 h self-completed home diary and normalised to a 16 h waking day. On time without troublesome dyskinesia is the sum of on time without dyskinesia and on time with non-troublesome dyskinesia. (B) Treatment difference from randomisation visit (week 0) to study endpoint (week 12). Error bars are 95% CI.



Michael Okun @MichaelOkun · Apr 9

Results are in for the **EARSTIM-PD trial**. The trial of intrinsic auricular muscle zone stimulation for Parkinson's disease: Phase II multi-center pilot study in @ParkinsonismD by Fernandez and colleagues.

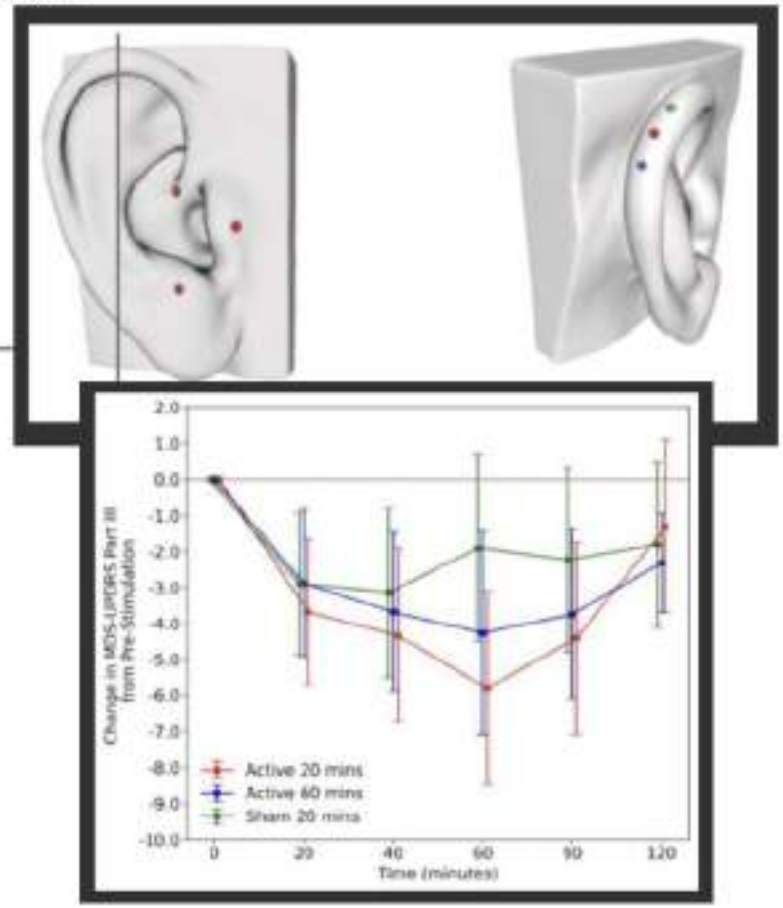
Key Points:

- **Intrinsic auricular muscle zone**l (IAMZ) stimulation has been

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Intrinsic auricular muscle zone stimulation for Parkinson disease: The *EARSTIM-PD* Phase II multi-center pilot study results

Hubert H. Fernandez, Eric A. Macklin, Robert A. Hauser, Kelvin L. Chou, Yusuf O. Cakmak, Burak Ozsoy, Stanley Fahn, and the Parkinson Study Group EARSTIM-PD Investigators

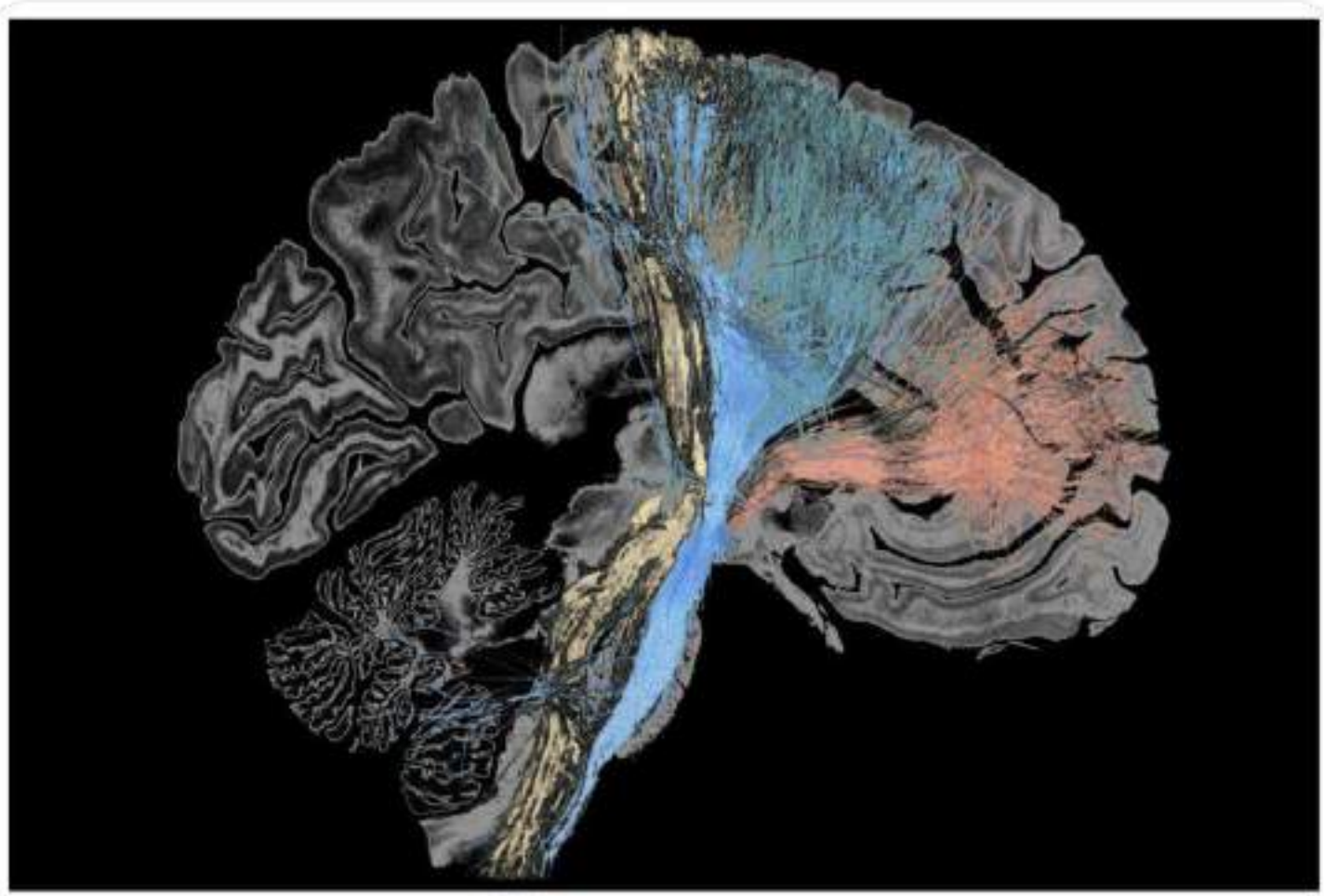




Michael Okun @MichaelOkun · Apr 16

Do you know what the **brain's 'dysfunctome' is**? Andy Horn and his team dubbed it the dysfunctome and he showed the set of circuits 'likely to be disrupted in those disorders.' The method, 'used to visualize fiber bundles in white matter, provides only an indirect assessment of

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Making maps: The 'dysfunctome' traces circuits that are likely disrupted across different brain disorders.

1 13 41 3.8K

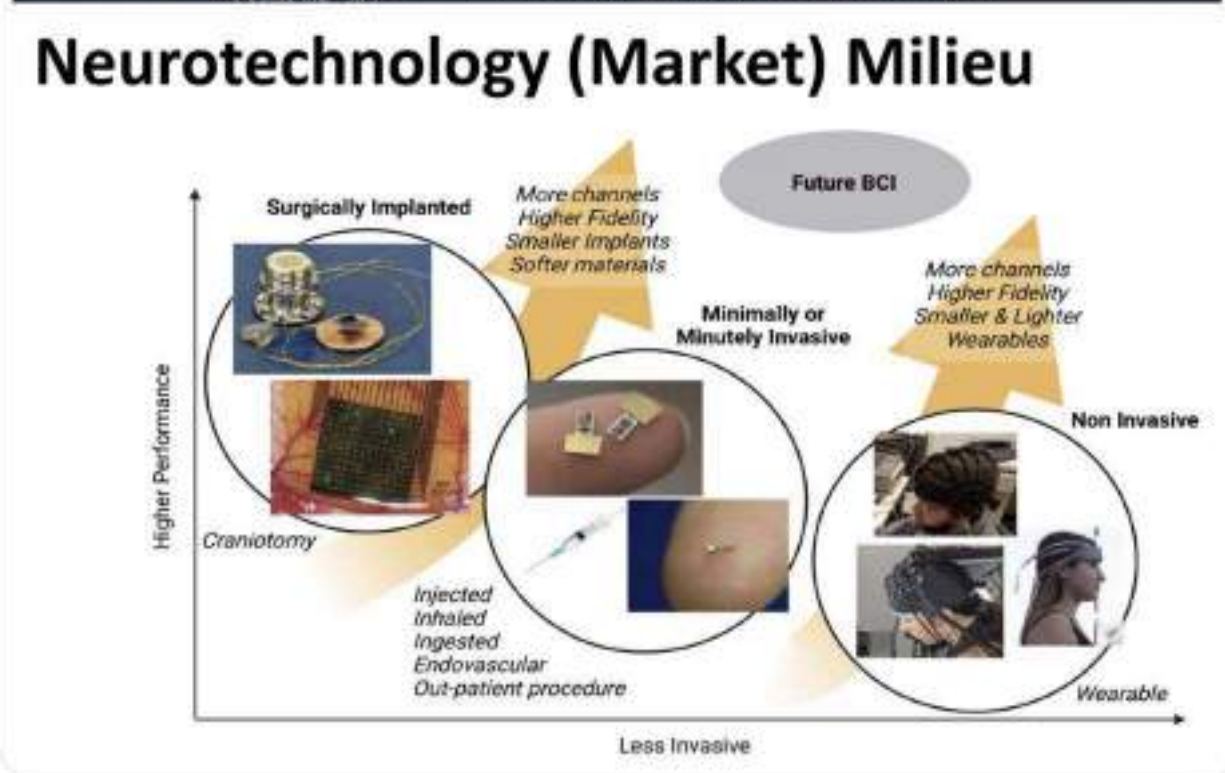


Michael Okun @MichaelOkun · Apr 18

Do you think there will be **direct to consumer brain implants**? You bet there will be, and we need to be ready. We need to create dialogue w/ all stakeholders. This is a GLOBAL challenge. Check out the multi-billion dollar market milieu. Are we 'leaning in' to this challenge or

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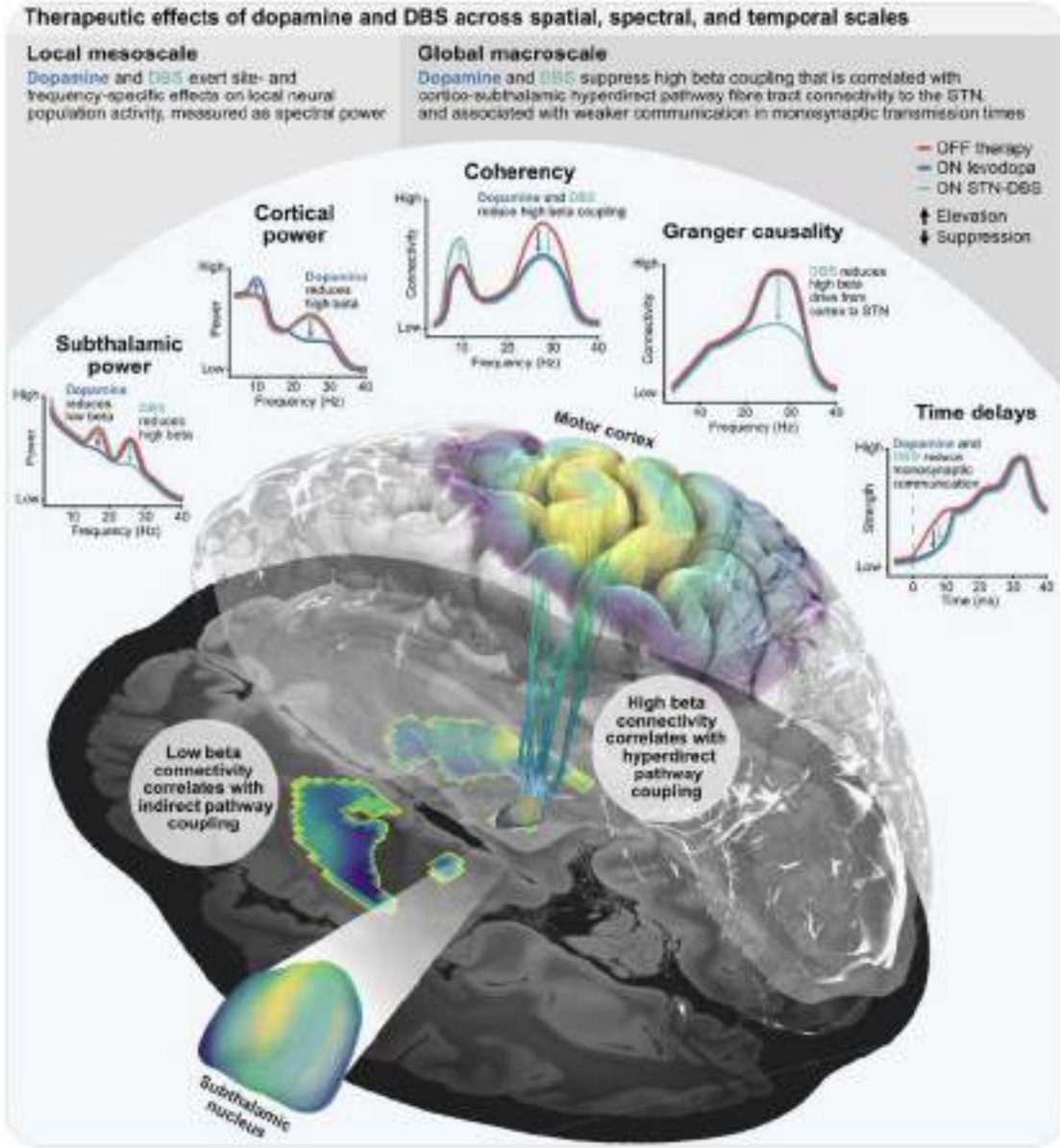


4 8 1.8K



Julian Neumann @neumann_wj · Apr 18

Preprint 🚨 This one is important for invasive #Parkinson #neurotech of the future. Deep brain stimulation suppresses oscillatory hyperdirect pathway communication. So does dopamine! Check our #Parkinson study spearheaded by @ECN_Berlin #PhD @tsbinns 🧵
biorxiv.org/content/10.110...



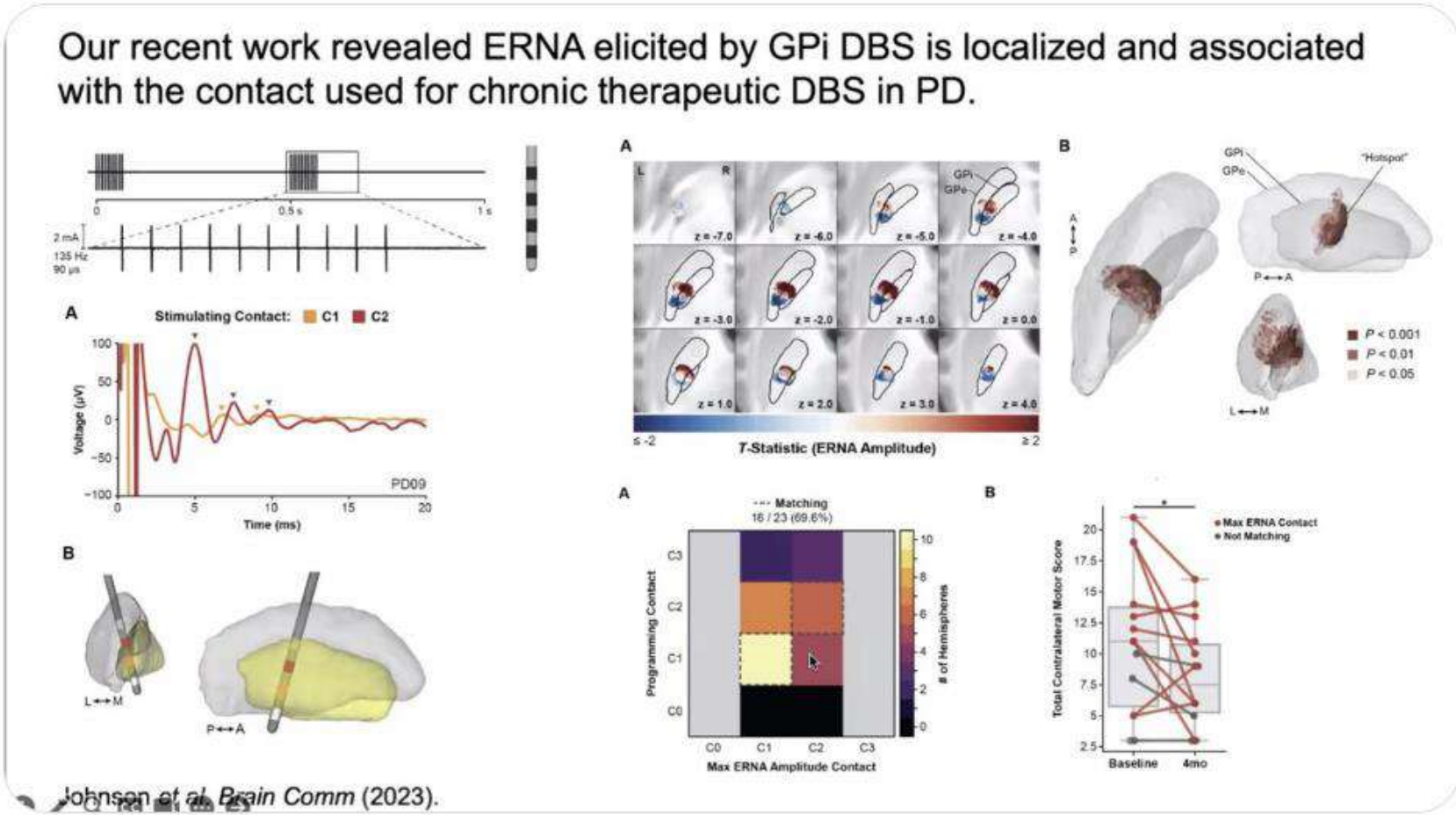
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Michael Okun @MichaelOkun · Apr 22

Kara Johnson kicked off the week w/ a presentation on her work using **evoked resonant neural activity (ERNA)** which is a high-frequency (~200–500 Hz) stimulation evoked response has been proposed as a candidate neural signal in **deep brain stimulation (DBS)** for **Parkinson's disease.**

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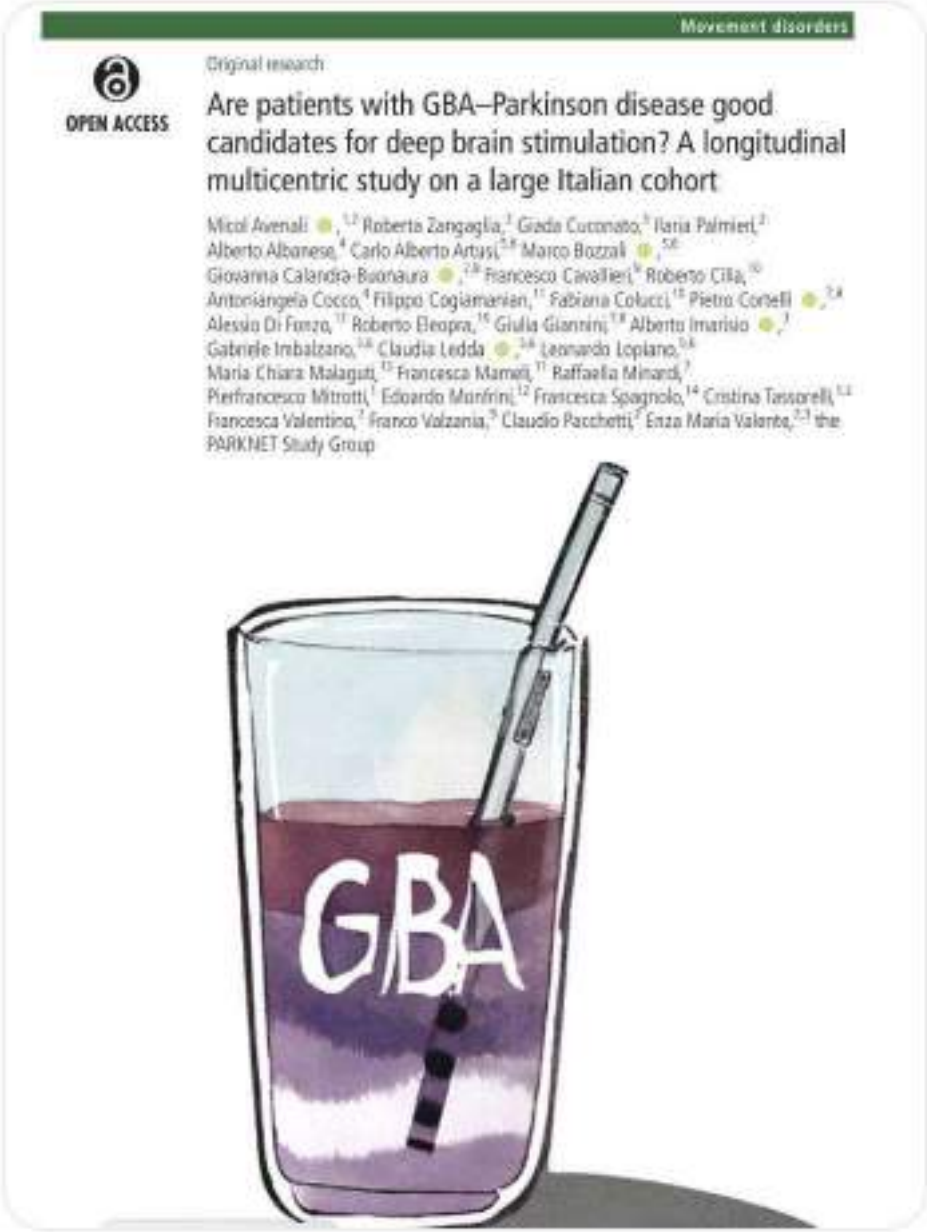


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Do we need **genetic testing** prior to offering **deep brain stimulation** for Parkinson's? A really important debate has recently broken out over GBA status and STN DBS. An early paper from Pal was followed by many multi-country papers. Now, we have a new Italian paper @bmj_latest and

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Movement disorders

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Original research

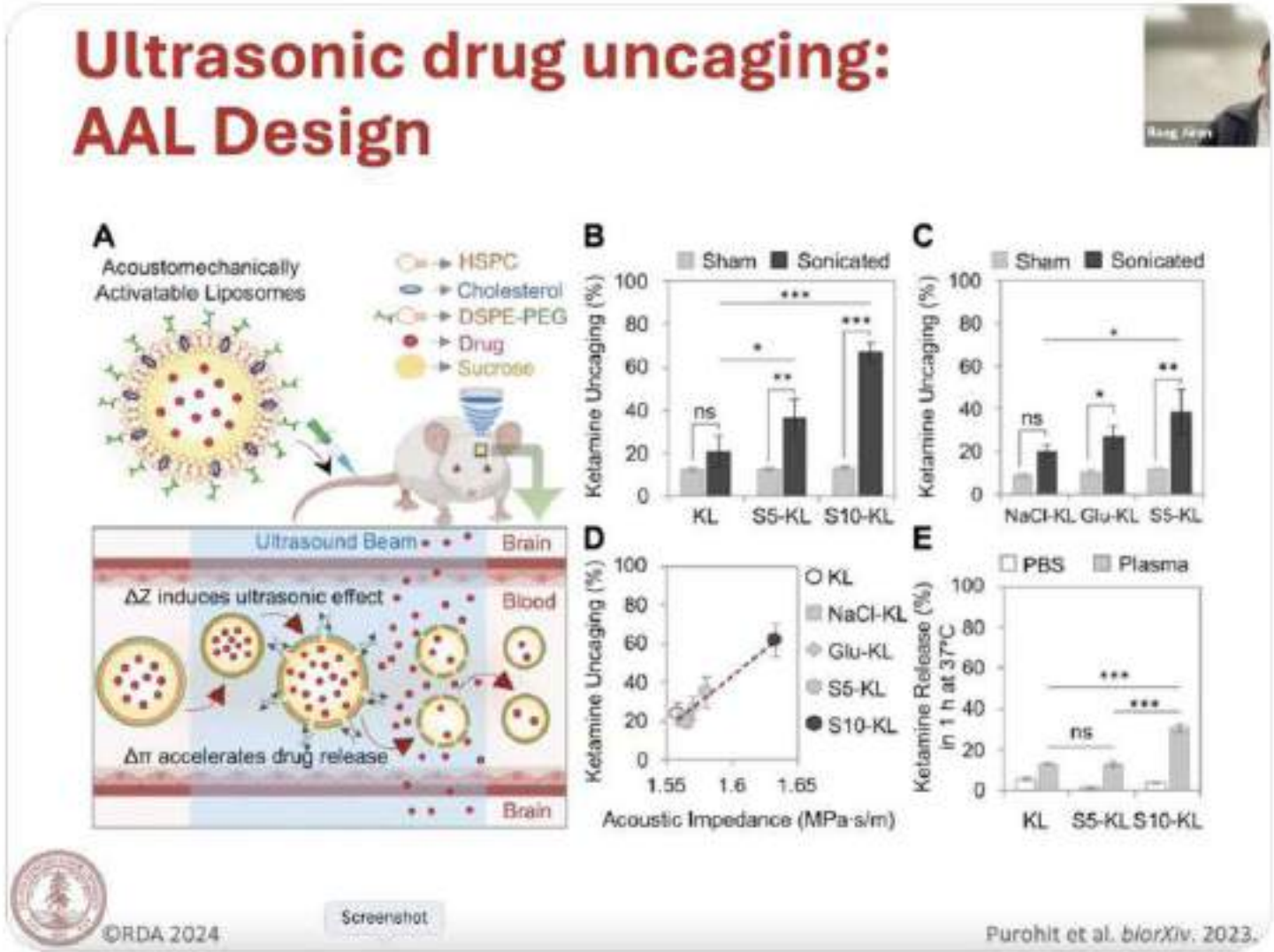
Are patients with GBA–Parkinson disease good candidates for deep brain stimulation? A longitudinal multicentric study on a large Italian cohort

Micol Avenali, Roberta Zangaglia, Giada Cuconato, Ilaria Palmieri, Alberto Albanese, Carlo Alberto Artusi, Marco Bozzali, Giovanna Calandra-Buonaura, Francesco Cavallieri, Roberto Cilia, Antoniangela Cocco, Filippo Cogiamanian, Fabiana Colucci, Pietro Cortelli, Alessio Di Fonzo, Roberto Eleopra, Giulia Giannini, Alberto Imarisio, Gabriele Imbalzano, Claudia Ledda, Leonardo Lopiano, Maria Chiara Malaguti, Francesca Mameli, Raffaella Minardi, Pierfrancesco Mitrotti, Edoardo Monfrini, Francesca Spagnolo, Cristina Tassorelli, Francesca Valentino, Franco Valzania, Claudio Pacchetti, Enza Maria Valente, the PARKNET Study Group



Michael Okun @MichaelOkun · May 6

Introducing the acoustomechanically activated liposome. Just add sugar and watch the drug delivered to the brain when hit with an ultrasound beam. Nice work by Raag Airan @Stanford.



6 14 2.4K



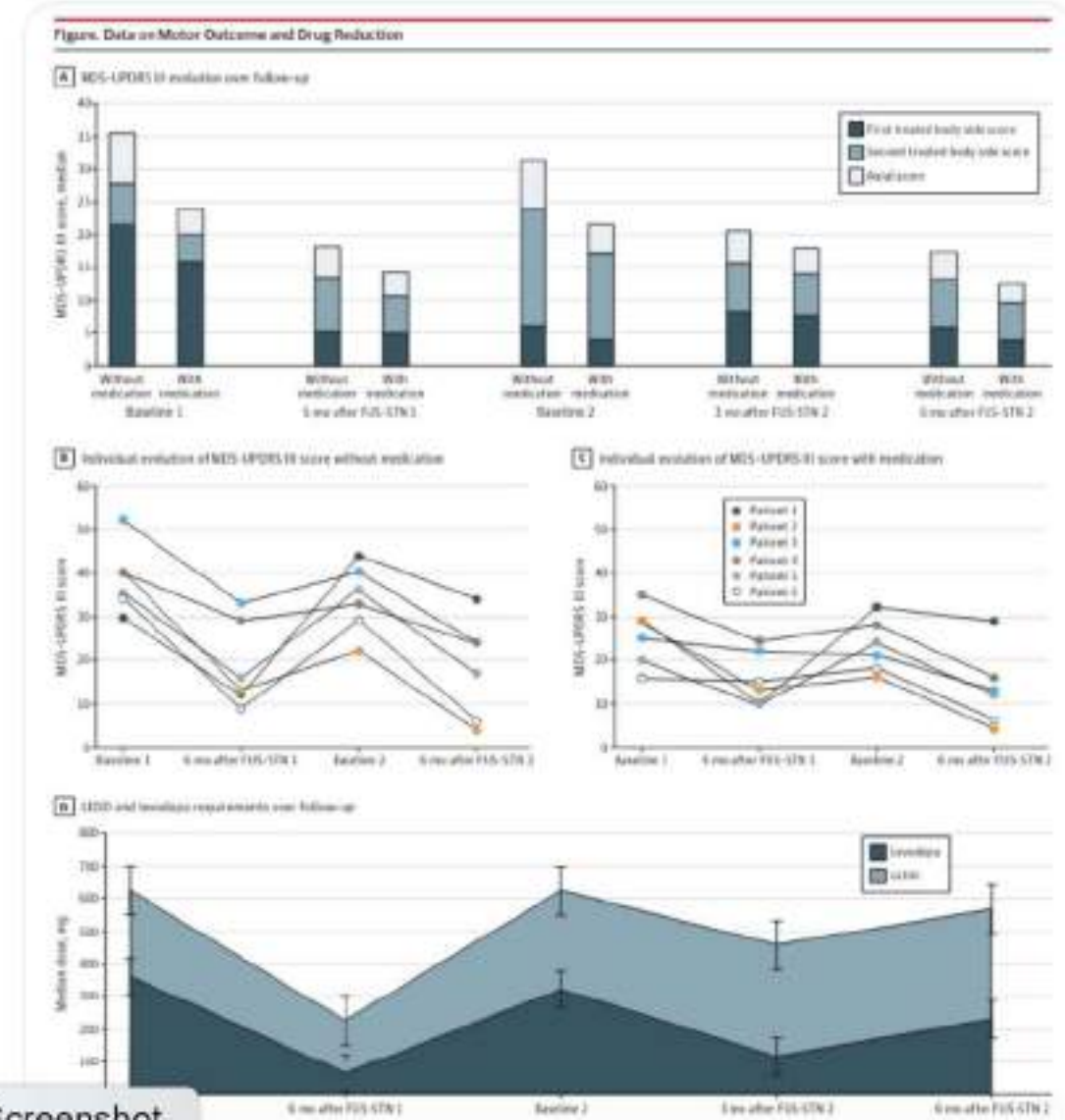
Michael Okun @MichaelOkun · May 18

Adding a **second-sided** MRI-guided **focused ultrasound subthalamotomy** for Parkinson's. Some important new data was just published @JAMANeuro from Raúl Martínez-Fernández, Jose Obeso and their team from Spain. Time to ab uno disce omnes.

Key Points:

- The authors asked whether **adding**

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Screenshot



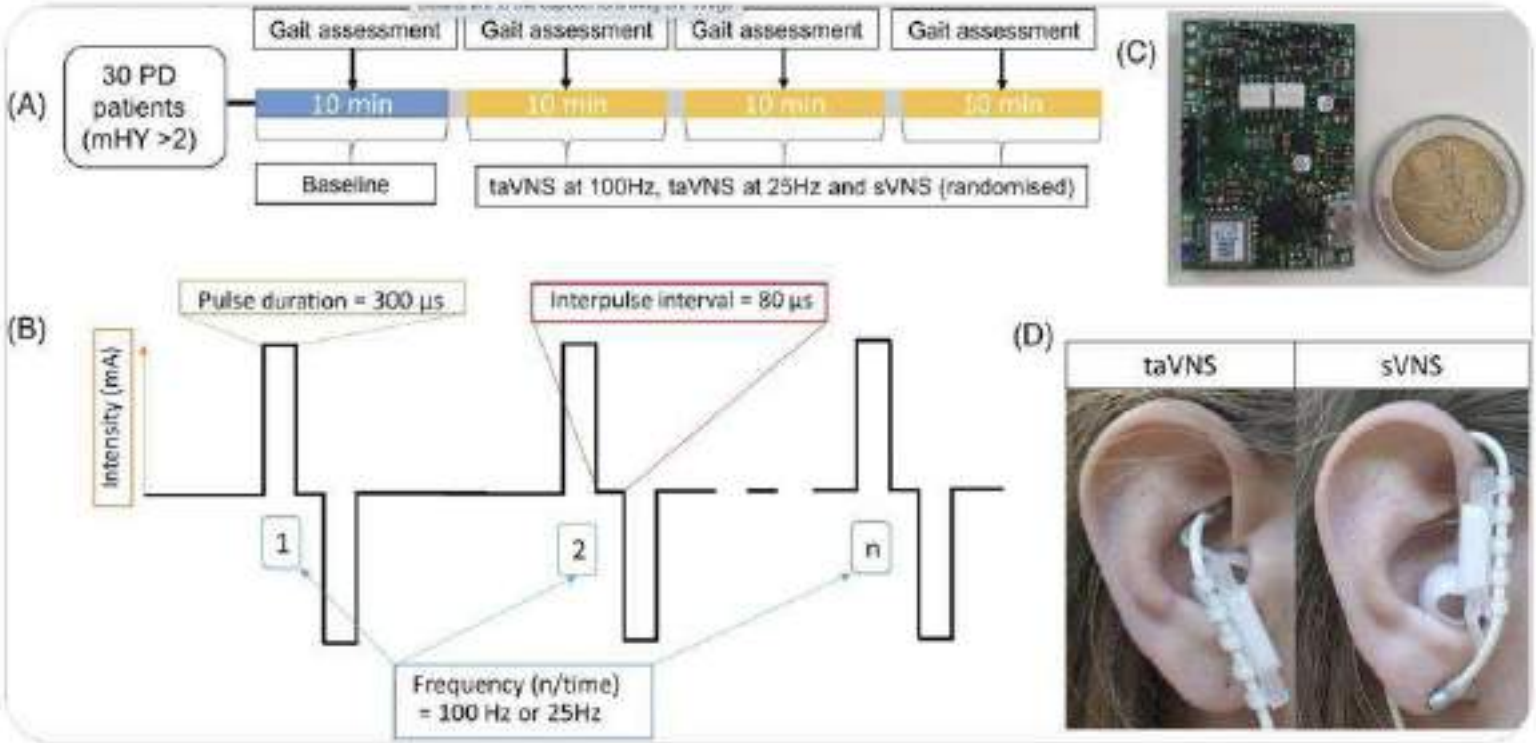
Michael Okun @MichaelOkun · May 22

Ear stimulation to treat walking in Parkinson's? **Transcutaneous** electrostimulation of the **auricular branch o**f the **vagal nerve**? YES says a new paper. Check out this randomized motion sensor study in Parkinson's by Vesna van Midden and colleagues @MDJ_Journal

Key Points:

-

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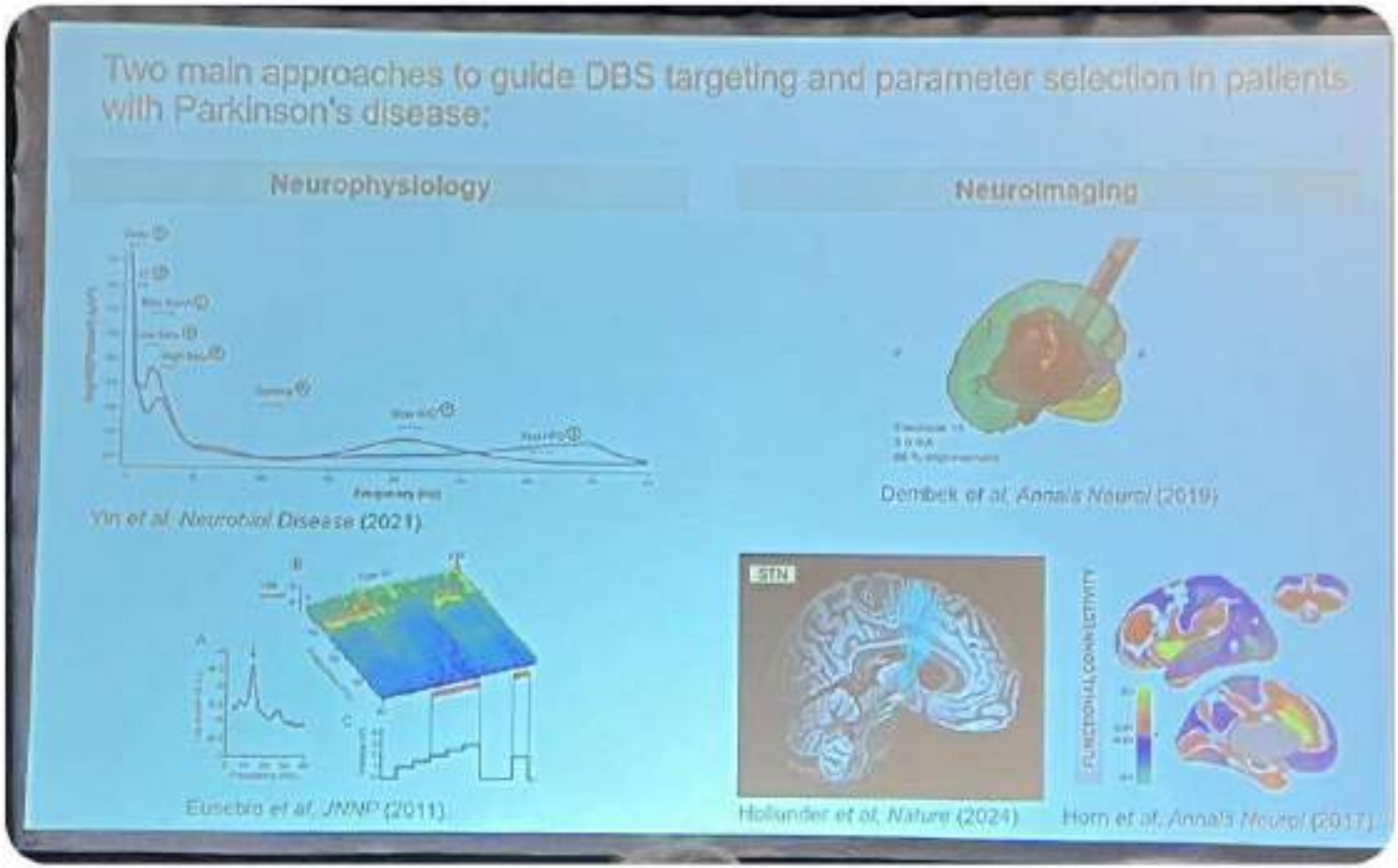


4 28 103 14K



Michael Okun @MichaelOkun · Jun 3

Do you know the two main approaches to guide programming deep brain stimulation? Neurophysiology and neuroimaging as @karaannjohnson delightfully blew our minds showing how ERNA could possibly be used to bridge gaps; guide clinicians of the future. @ASSFNeurosurg



8 30 4.9K



Michael Okun @MichaelOkun · Jun 4

How can focused ultrasound deliver cargo to the brain to treat human neurological diseases? Finnish physicist Kuellervo Hynyen shows us how the magic happens...

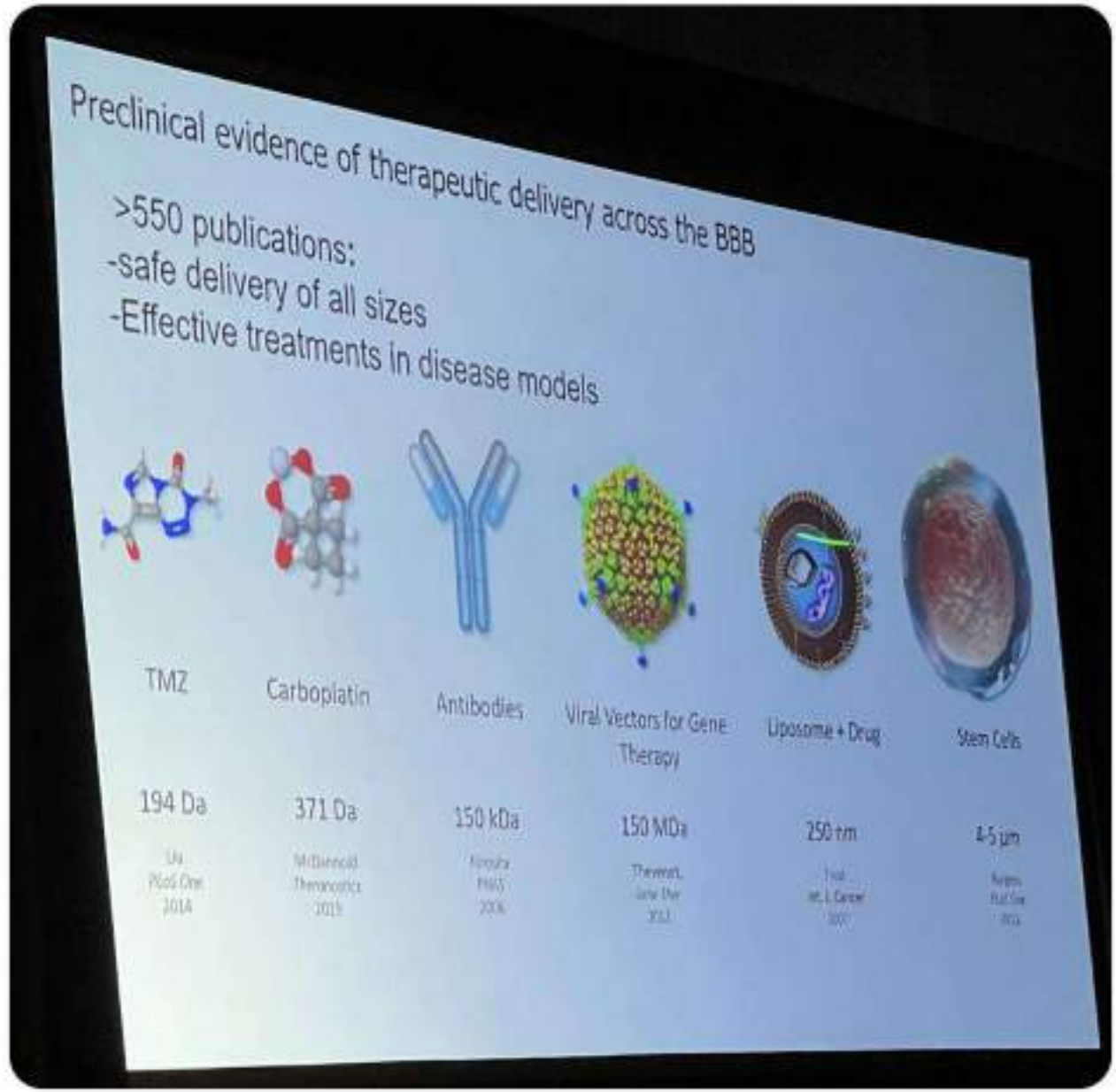


17 65 5.3K



Michael Okun @MichaelOkun · Jun 5

All shapes and sizes of cargo can be delivered to the brain by focused ultrasound. Great talk by the Finnish physicist and innovator Kuellervo Hynyen who is at @Sunnybrook #assfn

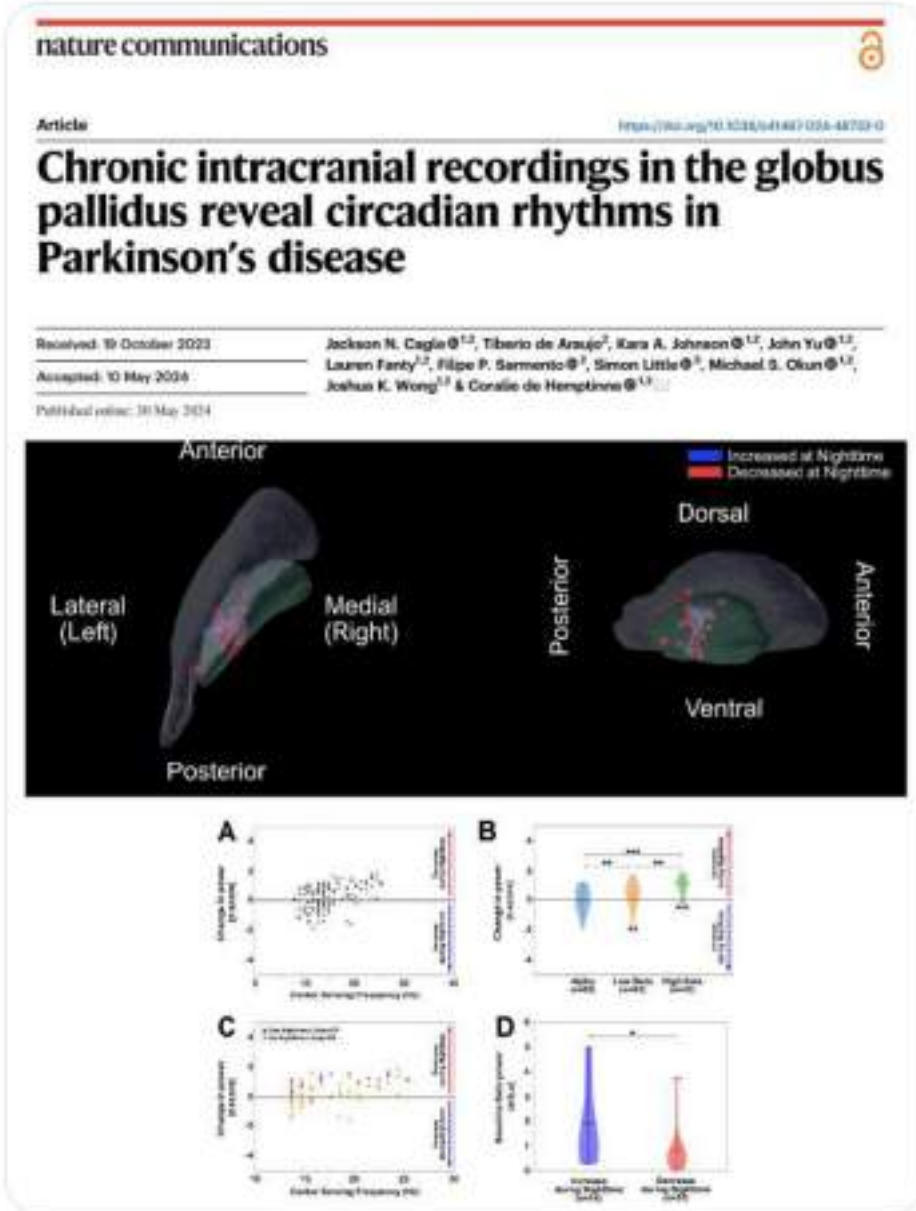




Michael Okun @MichaelOkun · Jun 5

Ever wonder how **circadian rhythms** are tracked in the brain? These rhythms represent the physical, mental, and behavioral changes experienced over a 24 hour cycle. Thus, it isn't just 'light and dark' which affect these rhythms and guess what? You can measure them in the human GPi

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nature communications

Article

Chronic intracranial recordings in the globus pallidus reveal circadian rhythms in Parkinson's disease

Received: 19 October 2023

Accepted: 10 May 2024

Published online: 30 May 2024

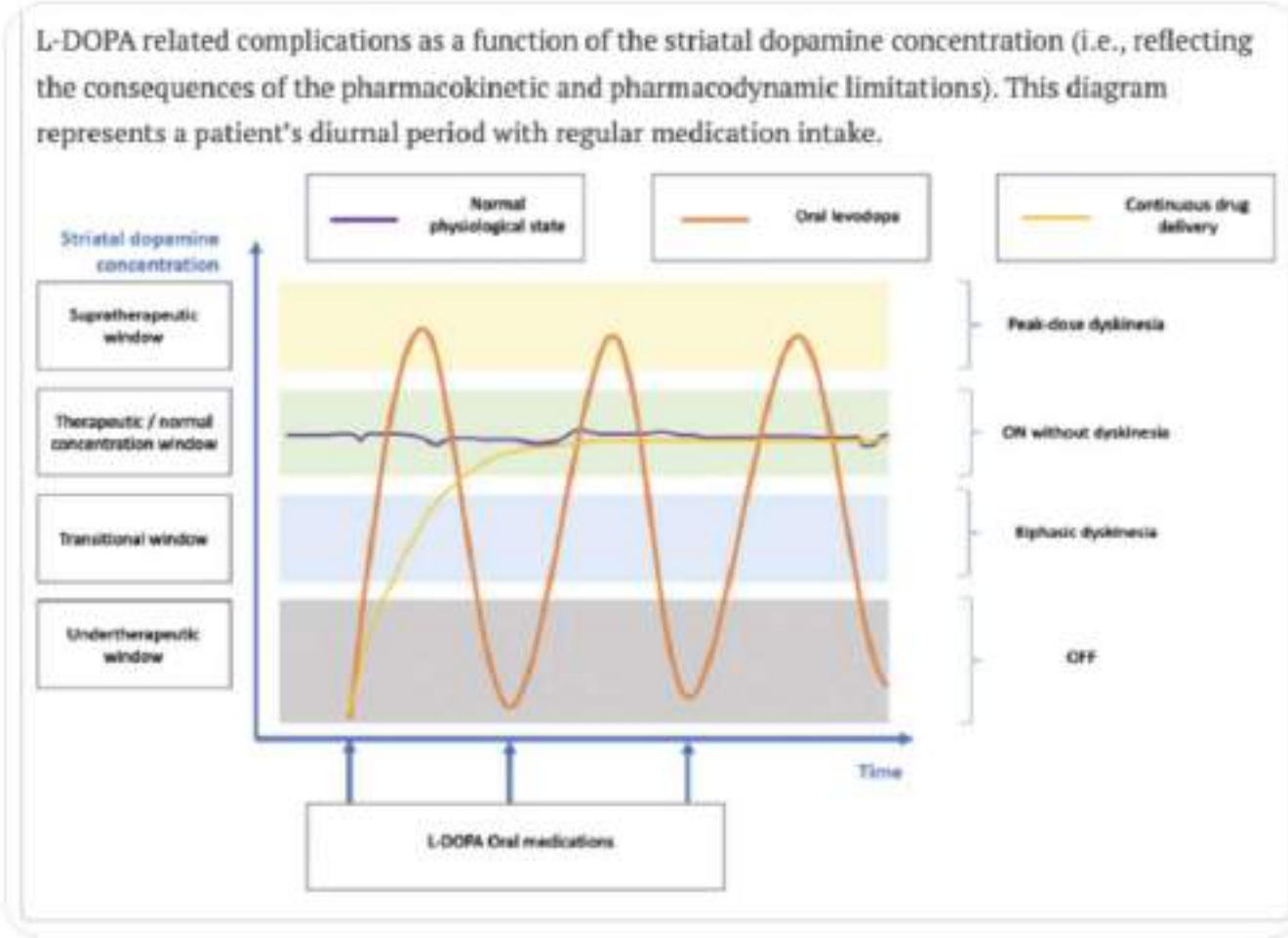
Jackson N. Cagle, Tiberio de Araujo, Kara A. Johnson, John Yu, Lauren Fanty, Filipe P. Sarmento, Simon Little, Michael S. Okun, Joshua K. Wong & Coralie de Hemptinne



Michael Okun @MichaelOkun · Jun 9

How effective are **continuous dopaminergic therapies** in **Parkinson's**? Can you name 6 limitations in current therapy? The shortcoming seems to be at least in part linked to the L-DOPA pharmacokinetics and pharmacodynamics as well as disease progression. Demailly, Moreau and Devos

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2 34 113 11K



Michael Okun @MichaelOkun · Jun 10

How about a **brain implant** that when '**squeezed or pressed**' it powers a neuromodulation device? The word **piezo** is derived from the Greek word πιέζω: to squeeze or to press. Hou and colleagues have a new paper in @NatureComms on a **novel implantable piezoelectric ultrasound**

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nature communications

Article | Open access | Published: 04 June 2024

An implantable piezoelectric ultrasound stimulator (ImPULS) for deep brain activation

Jason T. Hou, Md Osman Goni Naveen, Kian A. Caplan, Evan A. Ruesch, Albit Caban-Murillo, Ernesto Criado-Hidalgo, Sarah B. Ornellas, Brandon Williams, Ayella A. Pearce, Huseyin E. Dagdeviren, Michelle Surets, John A. White, Mikhail G. Shapiro, Fan Wang, Steve Ramirez & Canan Dagdeviren ✉

Nature Communications 15, Article number: 4601 (2024) | Cite this article

3068 Accesses | 61 Altmetric | Metrics



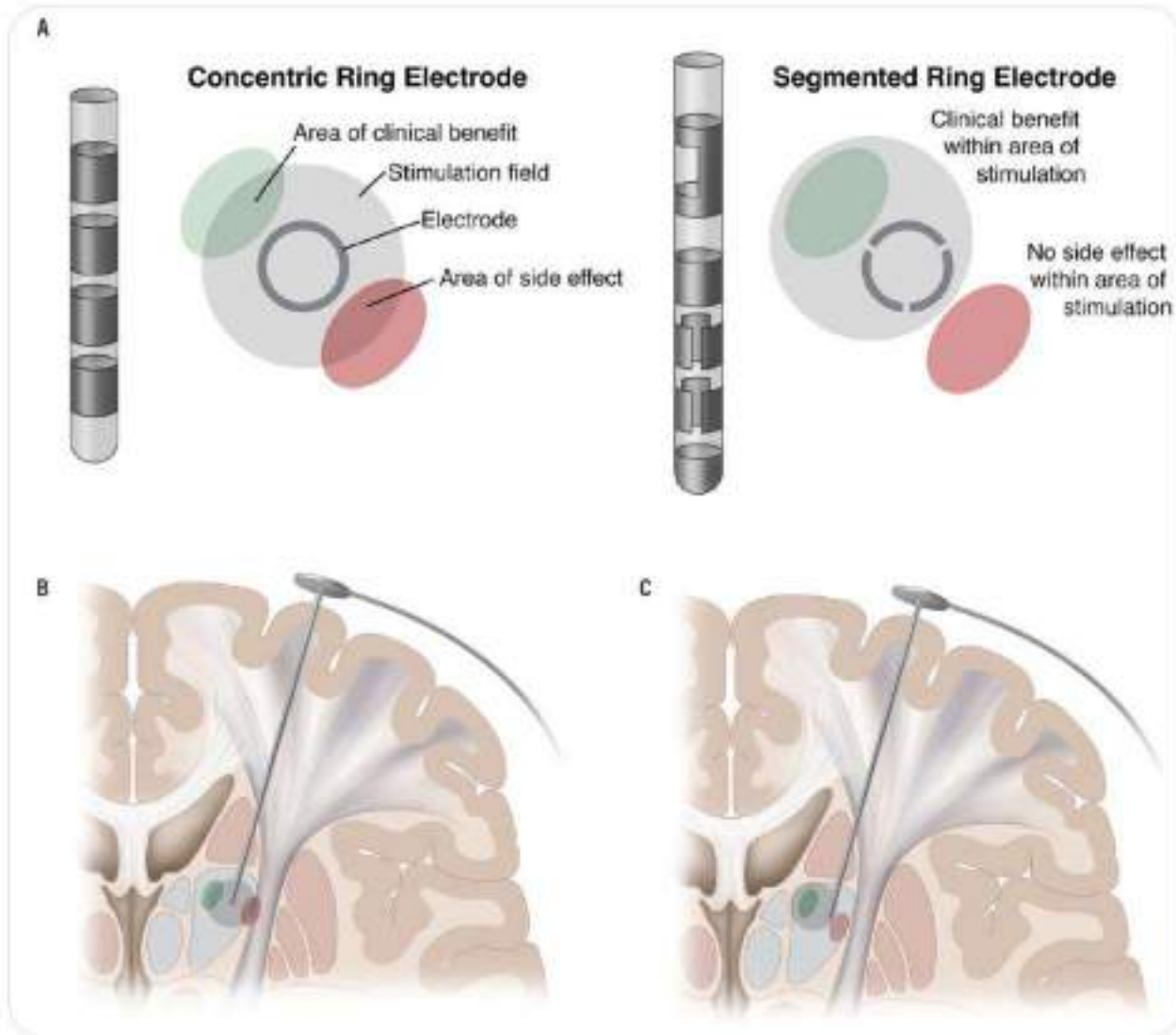
Michael Okun @MichaelOkun · Jun 11

Is **directional deep brain stimulation** programming the **bee's knees**? Is the segment clearly identifiable and stable over time? Spoiler alert: Nope. Karl, Verhagen and colleagues have a terrific new paper @MDCP_Journal.

Key Points:

- The authors noticed that when they programmed

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1 31 93 10K



Michael Okun @MichaelOkun · Jun 13

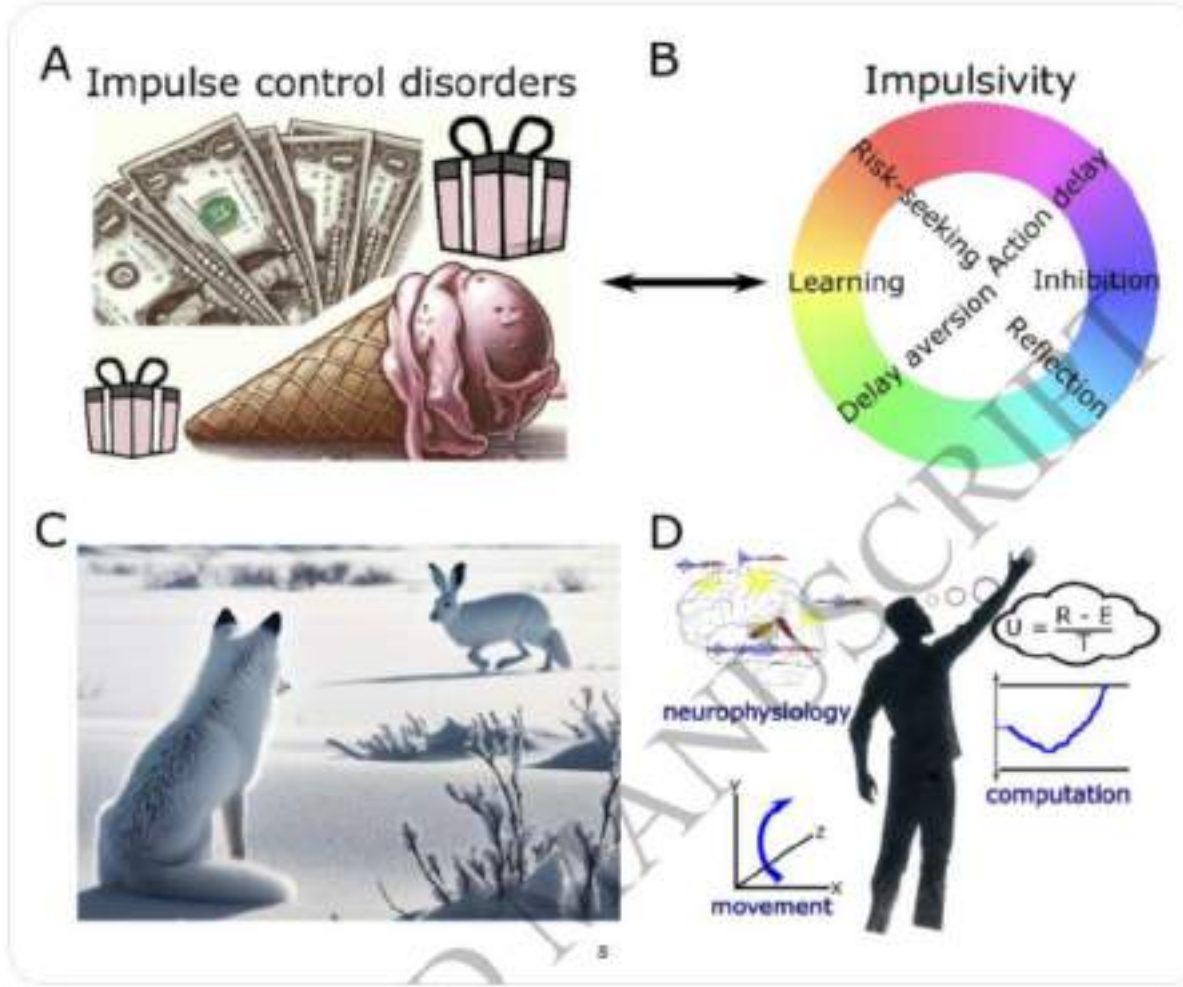
How does the **subthalamic nucleus** region control **impulsive actions**? Herz, Frank and colleagues use deep brain stimulation to teach us all about it @Brain1878.

Key Points:

- Basal ganglia dynamically control actions through recurrent **negative feedback loops**.

- The authors show us

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PLOS BIOLOGY

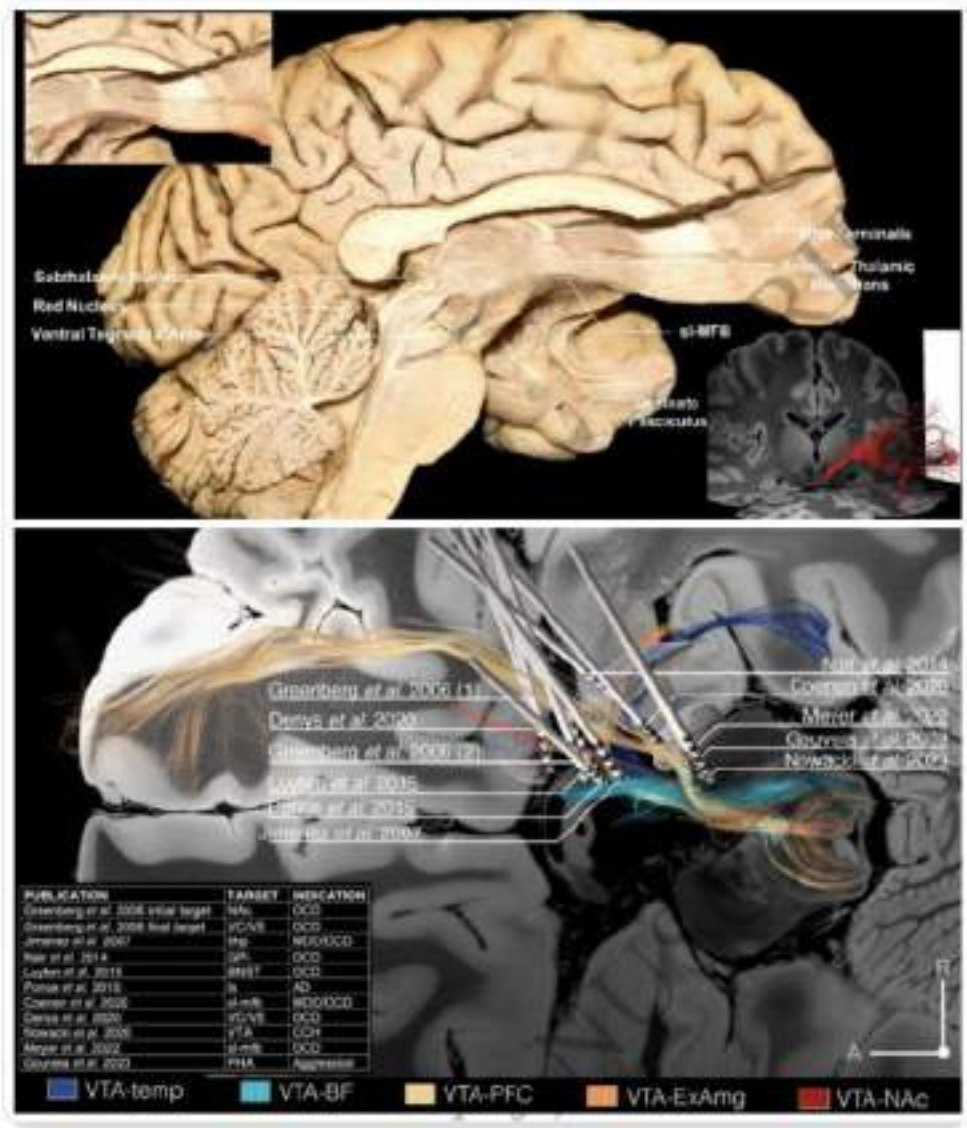
1 19 36 4K



Michael Okun @MichaelOkun · Jun 18

What if we performed **micro-dissections** of the human brain, uncovered its **connectivity** and merged it to **MRI based imaging.** Check out the incredible pictures in this article. Georgios Skandalakis and colleagues have a cool new paper on the midbrain region in the journal

Show more



21 79 6.6K



Michael Okun @MichaelOkun · Jun 20

Check out these three **'scary' scenarios** we should all proactively think about as **technology and brain implants surge**. Also, love the table by Hendriks and Grady @NEJM on considerations in **post-trial access**. 1- What happens when a brain device manufacturer **goes out of business** and

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FUNDAMENTALS OF MEDICAL ETHICS

Ethics and Highly Innovative Research on Brain Diseases

Saskia Hendriks, M.D., Ph.D., and Christine Grady, M.S.N., Ph.D.

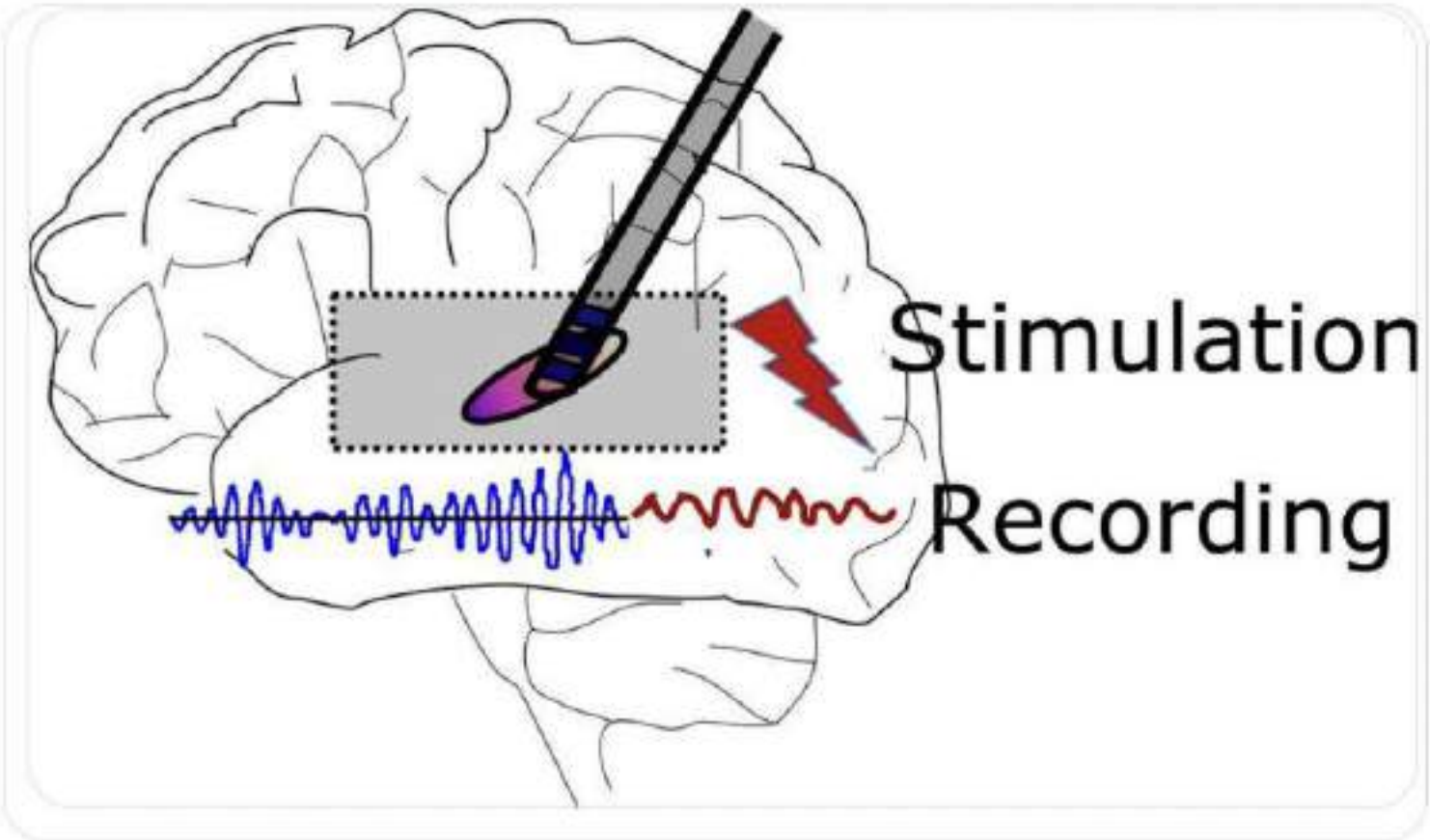
Selected Considerations and Responsibilities Related to Post-Trial Care after Brain Implant Trials.*

Professionals or Organizations	Considerations and Responsibilities
Research teams	Identify post-trial research-related risks, discomforts, and benefits by mapping out the patient journey in reasonable foreseeable scenarios (e.g., whether the device is commercialized) Identify continuing health care needs related to study participation. Minimize research-related post-trial risks and enhance potential benefits when designing the device, the study, and long-term care plans for former participants with implants. Describe post-trial care needs and plans in protocols for review by the IRB, the funder, and the FDA. Ensure that the informed consent process adequately informs patients about what happens after trials end (see "Reviewers" below for elements to be included). Within reasonable limits, ensure that appropriate referrals are made or remain available to provide necessary care that only the researchers can provide.
Research institutions	Consider contributing to critical unmet post-trial needs by waiving fees, providing financial support within limits, or both.
Device manufacturers	Minimize research-related post-trial risks and enhance potential benefits when designing the device, the study, and long-term care plans for former participants with implants. If hardware or software is incompatible with commercially available options, make a reasonable number of hardware replacements available (e.g., produce them up front) and provide software updates for a reasonable time. Consider contributing to critical unmet post-trial needs by providing financial support within limits. Establish industry standards to maximize compatibility where possible.
Funders	Request long-term plans and assess them. Consider contributing to critical unmet post-trial needs by providing financial support within limits.
Reviewers (IRBs, FDA)	Assess the adequacy of informed consent forms' description of what happens after trials end, including reasonably foreseeable post-trial risks, discomforts, and benefits, continuing medical care needs related to study participation, plans to provide or facilitate this care, and costs resulting from having participated in the trial. Include reasonably foreseeable research-related post-trial risks and benefits in the trial's risk–benefit analysis; ensure that these risks are also sufficiently minimized.



Michael Okun @MichaelOkun · Jun 22

'Subthalamic (STN) deep brain stimulation can lead to suboptimal choices by reducing the time that patients take for deliberation before committing to an action.' Love the discussion in @Brain1878 pubmed.ncbi.nlm.nih.gov/38869168/ @FixelInstitute @DBSThinkTank



20 51 3.4K



Michael Okun @MichaelOkun · Jun 27

Hey folks how about a simple 11 question scale to assess expectations for Parkinson's disease deep brain stimulation? Can this prevent **post-operative disappointment** and improve outcomes? Would you use or take it? Well, Meyer Mylène and colleagues have just published one in J

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Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns



Development and validation of the DBS-PS (Deep Brain Stimulation-Perception Scale): Assessing parkinsonian patients' expectations to prevent post-operative disappointment?

Meyer Mylène [a,*], Spitz Elisabeth [b], Colnat-Coulbois Sophie [c], Benatru
Guehl Dominique [e], Hainque Elodie [f], Rolland Anne-Sophie [g], Corvol J
Devilliers Hervé [h], Schwan Raymund [i,j], Devos David [a,k], the PREDIST

THE NEUROLOGIST

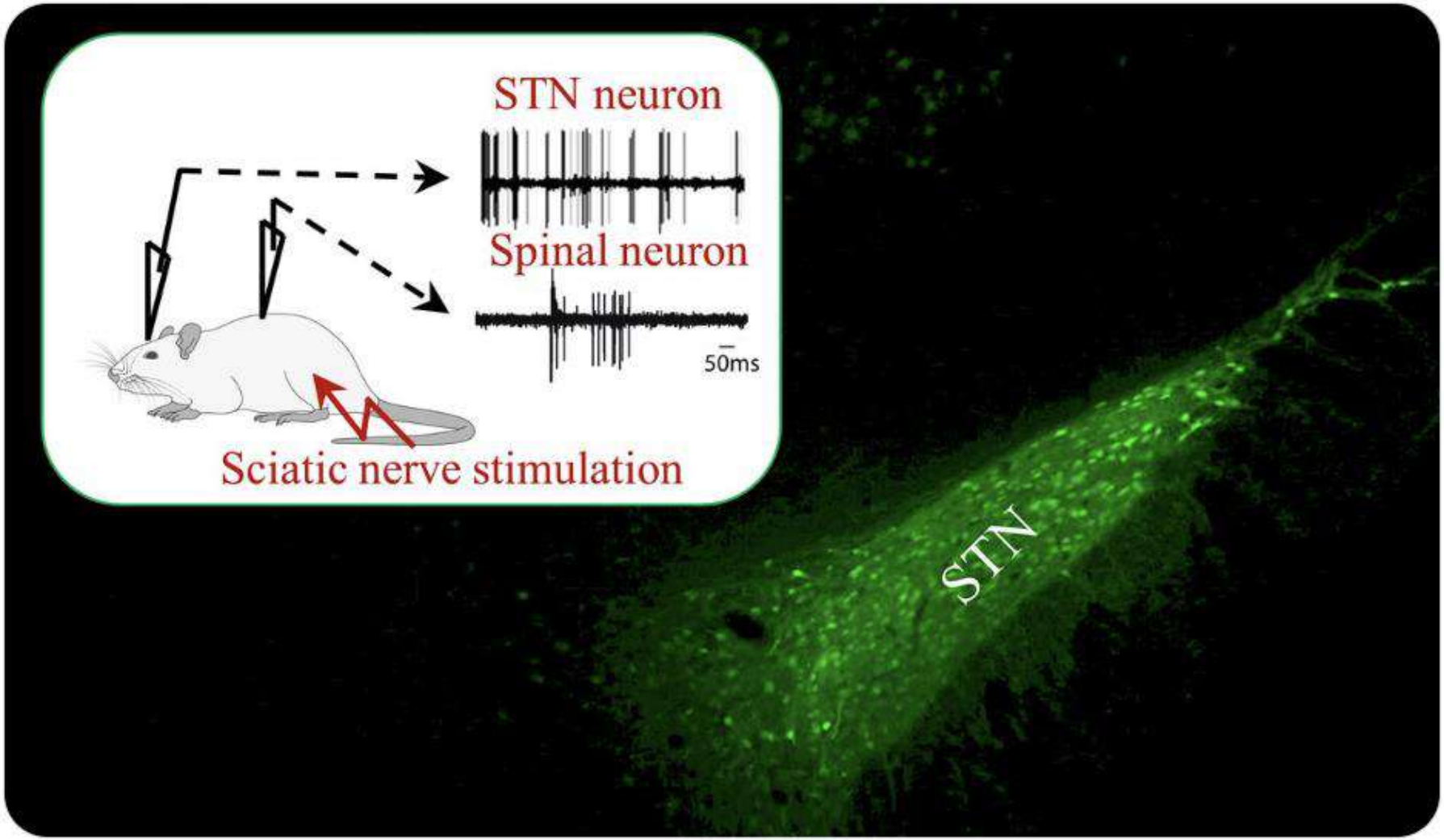


TABLE 1. University of Florida Mnemonic Device for Patients With PD Considering DBS

Does not cure.
Bilateral DBS is often required to improve gait, although sometimes unilateral DBS has a marked effect on walking.
Smooths out on/off fluctuations.
Improves tremor, bradykinesia (slowness), stiffness (rigidity), and dyskinesia in most cases, but may not completely eliminate them.
Never improves symptoms that are unresponsive to your best "on." For example, if gait or balance do not improve with best medication response, it is very unlikely to improve with surgery.
Programming visits are likely to occur many times during the first 6 months, and then follow-up visits as frequently as every 6 months. There will be multiple adjustments in the stimulator and in the medications.
Decreases medications in many, but not all patients.

Brain @Brain1878 · Jun 27

Charles et al. study the involvement of the STN in the perception of pain associated with Parkinson's disease, and conclude that it plays a central role in the pain circuitry through its interaction with the spinal cord.
tinyurl.com/yc443wxu

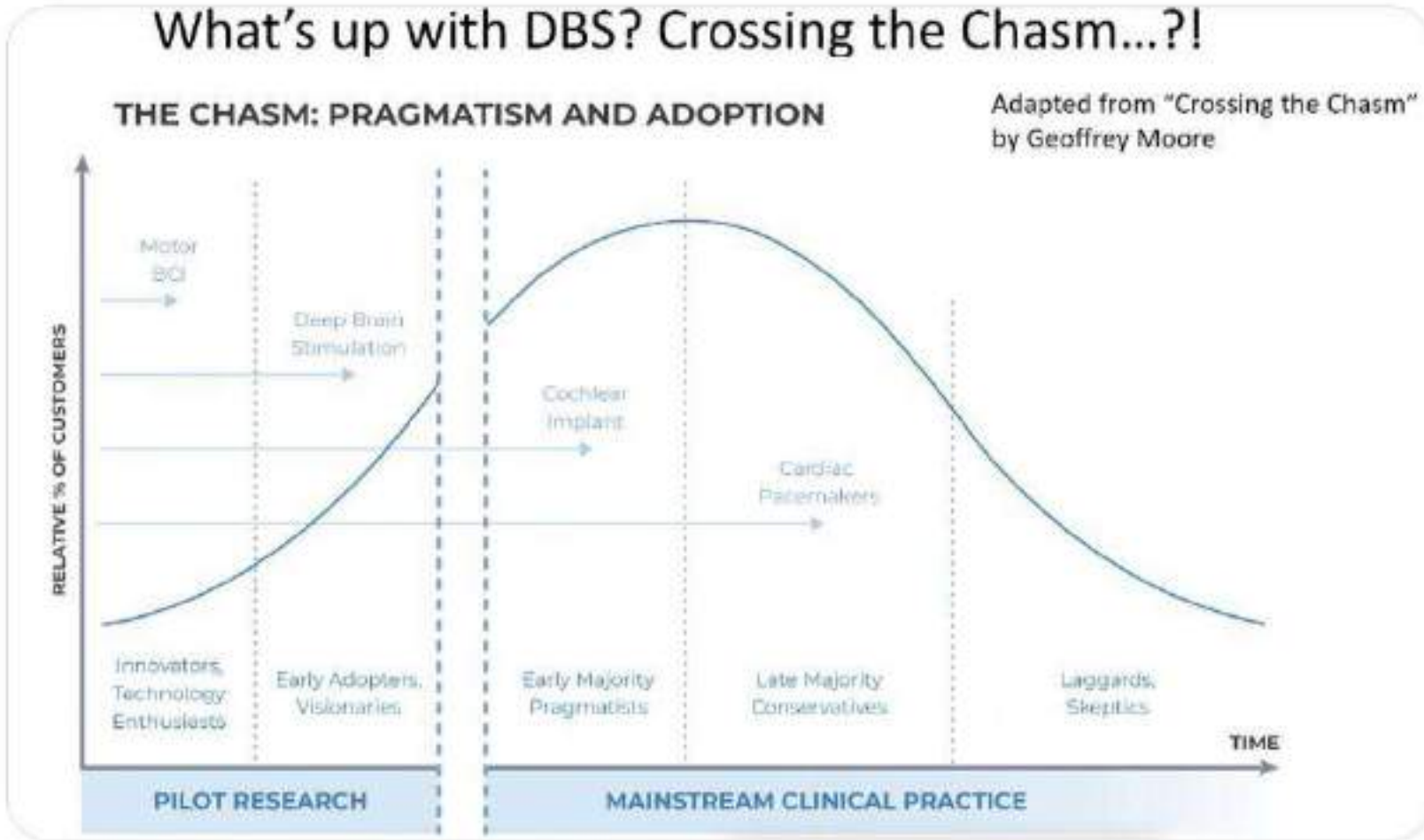




Michael Okun @MichaelOkun · Jul 3

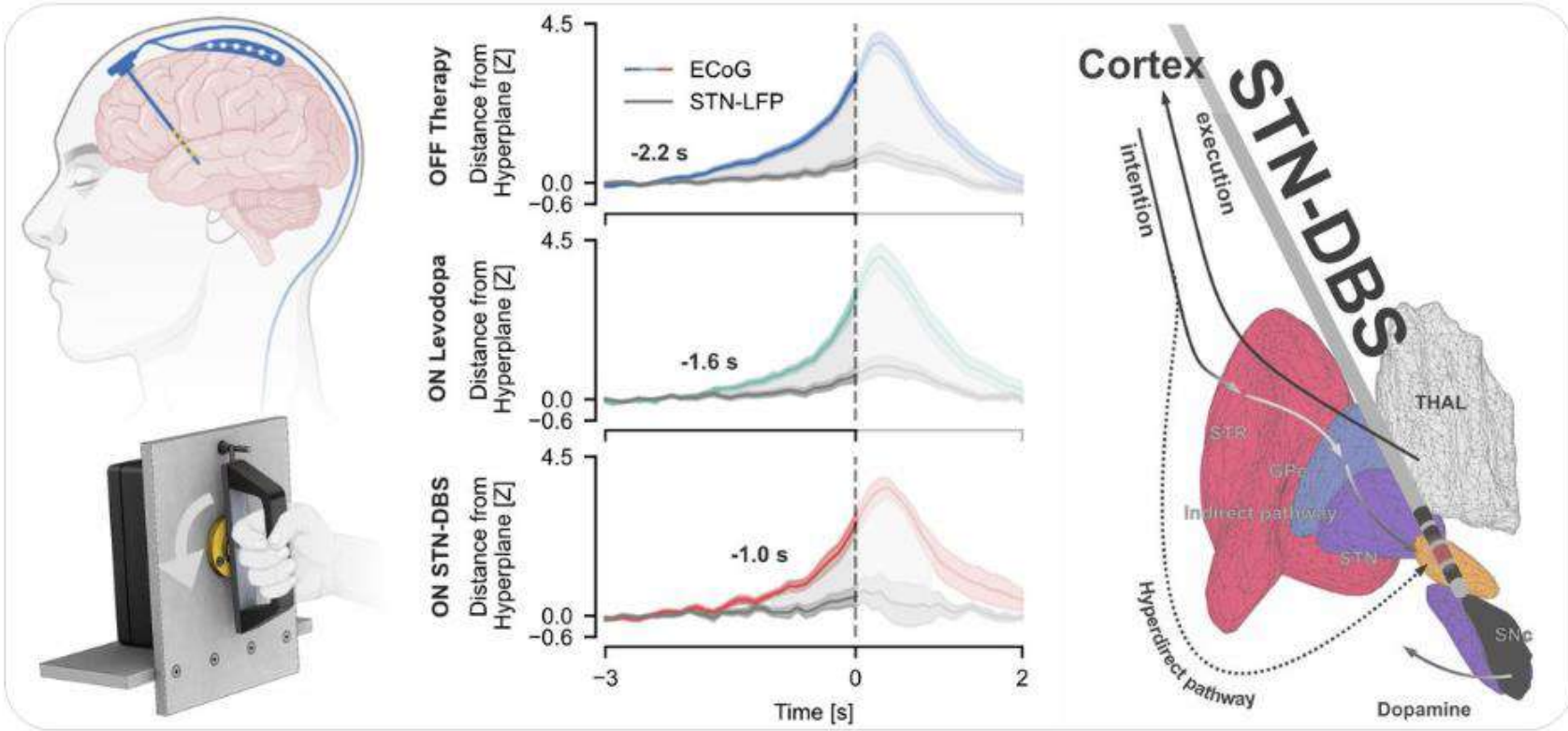
What are the **barriers to adopting implantable brain stimulation** into the standard of care across central nervous system disorders, and what are the potential strategies and collaborations to develop **sustainable and scalable utility** in the future? Great planning committee of the

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Brain @Brain1878 · Jul 4

By recording from sensorimotor cortex and the STN in patients with Parkinson's disease performing self-initiated movements, Köhler et al. obtain evidence that dopamine and DBS improve movement initiation via shared mechanisms of action. tinyurl.com/mwpusdew

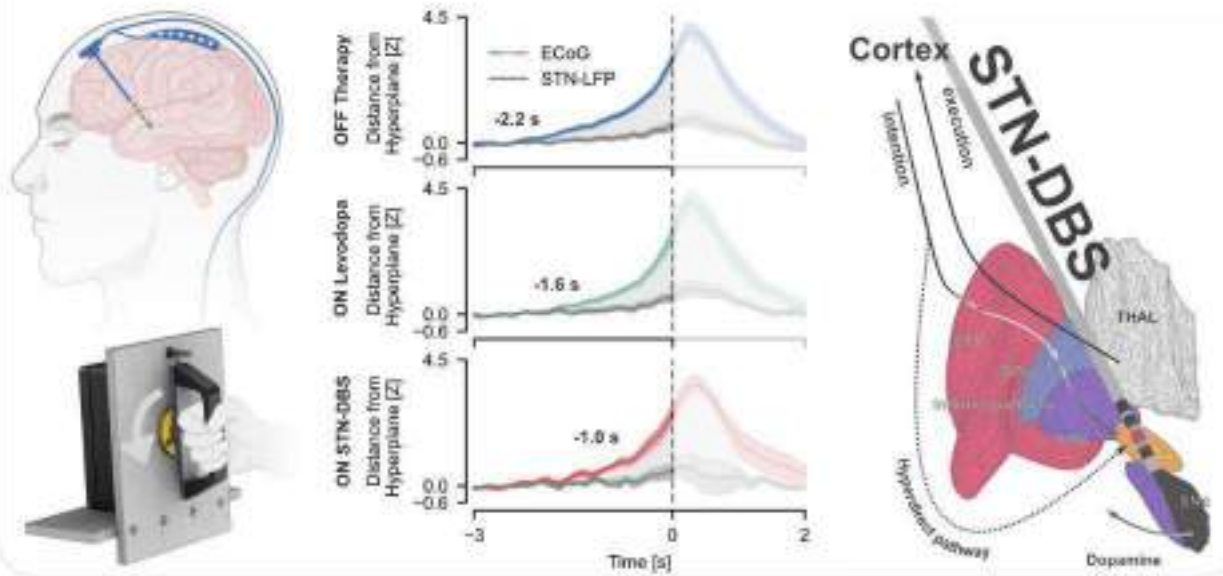


2 21 68 7.9K

Julian Neumann @neumann_wj · Jul 5

As young PI it's so exciting to see young talents excel. New @ICNeuromodulate study spearheaded by @rm_koehler out in @Brain1878. We used brain signal decoding to demonstrate that both dopamine and deep brain stimulation accelerate the neural dynamics of volitional action!

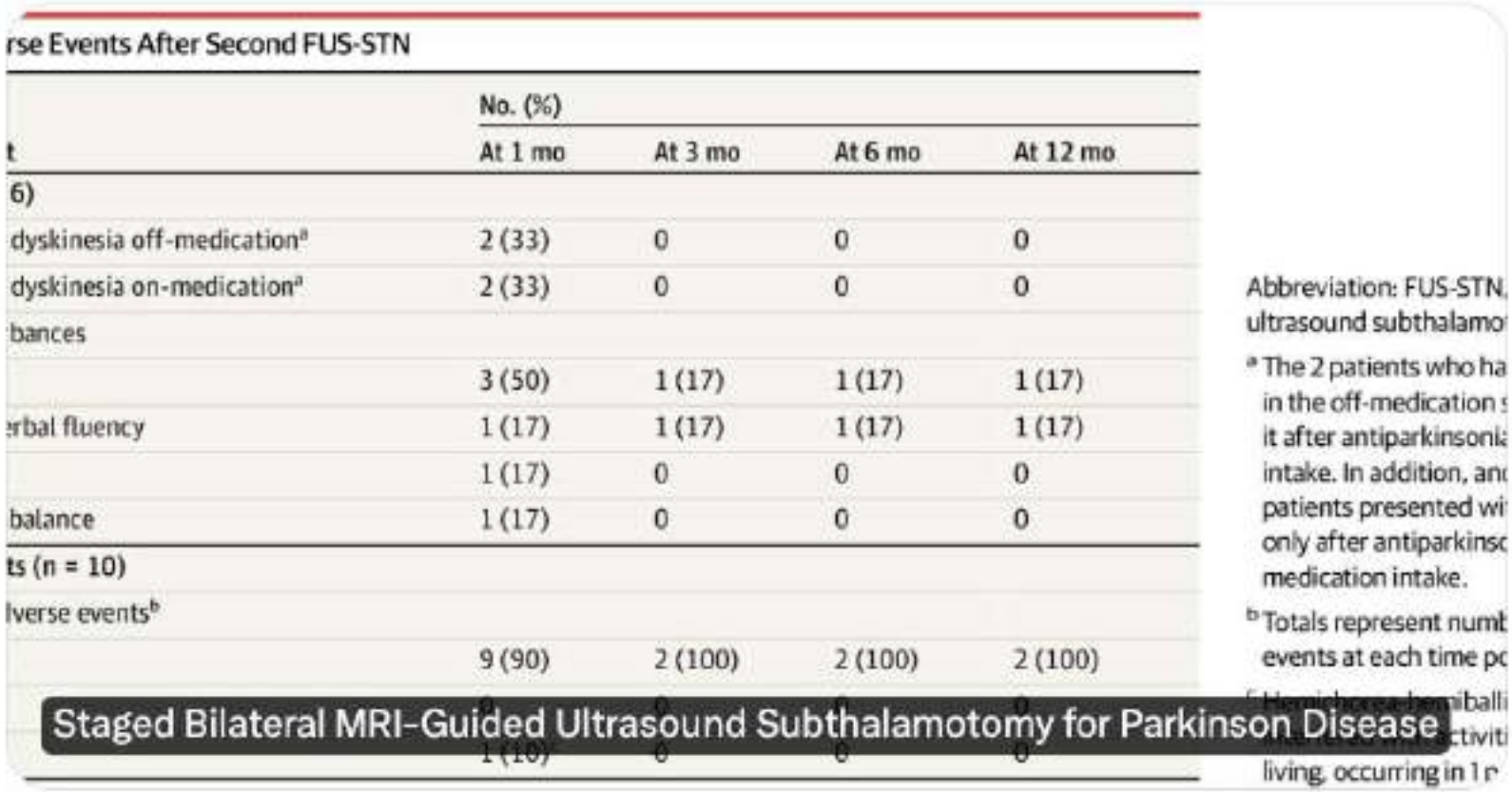
> **Brain** @Brain1878 · Jul 4
>
> By recording from sensorimotor cortex and the STN in patients with Parkinson's disease performing self-initiated movements, Köhler et al. obtain evidence that dopamine and DBS improve movement initiation via shared mechanisms of action. tinyurl.com/mwpusdew



14 35 3.9K

JAMA Neurology @JAMANeuro · Jul 4

Staged bilateral MRI–guided focused ultrasound subthalamotomy was associated with significant motor improvement among patients with Parkinson disease, finds open-label case series.



rse Events After Second FUS-STN

t	No. (%) At 1 mo	At 3 mo	At 6 mo	At 12 mo
6)				
dyskinesia off-medication[a]	2 (33)	0	0	0
dyskinesia on-medication[a]	2 (33)	0	0	0
bances				
	3 (50)	1 (17)	1 (17)	1 (17)
rbal fluency	1 (17)	1 (17)	1 (17)	1 (17)
	1 (17)	0	0	0
balance	1 (17)	0	0	0
ts (n = 10)				
lverse events[b]				
	9 (90)	2 (100)	2 (100)	2 (100)
	1 (10)	0	0	0

Abbreviation: FUS-STN, ultrasound subthalamo

[a] The 2 patients who ha in the off-medication s it after antiparkinsoni intake. In addition, an patients presented wi only after antiparkinso medication intake.

[b] Totals represent numb events at each time po

Staged Bilateral MRI-Guided Ultrasound Subthalamotomy for Parkinson Disease

living, occurring in 1 p

From jamanetwork.com

6 12 2.2K

‘Autoimmune Age’

Child's Nervous System (2022) 38:203–206
https://doi.org/10.1007/s00381-021-05152-5

CASE REPORT

Pediatric autoimmune Parkinsonism and response to deep brain stimulation

Yulia Salamatova[1] · Irene Malaty[2] · Suman Ghosh[3]

Child's Nervous System

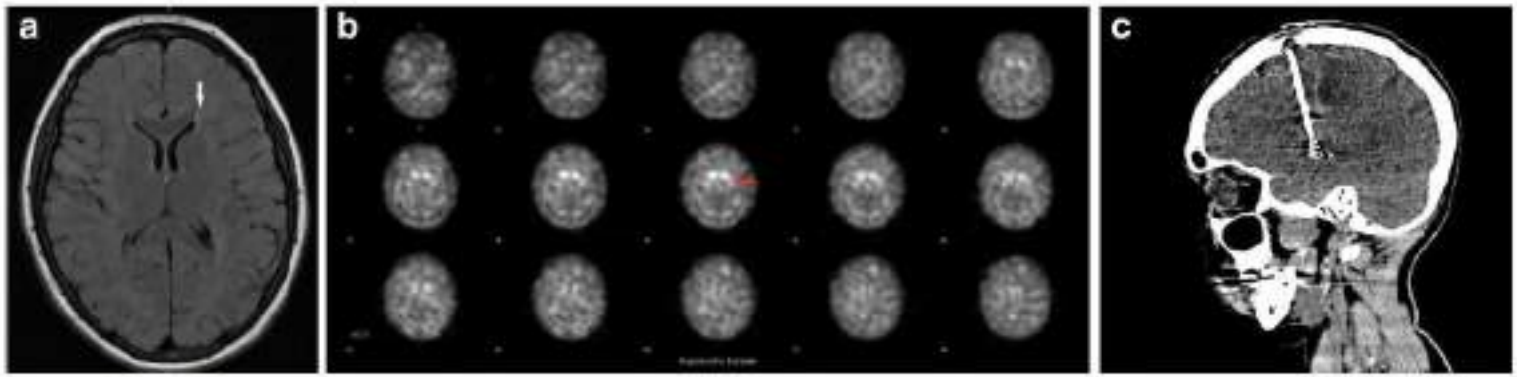


Fig. 1 a MRI FLAIR/T2 hyperintensity in the periventricular white matter (white arrow). b DAT scan pattern showing faint uptake in the caudates (red arrow) with no uptake in the putamen. c CT head with DBS placement

- 13 year old post-influenza
- Pediatric autoimmune parkinsonism with autoantibodies to dopamine D2L receptor: anti-DRD2L antibodies.
- Dyskinesia on levodopa.
- Bilateral GPi DBS nild improvements parkinsonism

npj | Parkinson's Disease

www.nature.com/np

ARTICLE OPEN

Systematic evaluation of levodopa-carbidopa intestinal gel patient-responder characteristics

David G. Standaert[1], James T. Boyd[2], Per Odin[3], Weining Z. Robieson[4], Jorge Zamudio[4] and Krai Chatamra[4]

- n=324 patients; 272 (84.0%) were Responders and 52 (16.0%) were Non-Responders
- Baseline characteristics were similar between all groups including Robust Responders.
- Identified baseline "Off" time as the only factor that had significant effect on Responder and Robust Responder status
- The safety profile of LCIG was similar between patient groups

Lesions

Solid evidence literature
Become less popular
"Reversibility" and AE's bilateral lesions

Research Review

Lesion Therapy for Parkinson's Disease and Other Movement Disorders: Update and Controversies

Michael S. Okun, MD,[1] and Arnold L. Vitek, MD, PhD[2]

Clinical Study

Stereotactic and Functional Neurosurgery

Clinical Cases where Lesion Therapy Was Chosen over Deep Brain Stimulation

Amanda K. Hooper Michael S. Okun Kelly D. Foote Hubert H. Fernandez
Charles Jacobson Pamela Zeilman Janet Romrell Ramon L. Rodriguez

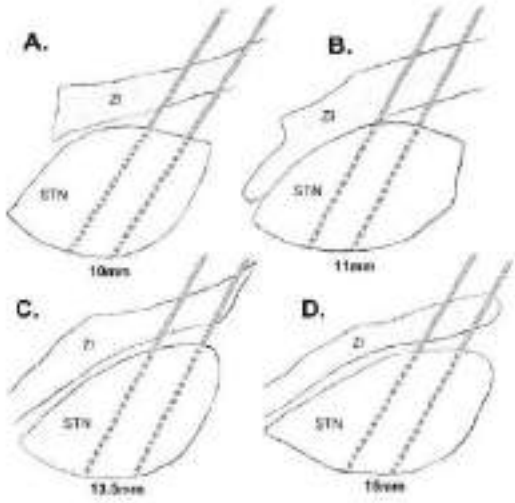


Table 1. Reasons to consider lesion therapy over DBS

Considerations for lesion therapy	Rationale
Immunocompromised health status	an implanted lead may provide a higher risk of infection
Access to care	frequent follow-up visits and device-related management by trained providers (management includes programming, examinations and battery replacements)
Old age/friable skin	loss of skin elasticity and thickness may result in more difficult healing in elderly patients
Children	small children under 8 (for example, dystonia patients) may develop skin erosions related to the size of the DBS hardware
Lack of expertise at a treating center	DBS requires trained staff and special equipment to be managed successfully
Unilateral procedures/athletes	a subset of patients may prefer to have a lesion without the excess management issues, especially if a unilateral procedure is all that is required some athletes may prefer lesions over DBS especially in contact-related sports
Reduce cost	battery changes, frequent doctor and nurse visits, and medication management can all add to the difficulty in managing patients with DBS; these issues may be less with lesion therapy

**Multiple Infections
Lesion through the device

History of Ablative Therapies

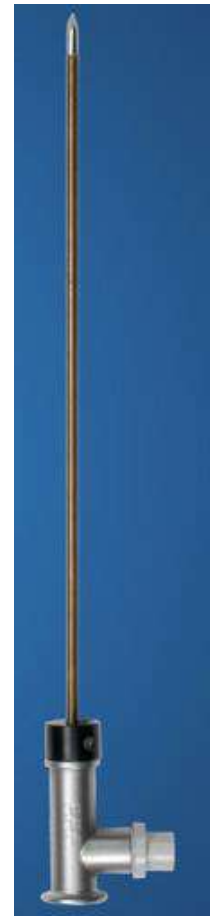
Radio-ablation also some alcohol ablation

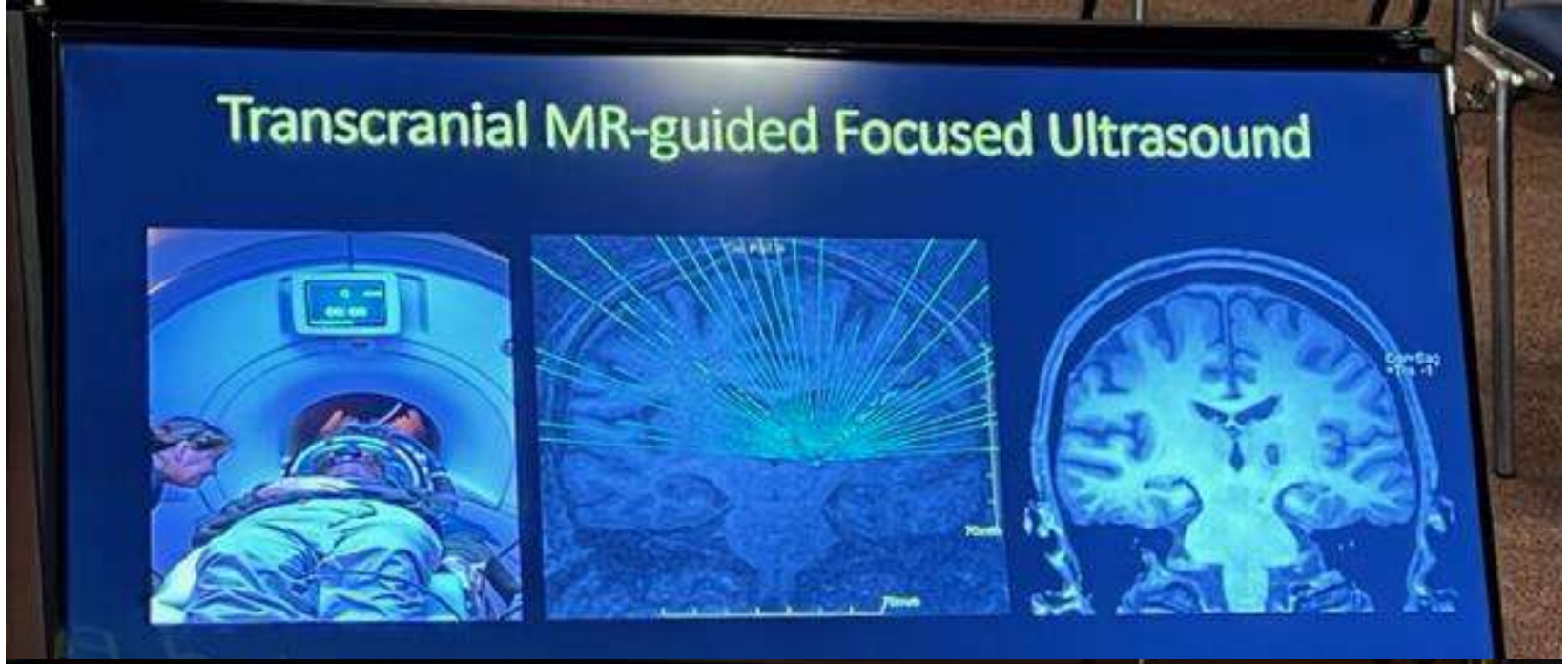
Slightly different AE profile; Similar outcomes unilateral DBS

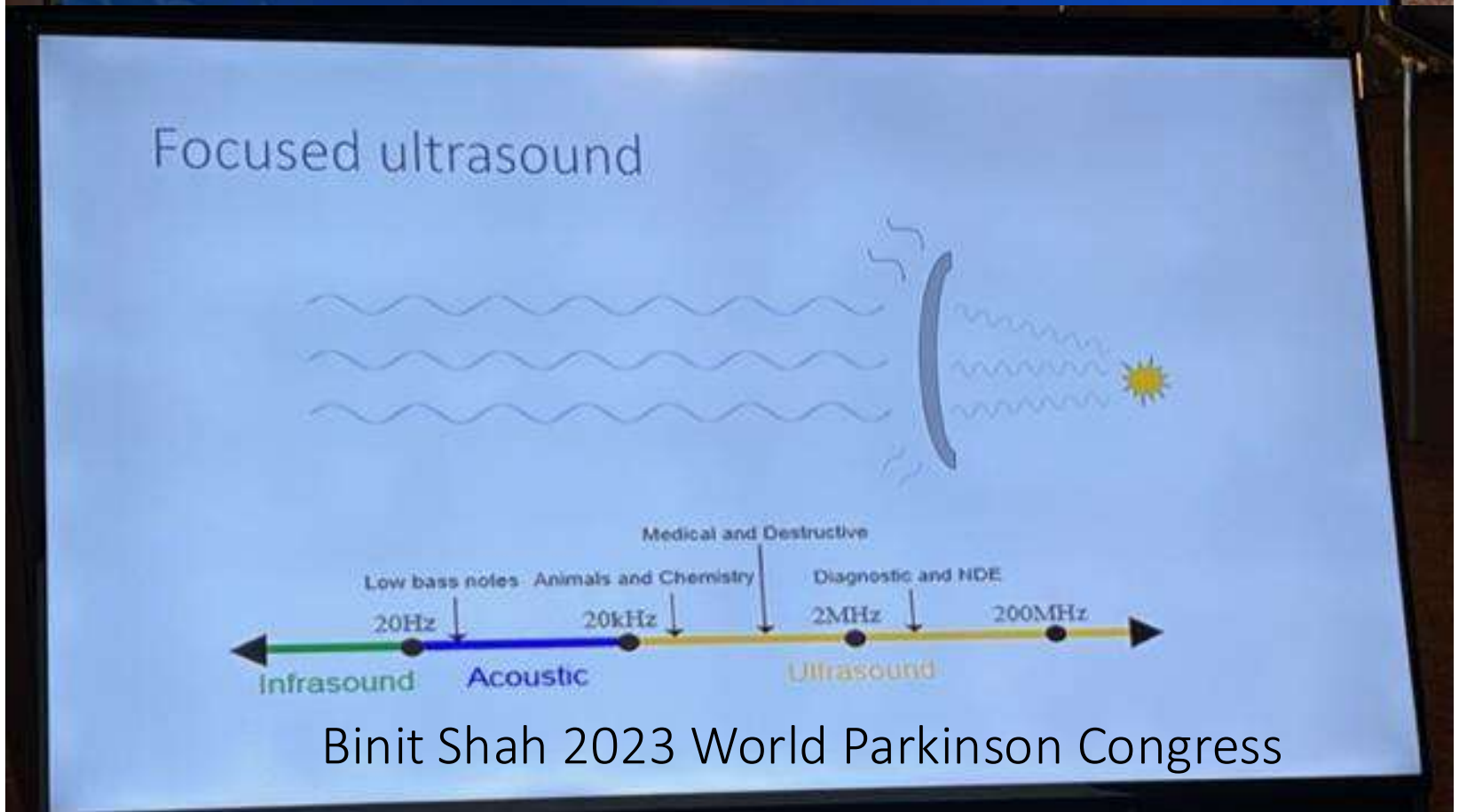


TABLE 1. *History of lesion therapy for Parkinson's disease and movement disorders*

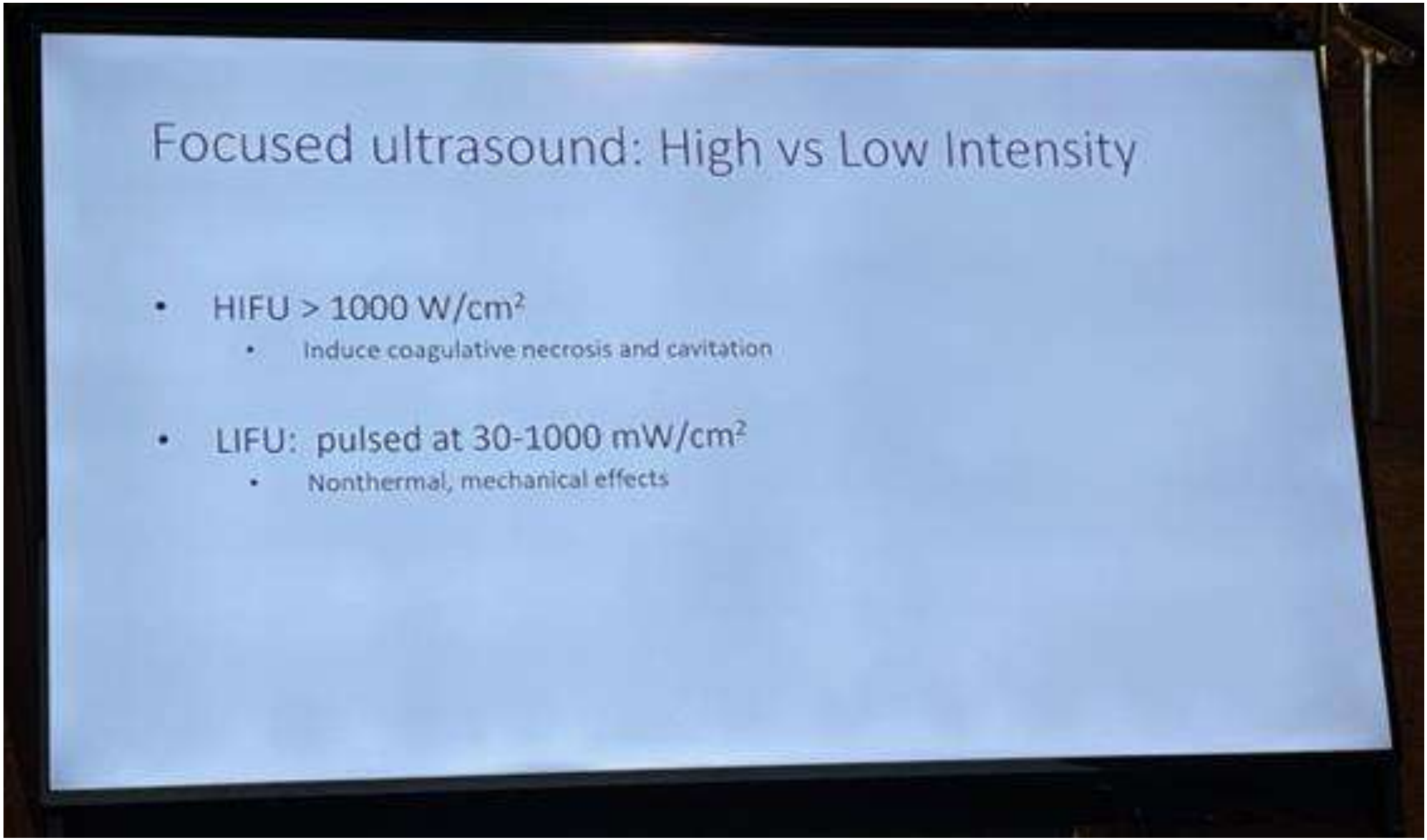
Reference	Therapy
Horsley et al., 1909	Excised motor cortex for treatment of athetosis
Bucy et al., 1939	Excised cortex for PD tremor
Bucy et al., 1950	Lesioned caudate and globus pallidus
Klemme et al., 1940	Resected portions of the pyramidal system
Meyers et al., 1942	Removed globus pallidus and sectioned efferent fibers
Spiegel et al., 1946–1947	Introduced stereotaxic surgery on the ansa lenticularis
Putnam et al., 1948	Incised pyramidal tract in upper cervical cord
Browder et al., 1948	Section anterior internal capsule, pallidum, putamen Rigidity and tremor improved; paralysis was partial
Browder et al., 1950	Sectioned cervical cord no change in rigidity or tremor
Walker et al., 1952	Section cerebral peduncles tremor affected by paralysis
Fenelon and Thiebaut, 1950	Coagulation of ansa lenticularis
Guiot and Brion et al., 1952	Coagulation of efferent fibers of pallidum (leucotome)
Cooper, 1953	Ligation of the anterior choroidal artery
Hassler, 1955	Performed some of the first thalamotomies
Cooper et al., 1954	Chemopallidectomy and chemothalamectomy (alcohol)
Cotzias et al., 1967	Introduction of L-dopa slowing development of surgical procedures
Narabayashi et al., 1973	Microelectrode recordings for thalamotomy
Laitinen et al., 1992	Reintroduction of pallidotomy
Gill, Alvarez et al., 1997–2001	Introduction of subthalamotomy for Parkinson's disease







Binit Shah 2023 World Parkinson Congress



Binit Shah 2023 World Parkinson Congress

Focused Ultrasound

- FDA approved as a therapy for Parkinson's disease (and approved ET)
- Risks lower (infection, hemorrhage) than conventional lesion
- Careful of term "scalpel-less"
- Bilateral lesions (cognition, swallowing, speech)
- 4/15 subjects (26.7%) had persistent sensory side effects (used test lesions)
- Microelectrode recording and physiological mapping cannot be used to refine brain targets in ultrasound therapy

Neurosurgery. 2016 Aug;63 Suppl 1:154. doi: 10.1227/01.neu.0000486702.18785.ff

132 A Randomized, Sham-Controlled Trial of Transcranial Magnetic Resonance-Guided Focused Ultrasound Thalamotomy Trial for the Treatment of Tremor-Dominant, Idiopathic Parkinson Disease.

Bond AE, Dallapiazza R, Huss D, Warren AL, Sperling S, Gwinn R, Shah BB, Elias WJ.

Article

A prospective single-blind study of Gamma Knife thalamotomy for tremor

Tatiana Witjas, MD, Romain Carron, MD, PhD, Paul Krack, MD, PhD, Alexandre Eusebio, MD, PhD, Marianne Vaugoyeau, PhD, Marwan Hariz, MD, PhD, Jean Philippe Azulay, MD, PhD and Jean Régis, MD

+ SHOW AFFILIATIONS | + SHOW FULL DISCLOSURES

Correspondence to Dr. Witjas: tatiana.witjas@ap-hm.fr

Published online before print October 7, 2015, doi: http://dx.doi.org/10.1212/WNL.0000000000002087

Neurology November 3, 2015 vol. 85 no. 18 1562-1568

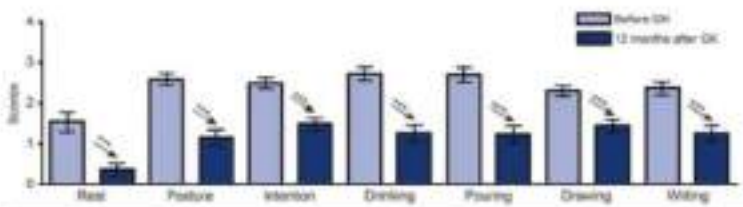


FIGURE 2 Pre- and post-GK comparison of the subscores for blinded assessments

Mean and SEM of each subscore. ***$p < 0.001$. All subscores improved after radiosurgery as before radiosurgery for the blinded rater. GK = Gamma Knife.

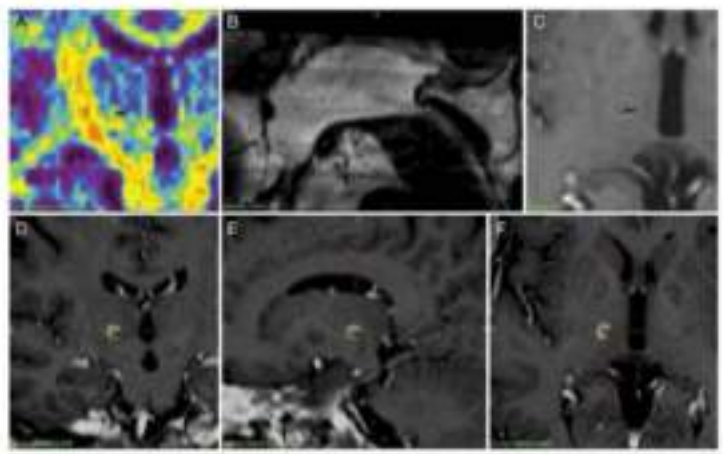


FIGURE 3 Treatment plan (upper panels) and 12-month neuroimaging follow-up (lower panels)

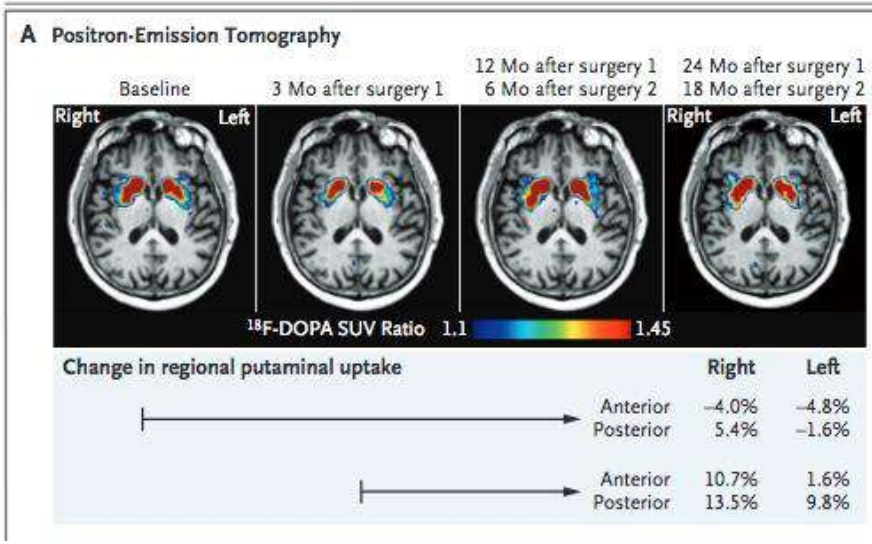
The thalamic lesion matches exactly with the planned target (as outlined by the 65-Gy (50%) isodose line). Upper panels: Diffusion tensor imaging coronal (A), T2-sagittal (B), and gadolinium-enhanced T1-weighted axial (C). Lower panels: Gadolinium-enhanced T1-weighted in coronal (D), sagittal (E), and axial (F) planes.

The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

Personalized iPSC-Derived Dopamine Progenitor Cells for Parkinson's Disease

Jeffrey S. Schweitzer, M.D., Ph.D., Bin Song, M.D., Ph.D., Todd M. Herrington, M.D., Ph.D., Tae-Yoon Park, Ph.D., Nayeon Lee, Ph. Sanghyeok Ko, Ph.D., Jeha Jeon, Ph.D., Young Cha, Ph.D., Kyungsang Kim,



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

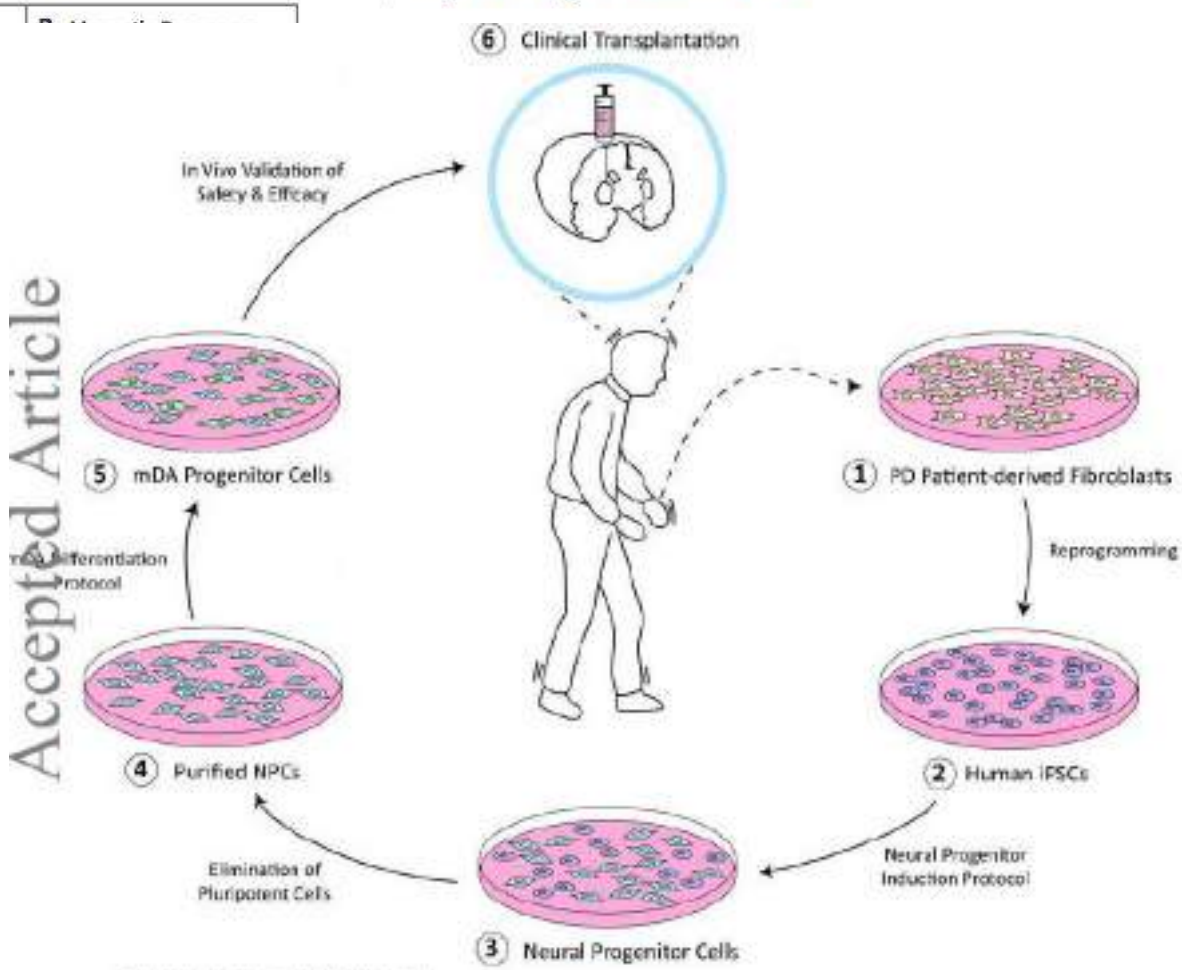
Viewpoint | Full Access

Stem Cells: Scientific and Ethical Quandaries of a Personalized Approach to Parkinson's Disease

Joseph Jankovic MD, Michael S. Okun MD, Jeffery H. Kordower PhD

2020 | https://doi.org/10.1002/mds.28187

Accepted Article



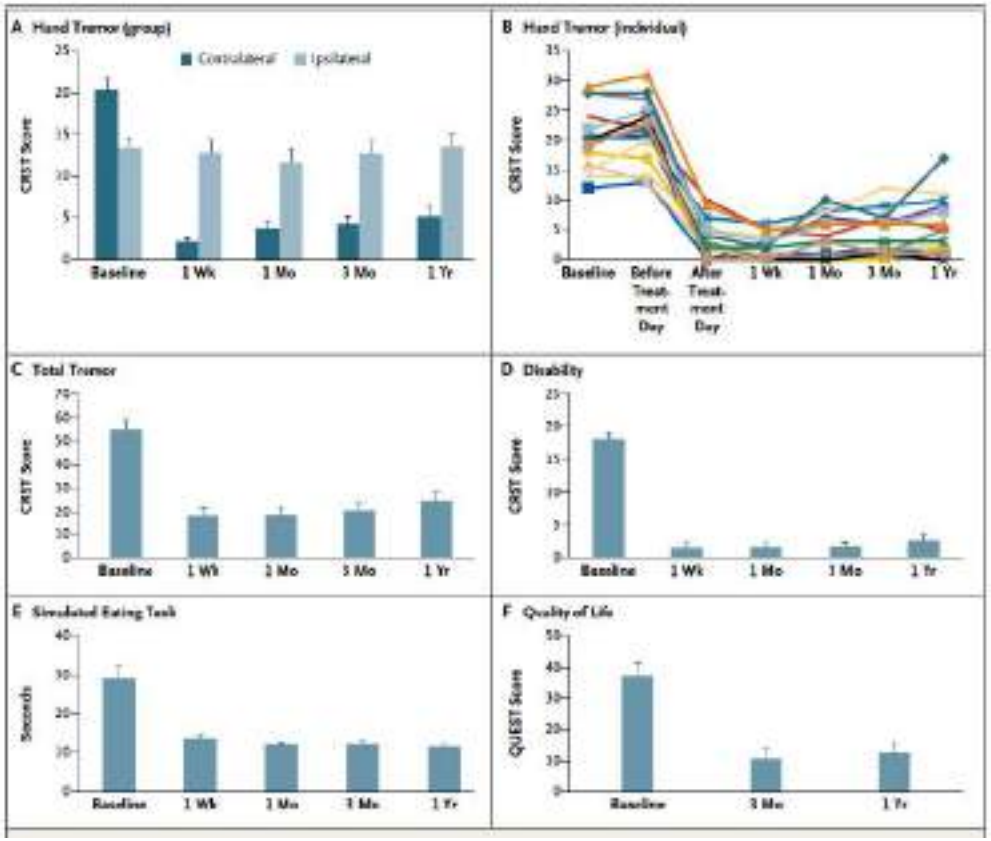
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Tremor creeps back following ultrasound

ORIGINAL ARTICLE

A Pilot Study of Focused Ultrasound Thalamotomy for Essential Tremor

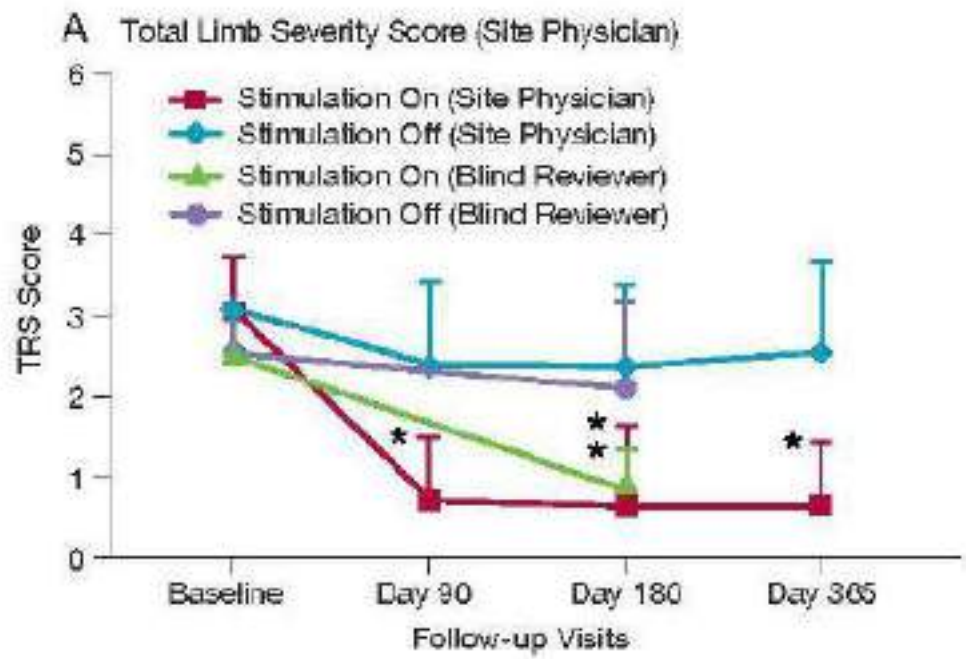
W. Jeffrey Elias, M.D., Diane Huss, P.T., D.P.T., N.C.S., Tiffini Voss, M.D., Johanna Loomba, B.S., Mohamad Khaled, M.D., Eyal Zadicario, M.Sc., Robert C. Frysinger, Ph.D., Scott A. Sperling, Psy.D., Scott Wylie, Ph.D., Stephen J. Monteith, M.D., Jason Druzgal, M.D., Ph.D., Binit B. Shah, M.D., Madaline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



Parkinsonism and Related Disorders

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

DBS sustained improvement 1 year 127 patients



AE's suggest ultrasound missed

Table 2. Adverse Events.*

Adverse Event	FUS Thalamotomy (N=56)							Sham Procedure (N=20)
	Total	1 Day	7 Days	1 Mo	3 Mo	6 Mo	12 Mo	
	number of patients (percent)							
Paresthesia or numbness								
Any region	21 (38)	18	17	16	14	11	8 (14)	1 (5)
Both face and hand	6 (11)	5	5	5	5	5	5 (9)	
Face, lips, and tongue	8 (14)	7	6	6	6	4	2 (4)	
Hand and fingers	6 (11)	5	5	4	2	1	1 (2)	1 (5)
Leg	1 (2)	1	1	1	1	1		
Taste disturbance	3 (5)	3	2	2	2	2	2 (4)	
Gait disturbance†								
Any, objective or subjective	20 (36)	19	18	13	9	7	5 (9)	1 (5)
Ataxia, noted objectively on examination	11 (20)	11	10	6	2	2	2 (4)	
"Unsteady" or "unbalanced," reported subjectively by examiner or patient	9 (16)	8	8	7	7	5	3 (5)	1 (5)
Dysmetria, limb	7 (12)	7	7	5	5	4	2 (4)	
Weakness, contralateral	2 (4)	2	2	2	2	2	1 (2)	

- Parasthesias face, lips, tongue, and leg 38%; 14%
- Gait disturbance (unilateral) 36%; 9%
- Persistent weakness in 2 patients

Ultrasound lesion violated the ventralis caudalis and the internal capsule

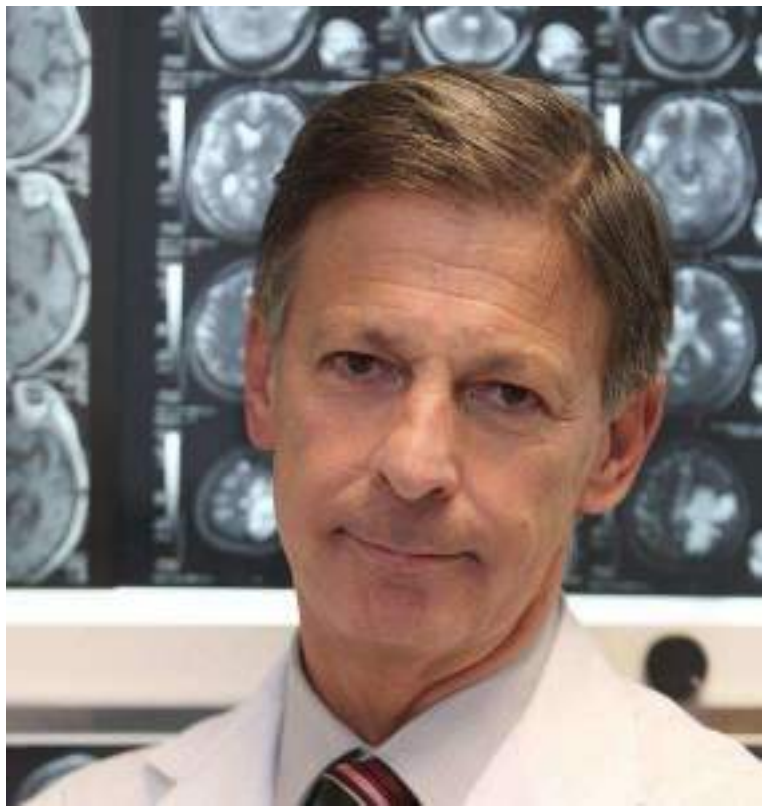
Articles

Focused ultrasound subthalamotomy in patients with asymmetric Parkinson's disease: a pilot study

Raul Martínez-Fernández, MD, Rafael Rodríguez-Rojas, MsC, Marta del Álamo, MD, Frida Hernández-Fernández, MsC, Jose A Pineda-Pardo, PhD, Michele Dileone, MD, Fernando Alonso-Frech, MD, Guglielmo Foffani, PhD, Ignacio Obeso, PhD, Carmen Gasca-Salas, MD, Esther de Luis-Pastor, MD, Lydia Vela, MD, Prof José A Obeso, MD

Published: 01 December 2017

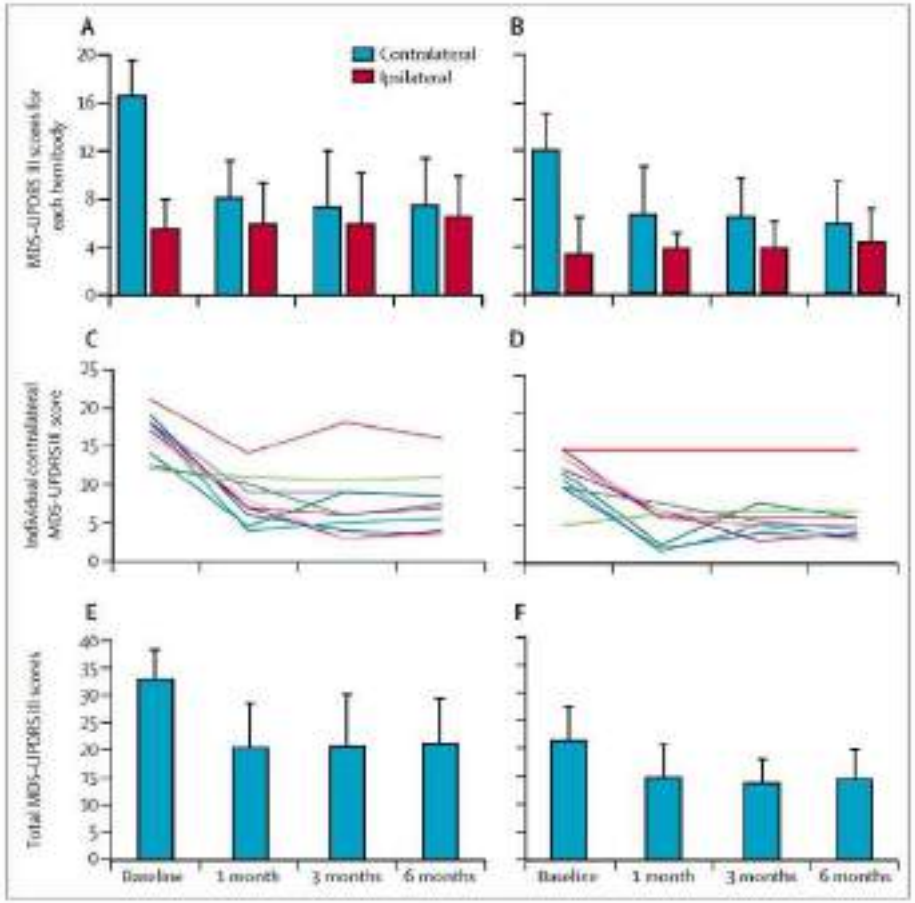
10 patients
53% Improvement UPDRS



Focused ultrasound subthalamotomy in patients with asymmetric Parkinson's disease: a pilot study

Raul Martínez-Fernández, Rafael Rodríguez-Rojas, Marta del Álamo, Frida Hernández-Fernández, Jose A Pineda-Pardo, Michele Dileone, Fernando Alonso-Frech, Guglielmo Foffani, Ignacio Obeso, Carmen Gasca-Salas, Esther de Luis-Pastor, Lydia Vela, José A Obeso

- 10 patients
- Unilateral STN

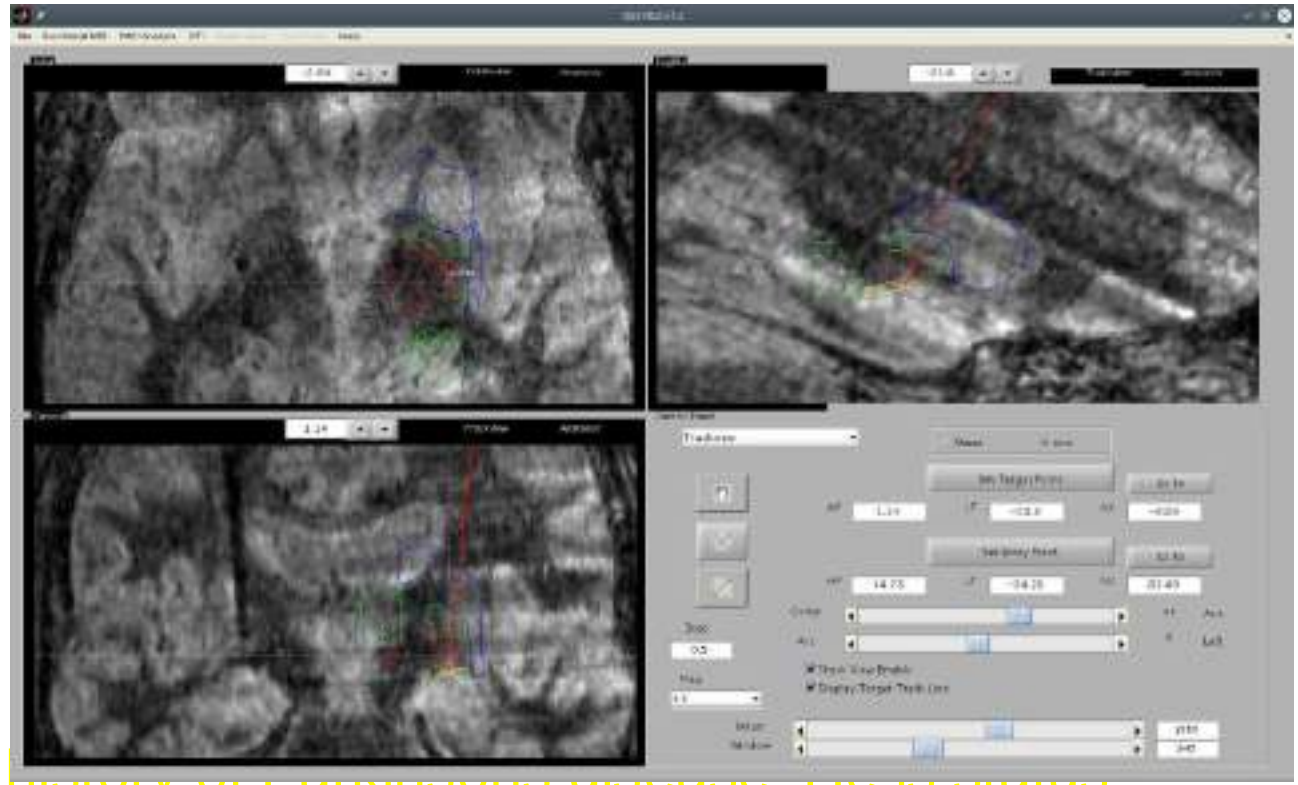




What symptoms respond to PD DBS?

- Symptoms responding to medications
- Tremors (which can be resistant to medications)
- UPDRS III motor does not characterize motor fluctuations and dyskinesia
- Postural instability, gait, and balance even if (rarely) improve “on” will progress
- Freezing sometimes improves with the “on”
- Could be any Hoehn and Yahr Stage





68 y.o. male with a history of Parkinsons disease. He is status post a bilateral GPi deep brain stimulator

Thresholds:

Ch 1: Lead 0 (v): 2 (1.7v RUE/RLE tremor 0/0 rigidity 1/1 taps 0 open 1 sup 1)
Ch 1: Lead 0 Side Effect Type: Motor, Other (pulling right shoulder, arm and hand, face, dysarthria)
Ch 1: Lead 1 (v): 3 (2.9v RUE/RLE tremor 0/0 rigidity 1/1 taps 0 open 1 sup 1)
Ch 1: Lead 1 Side Effect Type: Other, Motor (right hand pulling and anxiety)
Ch 1: Lead 2 (v): 3.2 (3.1v RUE/RLE tremor 0/0 rigidity 1/1 taps 0 open tr sup 1)
Ch 1: Lead 2 Side Effect Type: Motor, Other (right hand pulling, anxiety)
Ch 1: Lead 3 (v): 5.4 (5.3v RUE/RLE tremor 0/0 rigidity 1/1 taps 0 open 0 sup 1)
Ch 1: Lead 3 Side Effect Type: Motor (right hand pulling)

Lead 1, 2 and 3 seemed the best. Lead 2 and 3 may possibly increase RLE dyskinesia with Freq at 180 Hz. Contact 3 is the best

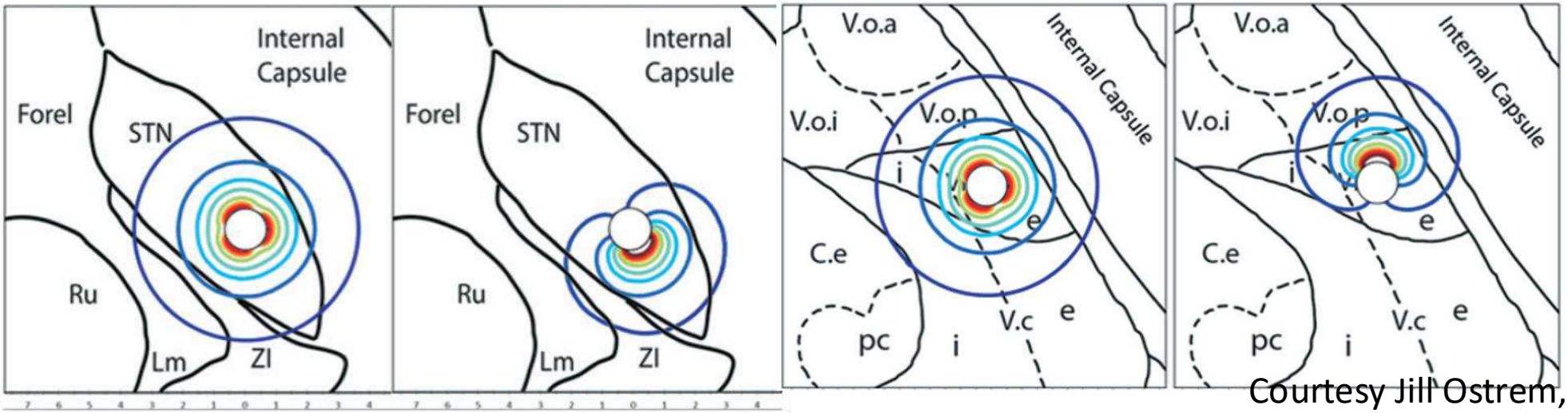
Novel Mode of DBS Stimulation
Current Steering/Directional Stimulation

- No publications with US commercial device (St Jude Medical)
- Allows for stimulation perpendicular to the lead axis/not circumferential
- First temporary steering electrodes implanted (6 contacts)-showed wider therapeutic programming window at lower current (Pollo C et al Brain 2014)

BRAIN
A JOURNAL OF NEUROLOGY

Directional deep brain stimulation: an intraoperative double-blind pilot study

Claudio Pollo,[1] Alain Kaelin-Lang,[2] Markus F. Oertel,[1] Lennart Stieglitz,[1] Ethan Taub,[3] Peter Fuhr,[4] Andres M. Lozano,[5] Andreas Raabe[1] and Michael Schüpbach[2]



Courtesy Jill Ostrem, U

SCIENTIFIC REPORTS
nature research
Check for updates

OPEN

Assessing the effect of current steering on the total electrical energy delivered and ambulation in Parkinson's disease

Daphne Hui[1 ✉], Aditya A. Murgai[2], Greydon Gilmore[2,3], Shabna I. Mohideen[1], Andrew G. Parrent[2] & Mandar S. Jog[1,2,3]

vCS reduced the TEED and side-effects at higher amplitudes

Gait improved with single contact or vCS

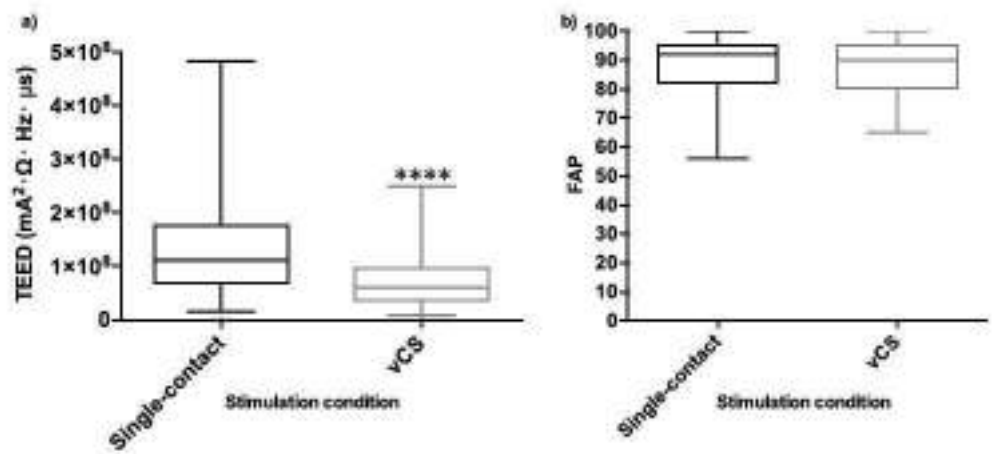


Figure 1. Effect of single-contact and vCS stimulation on TEED and FAP values. Means of TEED values and FAP scores compared in single-contact and vCS stimulation at all amplitude stages (around 20%, 40%, 60%, and 80% of the TW). Boxplots with N = 7; solid horizontal lines represent the median and the upper and lower whiskers represent the maximum and minimum values, respectively. (a) TEED values on average were significantly lower with vCS compared to single-contact stimulation (****, $P < 0.0001$; two-tailed, Wilcoxon matched-pairs signed rank test). (b) FAP scores on average were not different in the two stimulation conditions ($P = 0.786$; two-tailed, Wilcoxon matched-pairs signed rank test).

VIEWPOINT

Tips for Choosing a Deep Brain Stimulation Device

Michael S. Okun, MD
Fixel Institute for Neurological Diseases, Department of Neurology, University of Florida Program for Movement Disorders and Neurorestoration, Gainesville.

Table. Comparison of Deep Brain Stimulation Devices

Device Capabilities	Medtronic	Abbott Infinity	Boston Scientific Vercise
Approved indications	Bilateral STN and GPi DBS for PD; bilateral STN and GPi for dystonia[a]; unilateral VIM for tremor; bilateral anterior limb of the internal capsule for refractory OCD[a]	Bilateral STN for PD; unilateral or bilateral VIM for ET	Bilateral STN for PD
Directional lead approval	Not available	(2016) Segmented 1-3-3-1 lead, current steering	(2019) Segmented lead 1-3-3-1, current shaping and with multiple independent current control
Sensing capabilities	Advanced sensing platform NEXUS, not yet available commercially	Not available	Not available
System battery life	Medtronic Activa SC (single chamber) and PC (dual chamber) estimated 3- to 5-y battery[b]; Medtronic Activa RC; 15 y after recent software update	Abbott Infinity (dual chamber and nonrechargeable), estimated 4 to 5 y of battery life[b]	Vercise Primary Cell Battery (dual chamber), estimated 4.5 y of battery life, and the Vercise Gevia, rechargeable systems, estimated 15-y approval in United States and 25-y in Europe (no shutoff)[a]
MRI use	Conditional	Conditional	Not available
No. of stimulation contacts	8 Contacts (2 × 8)	16 Contacts (2 × 8)	16 Contacts (2 × 8)
Wireless remote control	None	1 to 2 m in telemetry	91.4 cm (36 in) telemetry
Programming features	Frequency 2-250 Hz; pulse width 60-450 μs; maximum amplitude 10.5 V (voltage mode)/ 25.5 mA (current mode)	Frequency 2-240 Hz; pulse width 20-500 μs; maximum amplitude 12.75 mA	Frequency 2-250 Hz; pulse width 20-450 μs; maximum amplitude 12.7 mA per contact (20 mA total)
Programming platform	Samsung Galaxy Tab S2 tablet interface; visual and task-based workflow interface	Directional lead with current steering; wireless programming platform using an iOS software and Apple mobile digital devices for patient programming[a]	Directional lead current shaping; touch screen interface with steer up or down on the lead and increase or decrease amplitude through the control pad; visualization of the volume of tissue being activated for the selected stimulation settings.
Independent frequency control	Not available	Available (up to 2 independent frequencies per program)	Available (up to 4 independent frequencies per program)

Abbreviations: DBS, deep brain stimulation; ET, essential tremor; GPi, globus pallidus interna; iOS, iPhone operating system; MRI, magnetic resonance imaging; OCD, obsessive-compulsive disorder; PC, dual channel; PD, Parkinson disease; RC, rechargeable; SC, single chamber; STN, subthalamic nucleus; VIM, ventral intermediate nucleus.

[a] Humanitarian device exception.

[b] Mean battery duration (noting the influence of programming parameters on battery life).

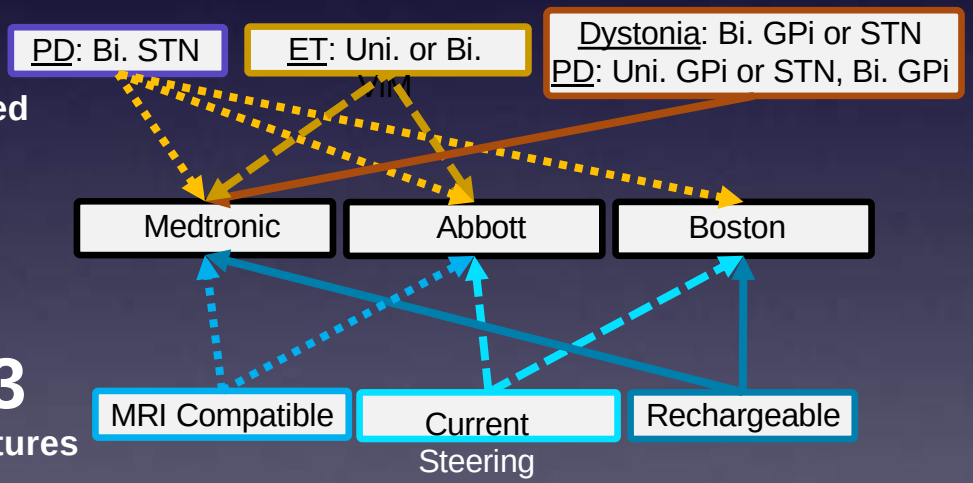
Precision Medicine: Last Choice is Device



1
Prerequisites

- Multidisciplinary clinical screening
- Availability of support services from different vendors (geographical and access to care limitations)
- Insurance coverage
- Providers trained on specific DBS platforms (additional training required)
- Providers can manage additional time demands for new features (directional leads, additional lead contacts and programming options)

2
FDA-approved indications



3
Features

JAMA Neurology: In Press



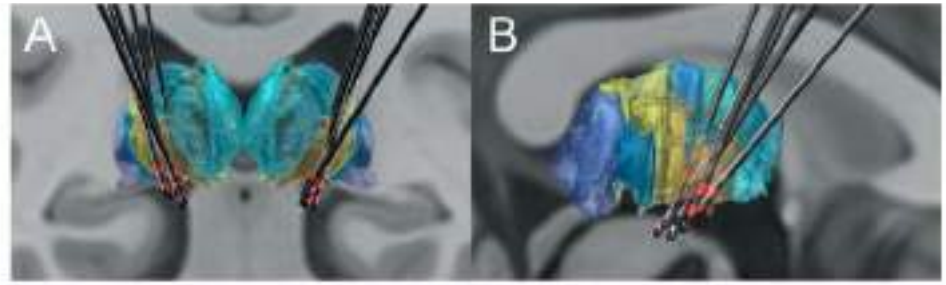
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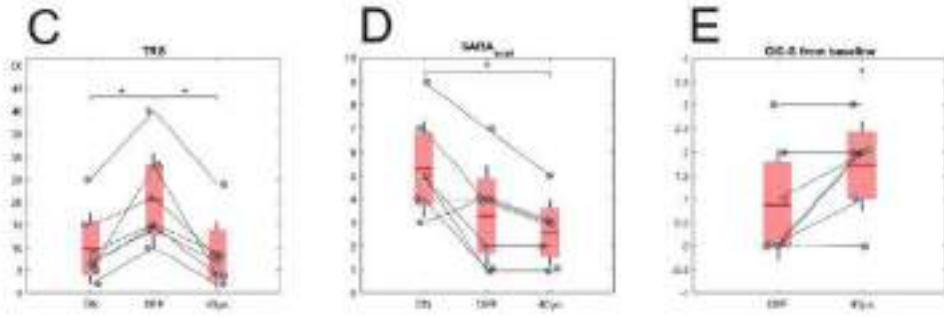
SHORT REPORT

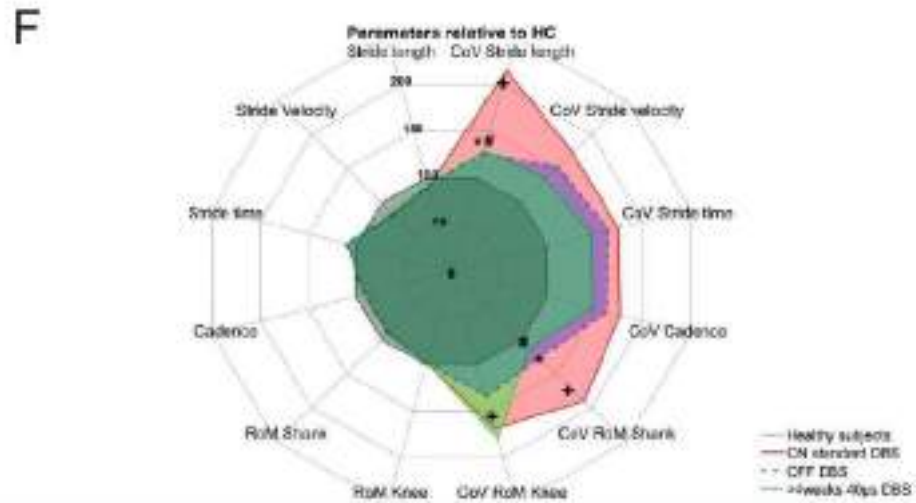
Shorter pulse width reduces gait disturbances following deep brain stimulation for essential tremor

Daniel Kroneberg,[1] Siobhan Ewert,[1] Anne-Christiane Meyer,[1] Andrea A Kühn[1,2]

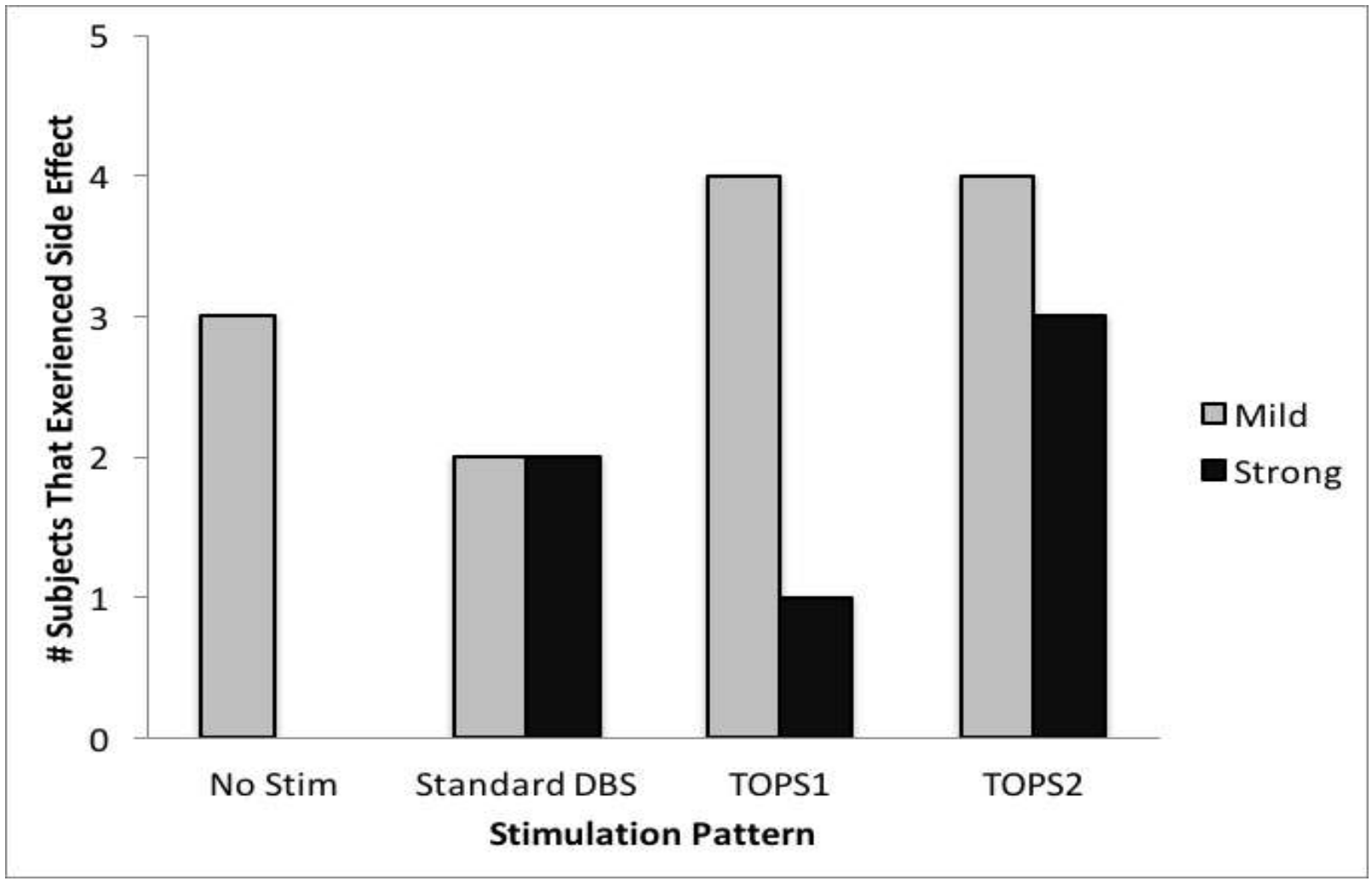
J Neurol Neurosurg Psychiatry: fi







Temporally Optimized Patterns of Stimulation (TOPS)

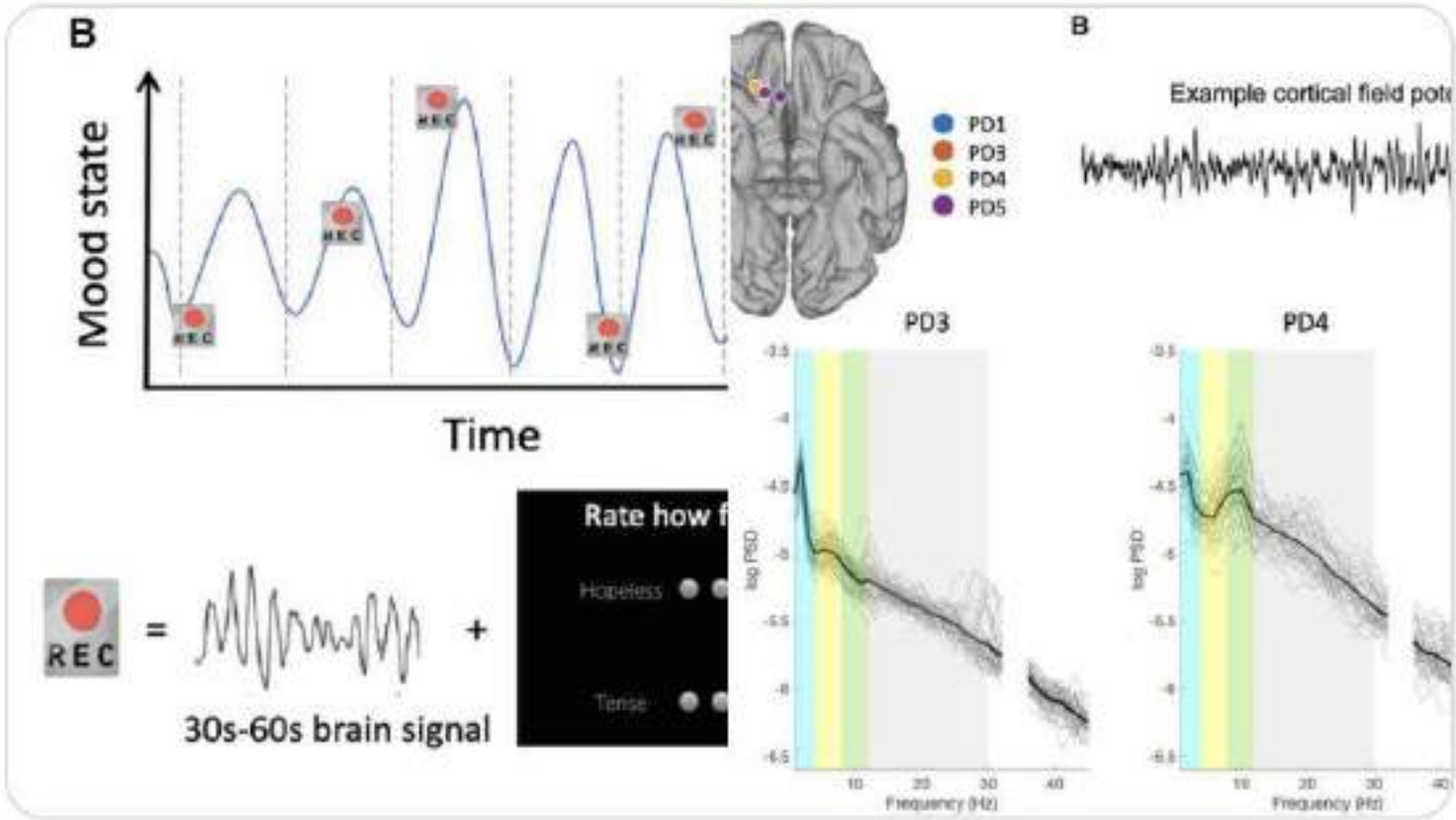


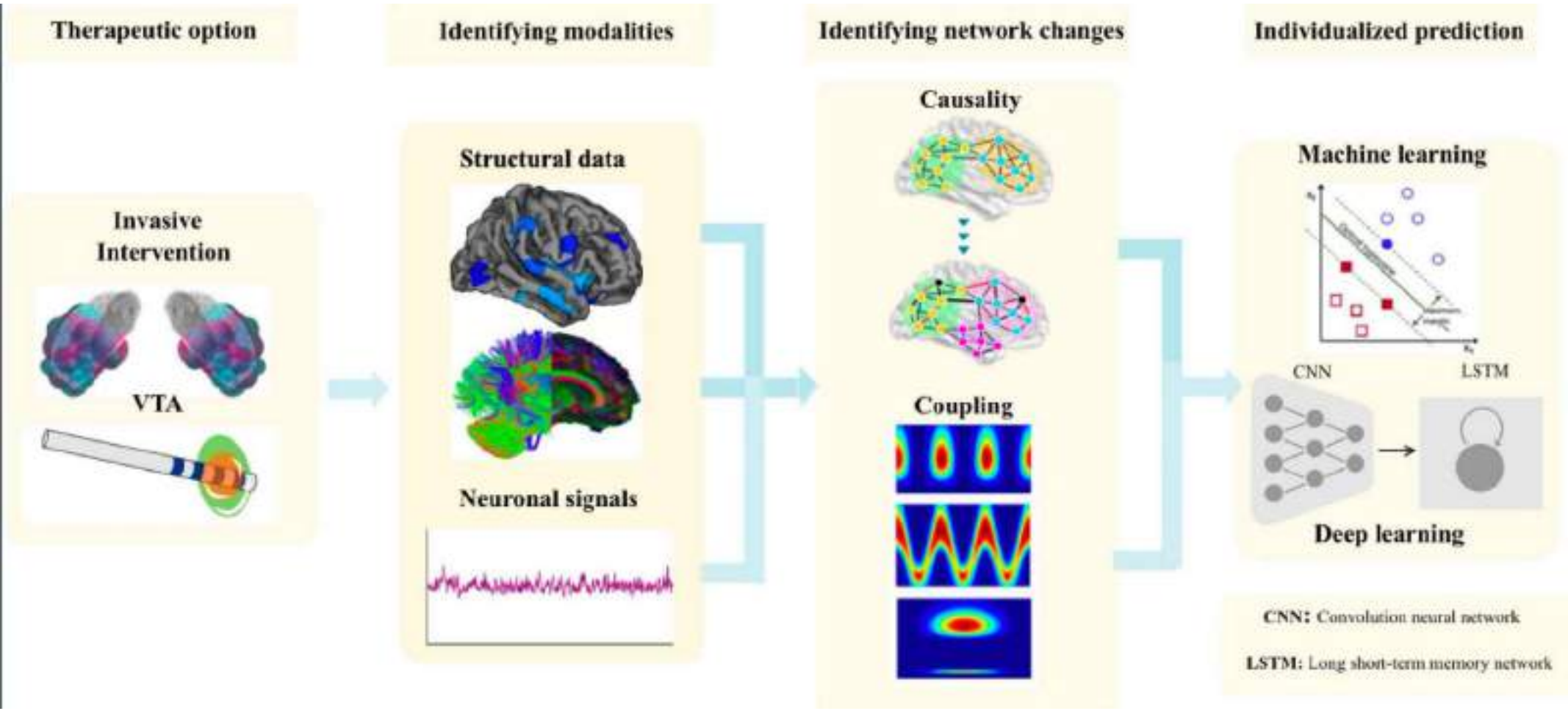
W. Grill

DBS Think Tank
@DBSThinkTank

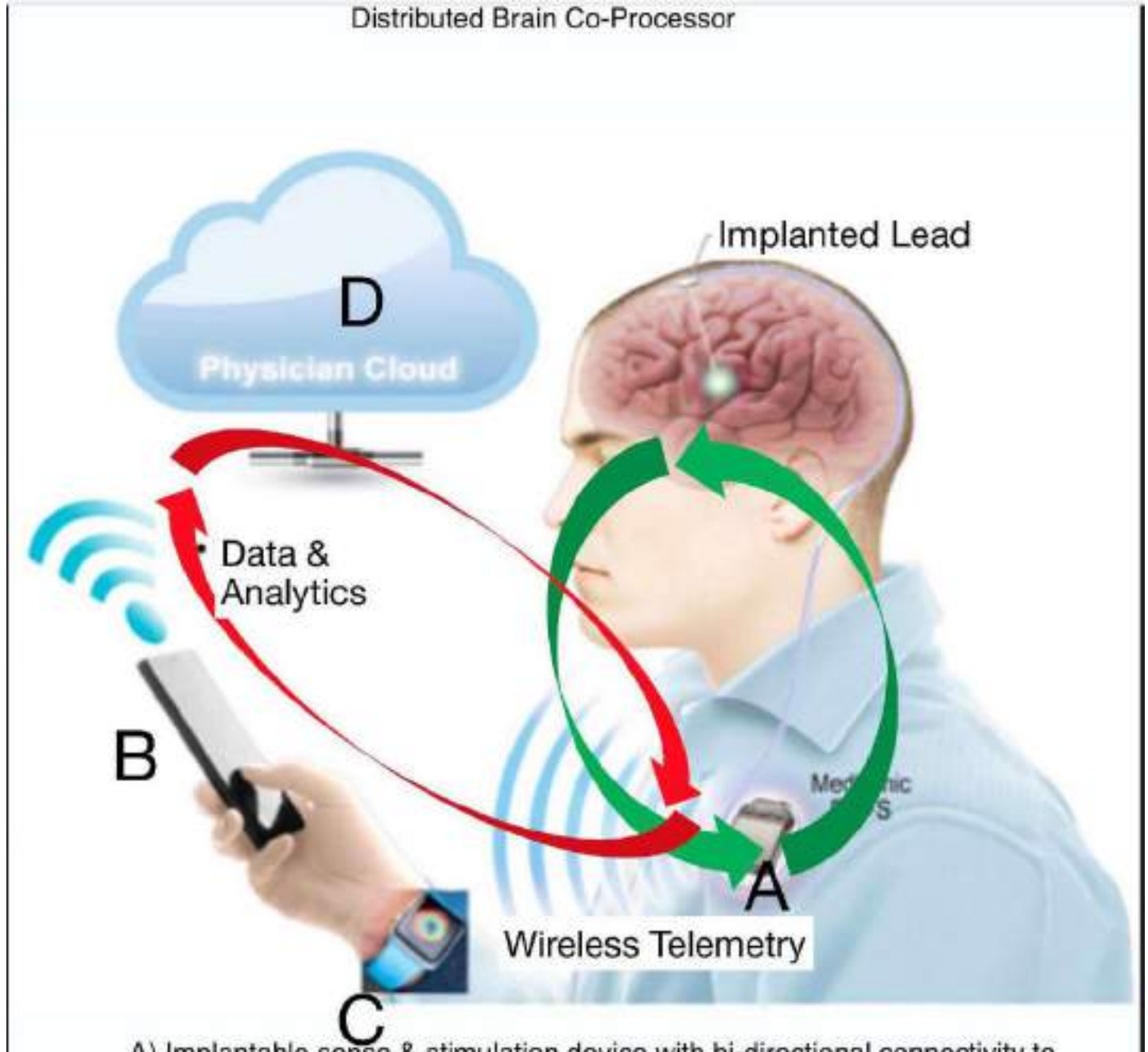


Great study by Cora de Hemptinne et al. showing electrophysiological correlations of non-motor symptoms in Parkinson's disease. We need more focus for NMS in PD! frontiersin.org/articles/10.33...




Therapeutic option
Identifying modalities
Identifying network changes
Individualized prediction
Invasive Intervention
VTA
Structural data
Neuronal signals
Causality
Coupling
Machine learning
CNN
LSTM
Deep learning
CNN: Convolution neural network
LSTM: Long short-term memory network

Distributed Brain Co-Processor



A) Implantable sense & stimulation device with bi-directional connectivity to smartphone. Short time latency adaptive stimulation (green arrows) with embedded computing

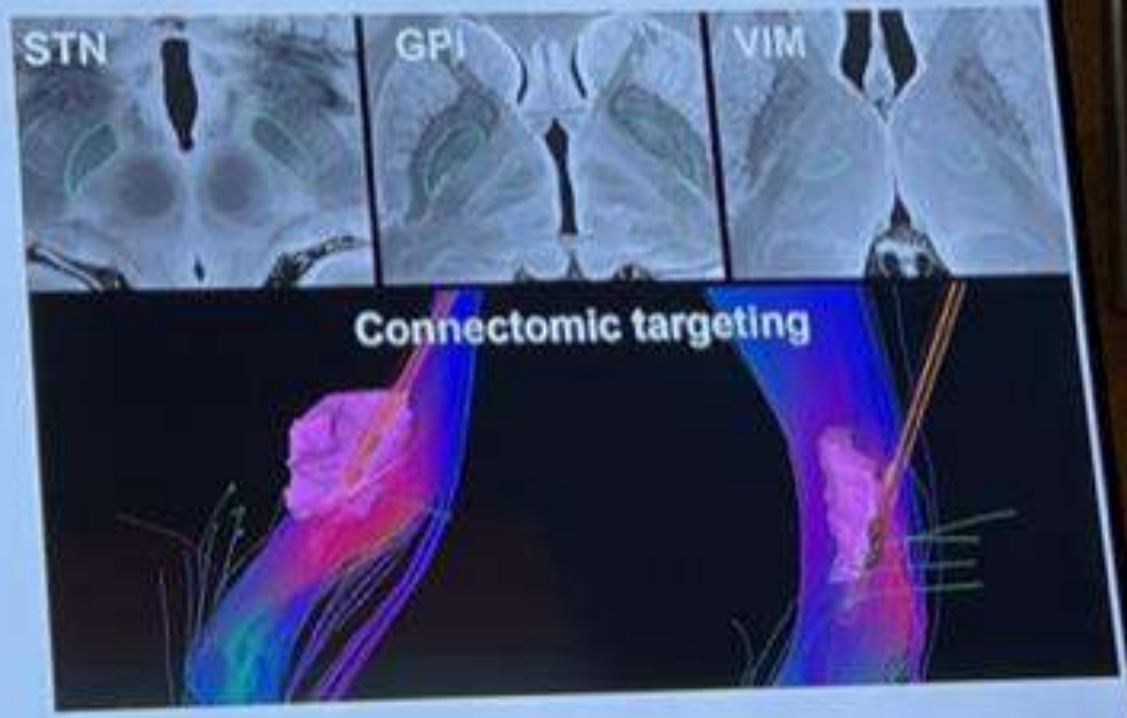
B) Local handheld computer (smartphone) for integrating devices and long latency adaptive stimulation (red arrows).

C) Wearable sensors D) Cloud platform for data storage, analytics and web epilepsy dashboard.

Connectomic DBS Targeting

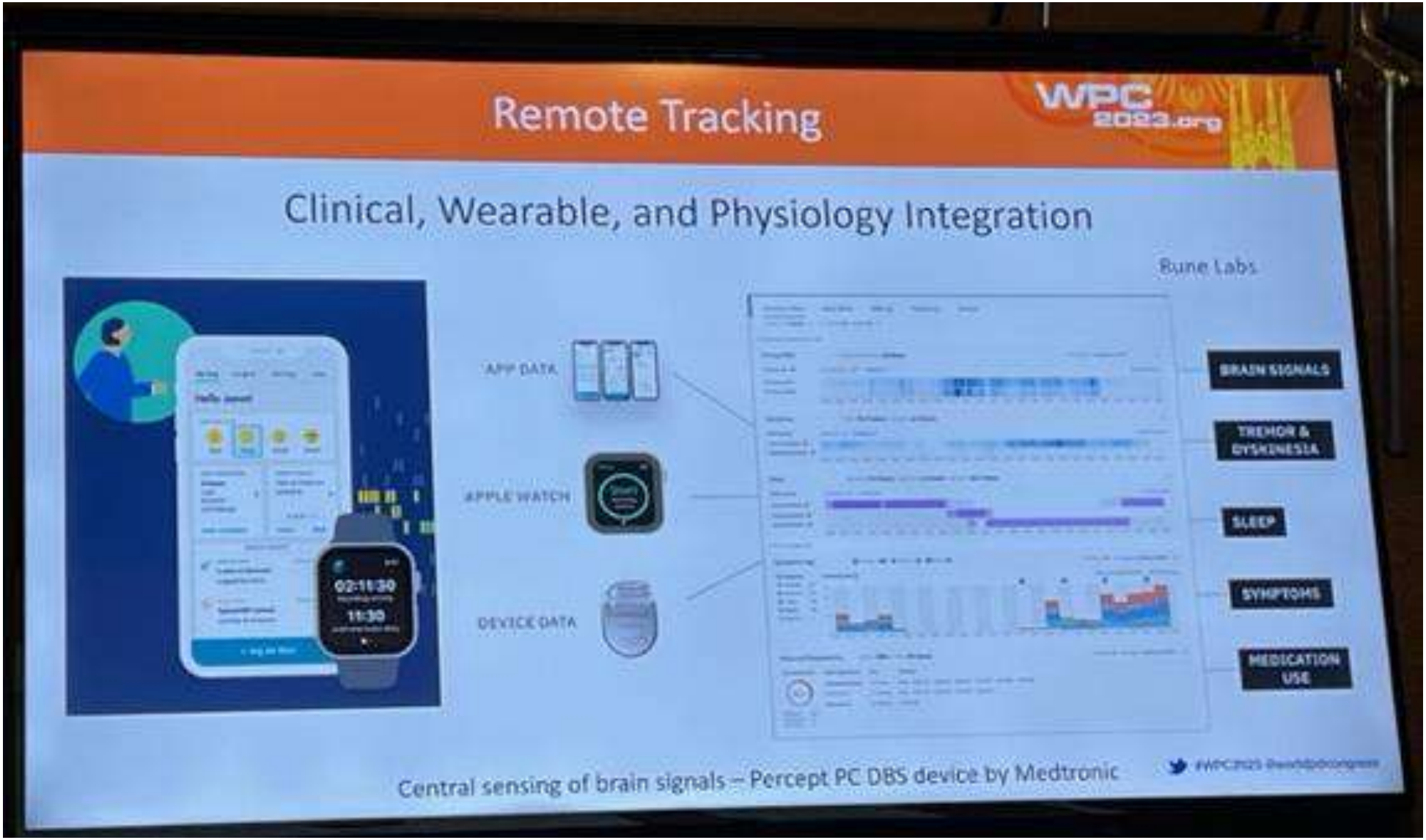
WPC 2023.org

- Strategy: Target a pathway or influence a brain network over just a target nucleus
- Neuroimaging modalities for deriving connectivity measures:
  - Diffusion tensor imaging (DTI) for structural connectivity
  - Functional MRI (fMRI) for functional connectivity.



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Jill Ostrem 2023 World Parkinson Congress



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Brain Stimulation 13 (2020) 280–283

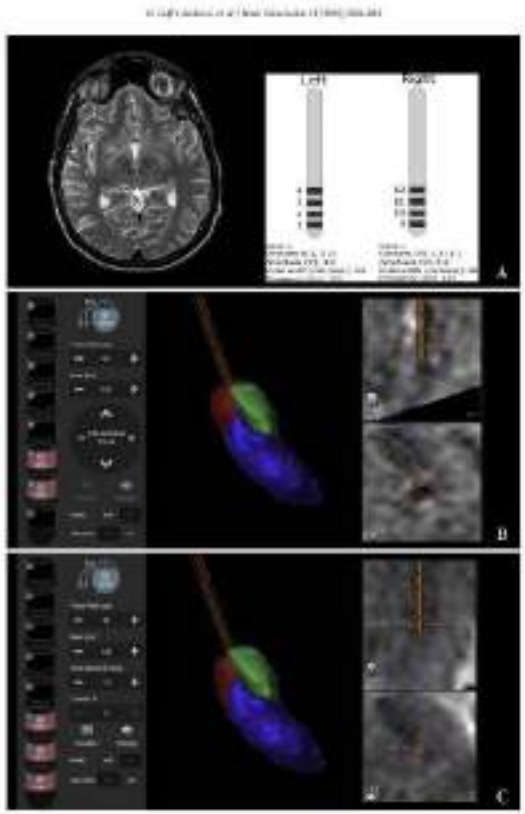
Contents lists available at ScienceDirect

Brain Stimulation

journal homepage: http://www.journals.elsevier.com/brain-stimulation

Deep brain stimulation and refractory freezing of gait in Parkinson's disease: Improvement with high-frequency current steering co-stimulation of subthalamic nucleus and substantia Nigra

- Improve disabling FoG without negatively affecting other PD cardinal
- Fine tuning of DBS by volumetric estimation of the electric field to both the SNr and STN



THE LANCET Neurology

Volume 9, Issue 6, June 2010, Pages 581–591



Articles

Deep brain stimulation plus best medical therapy versus best medical therapy alone for advanced Parkinson's disease (PD SURG trial): a randomised, open-label trial

Prof Adrian Williams, MD[a,*], Prof Steven Gill, FRCS[b], Thelekat Varma, FRCS[Ed][c], Prof Crispin Jenkinson DPhil[d], Prof Niall Quinn, MD[e], Rosalind Mitchell, FRCS[a], Richard Scott, PhD[f], Natalie Ives, MSc[g], Caroline Rick, PhD[g], Jane Daniels, MSc[g], Smitaa Patel, MSc[g], Prof Keith Wheatley, DPhil[g,*], on behalf of the PD SURG Collaborative Group[†]

THE LANCET Neurology

Volume 11, Issue 2, February 2012, Pages 140–149



Articles

Subthalamic deep brain stimulation with a constant-current device in Parkinson's disease: an open-label randomised controlled trial

Dr Michael S Okun, MD[a], Bruno V Gallo, MD[c], George Mandybur, MD[e], Jonathan Jagid, MD[d], Kelly D Foote, MD[b], Fredy J Revilla, MD[f], Ron Alterman, MD[g], Joseph Jankovic, MD[i], Richard Simpson, MD[j], Fred Junn, MD[k], Leo Verhagen, MD[l], Jeff E Arle, MD[m], Blair Ford, MD[n], Robert R Goodman, MD[o], R Malcolm Stewart, MD[p], Stacy Horn, DO[q], Gordon H Baltuch, MD[r], Brian H Kopell, MD[s], Frederick Marshall, MD[t], DeLea Peichel, BS[u], Rajesh Pahwa, MD[v], Kelly E Lyons, PhD[v], Alexander I Tröster, PhD[w], Jerrold L Vitek, MD[x], Michele Tagliati, MD[h], for the SJM DBS Study Group ‡

- Bilateral STN DBS improved motor function
- Use of a constant current device
- 25% of subjects not activated until 3 months

Neurol Ther (2021) 10:7–30
https://doi.org/10.1007/s40120-020-00220-5

COMMENTARY

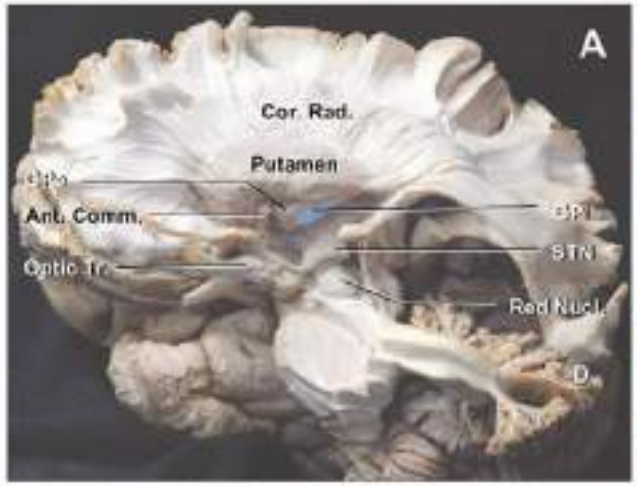
Globus Pallidus Internus (GPi) Deep Brain Stimulation for Parkinson's Disease: Expert Review and Commentary

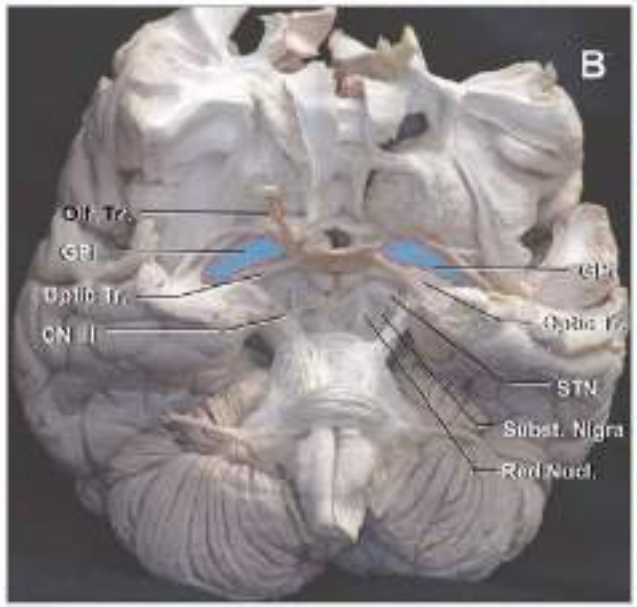
Ka Loong Kelvin Au · Joshua K. Wong · Takashi Tsuboi · Robert S. Eisinger · Kathryn Moore · Janine Lemos Melo Lobo Jofili Lopes · Marshall T. Holland · Vanessa M. Holanda · Zhongxing Peng-Chen · Addie Patterson · Kelly D. Foote · Adolfo Ramirez-Zamora · Michael S. Okun · Leonardo Almeida

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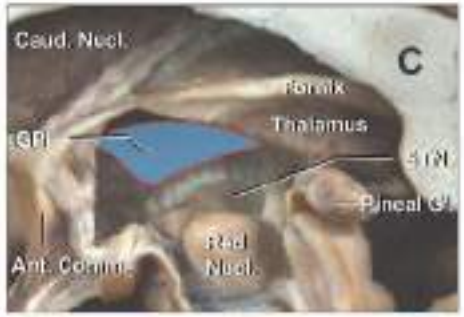




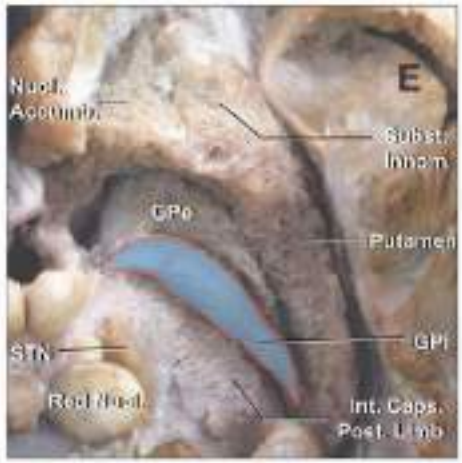












Subthalamic nucleus deep brain stimulation with a multiple independent constant current-controlled device in Parkinson's disease (INTREPID): a multicentre, double-blind, randomised, sham-controlled study

Jerrold L Vitek, Roshini Jain, Lilly Chen, Alexander I Tröster, Lauren E Schrock, Paul A House, Monique L Giroux, Adam O Hebb, Sierra M Farris, Donald M Whiting, Timothy A Leichliter, Jill L Ostrem, Marta San Luciano, Nicholas Galifianakis, Leo Verhagen Metman, Sepehr Sani, Jessica A Karl, Mustafa S Siddiqui, Stephen B Tatter, Ihtsham ul Haq, Andre G Machado, Michal Gostkowski, Michele Tagliati, Adam N Mamelak, Michael S Okun, Kelly D Foote, Guillermo Moguel-Cobos, Francisco A Ponce, Rajesh Pahwa, Jules M Nazzaro, Cathrin M Buetefisch, Robert E Gross, Cornelu C Luca, Jonathan R Jagid, Gonzalo J Revuelta, Istvan Takacs, Michael H Pourfar, Alon Y Mogilner, Andrew P Duker, George T Mandybur, Joshua M Rosenow, Scott E Cooper, Michael C Park, Suketu M Khandhar, Mark Sedrak, Fenna T Phibbs, Julie G Pilitsis, Ryan J Uitti, Philip A Starr

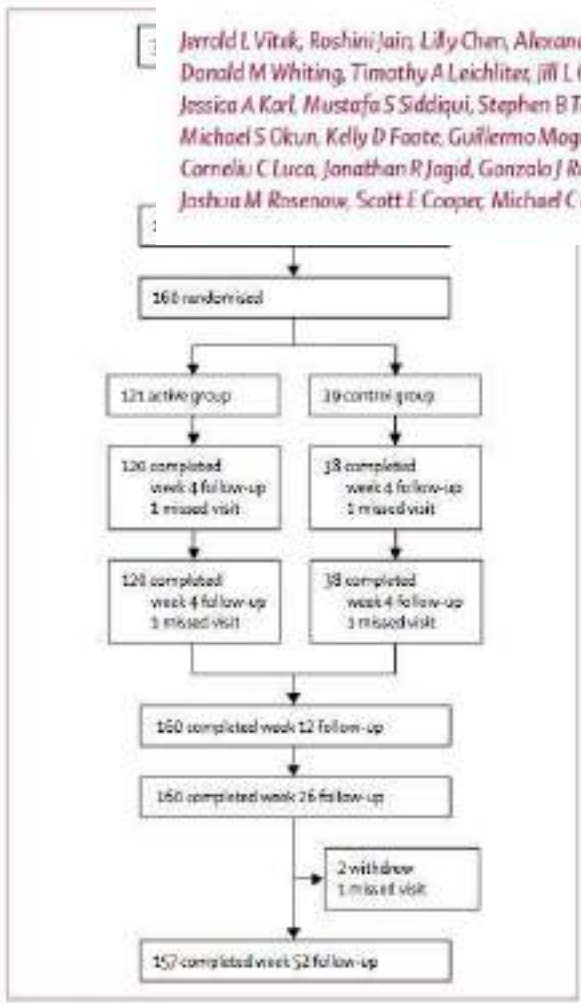


Figure 2: Trial profile
Only the prespecified cohort of the first 160 randomly assigned patients were included in the interim analysis, which we report in this Article. The remaining patients who received implant continued in the study but were not included in this interim analysis. The blinded period lasted 3 months, after which all patients entered the open-label period of up to 5 years.

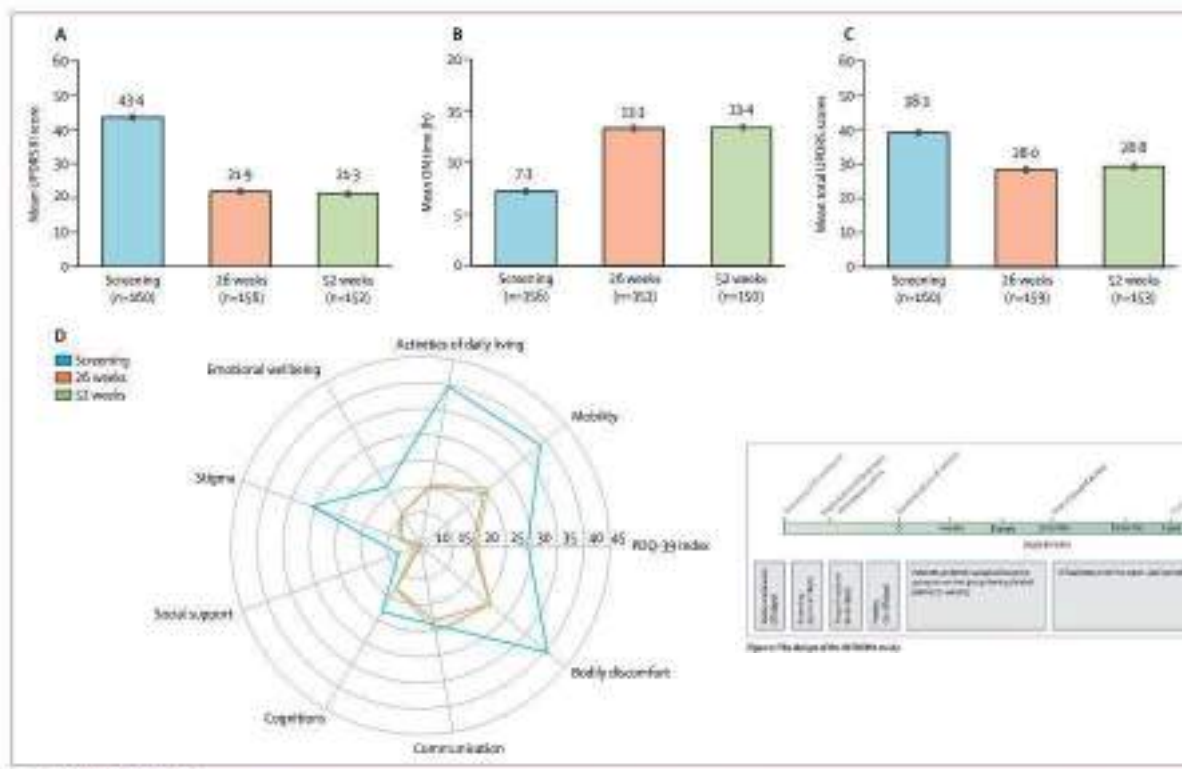


Figure 3: 1-year study outcomes
(A) Mean UPDRS III scores in stimulation ON and medications OFF condition. (B) Mean ON time without troublesome dyskinesias, as recorded by the Parkinson's disease diary. (C) Mean total UPDRS scores in stimulation ON and medications ON condition. The marked intervals in panels A, B, and C indicate SE. (D) PDQ-39 index. UPDRS=Unified Parkinson's Disease Rating Scale. UPDRS III=part 3 of the UPDRS. PDQ-39=Parkinson's Disease Questionnaire.

Brain Stimulation 11 (2018) 904–912

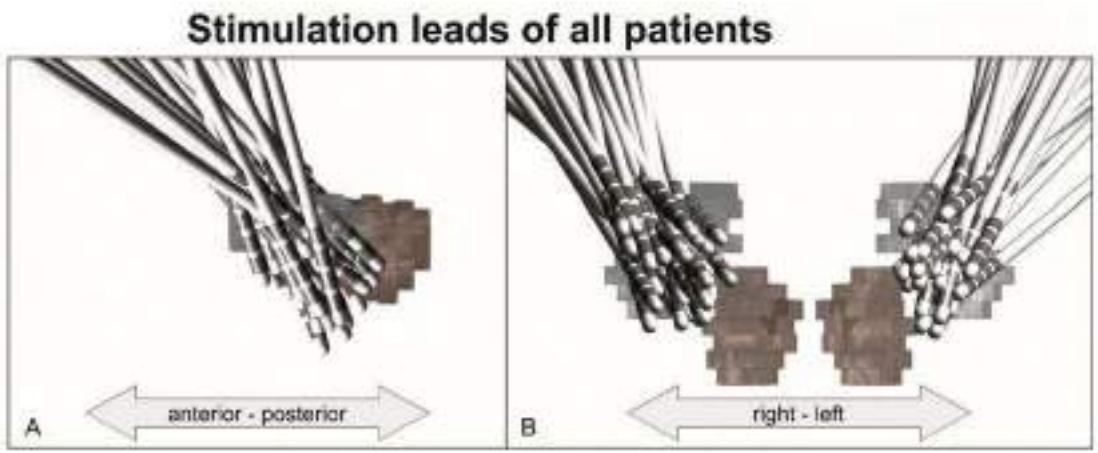
Contents lists available at ScienceDirect

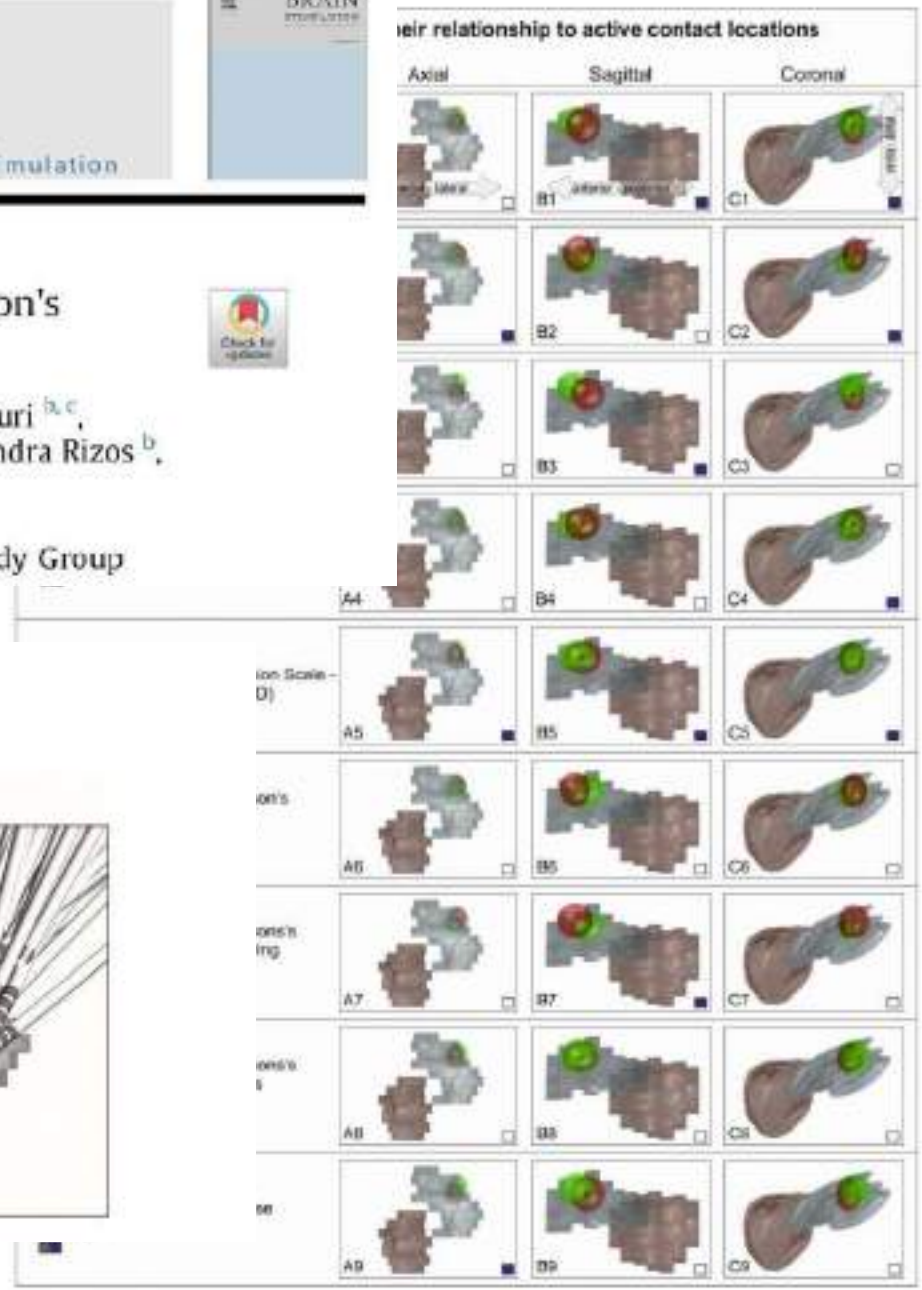
Brain Stimulation

journal homepage: http://www.journals.elsevier.com/brain-stimulation

Non-motor outcomes of subthalamic stimulation in Parkinson's disease depend on location of active contacts

Haidar Salimi Dafsari [a, b, *, 1, 2], Jan Niklas Petry-Schmelzer [a, 2], K. Ray-Chaudhuri [b, c], Keyoumars Ashkan [b], Luca Weis [d], Till A. Dembek [a], Michael Samuel [b], Alexandra Rizos [b], Monty Silverdale [e], Michael T. Barbe [a], Gereon R. Fink [a, f], Julian Evans [d], Pablo Martinez-Martin [g], Angelo Antonini [d], Veerle Visser-Vandewalle [h], Lars Timmermann [a, f], On behalf of EUROPAR, the IPMDS Non Motor PD Study Group





Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

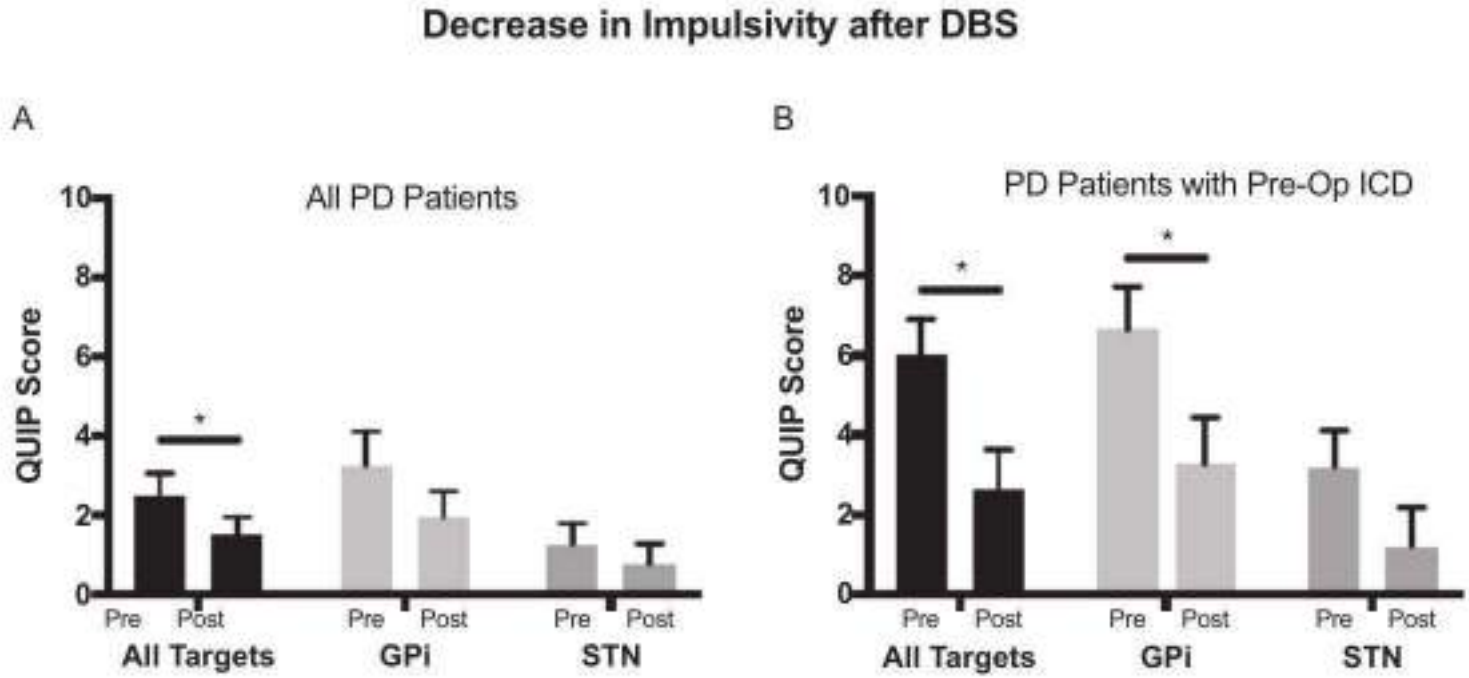
Measures of impulsivity in Parkinson's disease decrease after DBS in the setting of stable dopamine therapy

P. Justin Rossi [a,*], Sol De Jesus [a], Christopher W. Hess [a], Daniel Martinez-Ramirez [a], Kelly D. Foote [a], Aysegul Gunduz [b,1], Michael S. Okun [a,1]

[a] Center for Movement Disorders and Neurorestoration, University of Florida, 3450 Hull Road, Gainesville, FL 32607, USA
[b] J. Crayton Pruitt Family Department of Biomedical Engineering, University of Florida, 1275 Center Drive, Gainesville, FL 32610, USA

- [illegible]
- 14 with ICD



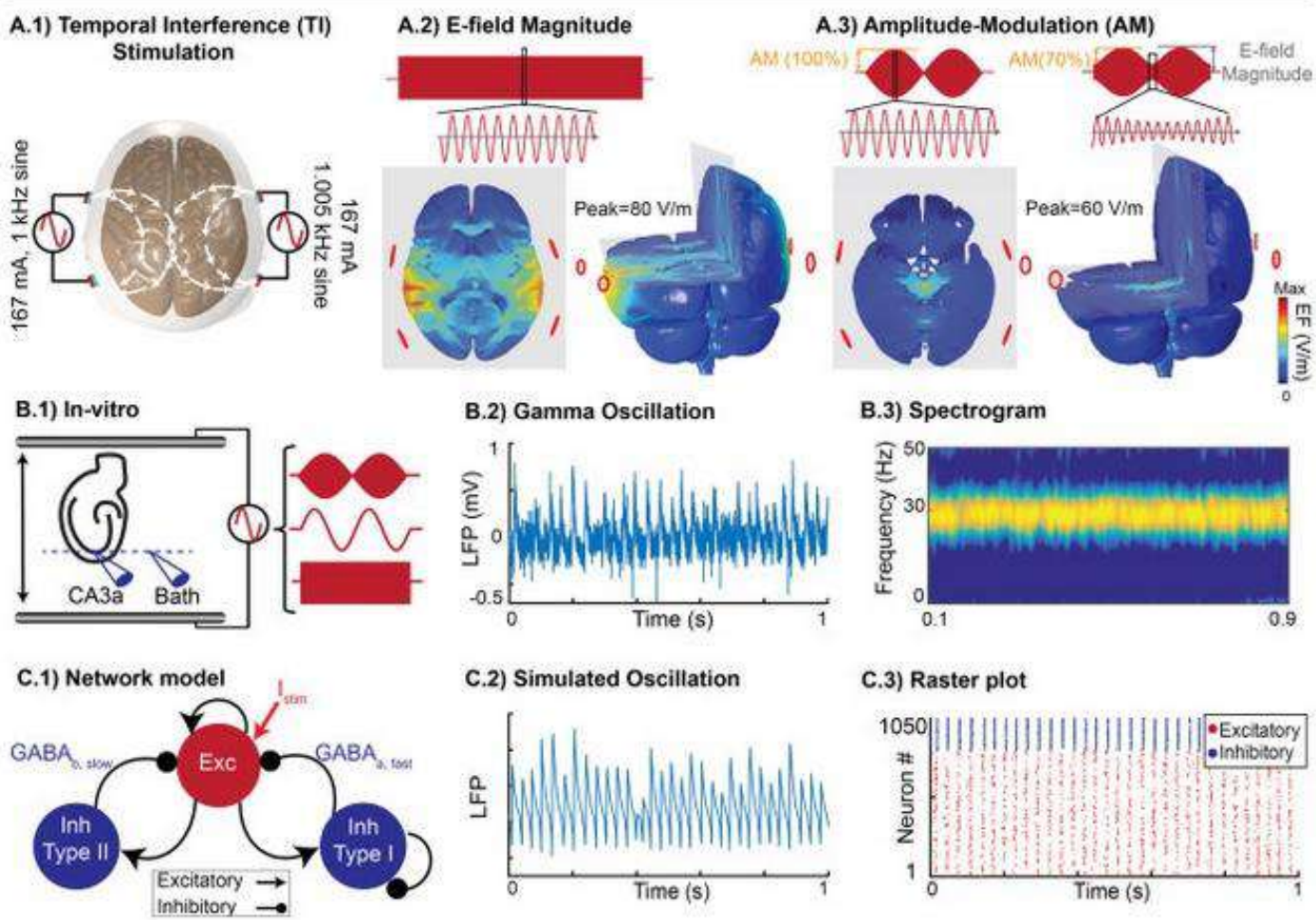


Brain Stimulation
Volume 14, Issue 1, January–February 2021, Pages 55-65

Temporal interference stimulation targets deep brain regions by modulating neural oscillations

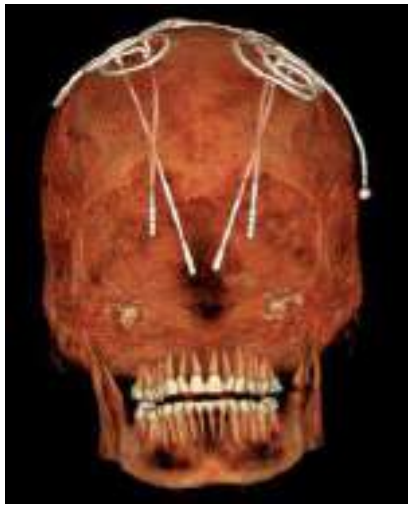
Zeinab Esmaeilpour [a] [c], Greg Kronberg [a], Davide Reato [b], Lucas C. Parra [a], Marom Bikson [a]

Show more



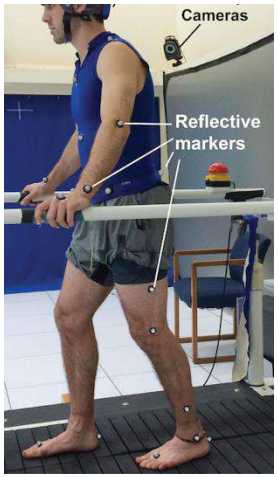
PPN DBS Parkinson's Disease

- Multiple small studies
- PPN uni vs. bilateral
- Plus or minus GPi/STN
- Study group MDS publishing results
- Collectively may improve freezing more than other symptoms
- Potential higher risk





Video Courtesy of Elena Mor









- Welcome to the “Aspen Movement Disorders Raceway”
- Move fast
- Show you newest sleekest and most interesting cars (patients)
- Sit back and enjoy both live and the video replay
- Try not to worry as all the drivers have provided their secrets (slides and tips)
- Look for the pearls 

Rescue Duopa after DBS

- In our series, LCIG seems a promising rescue strategy to:
  - Significantly reduce OFF times
  - Improve in patients' quality of life (PDQ-39)
    - ADLs
    - Mobility
    - Social
    - Body discomfort



AAN, 2018

- Identification of potential candidates is crucial and may include
  - Suboptimally placed DBS leads
  - High risk for further DBS surgeries
  - Patients unwilling to pursue further DBS surgeries
  - Patients with recurrent and unpredictable fluctuations, maximized on oral and DBS therapies


ANNALS of Clinical and Translational Neurology

RESEARCH ARTICLE

Rescue levodopa-carbidopa intestinal gel (LCIG) therapy in Parkinson's disease patients with suboptimal response to deep brain stimulation

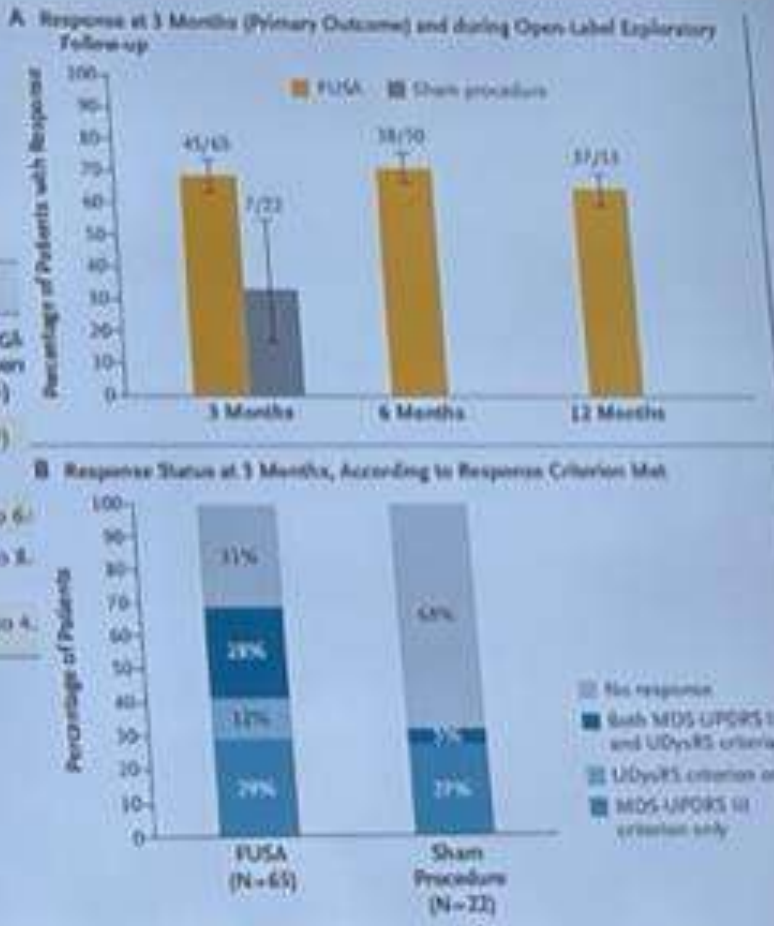
- Further studies are needed to identify potential candidates for early intervention of combined LCIG and DBS

UF UNIVERSITY of FLORIDA

FUS Pallidotomy

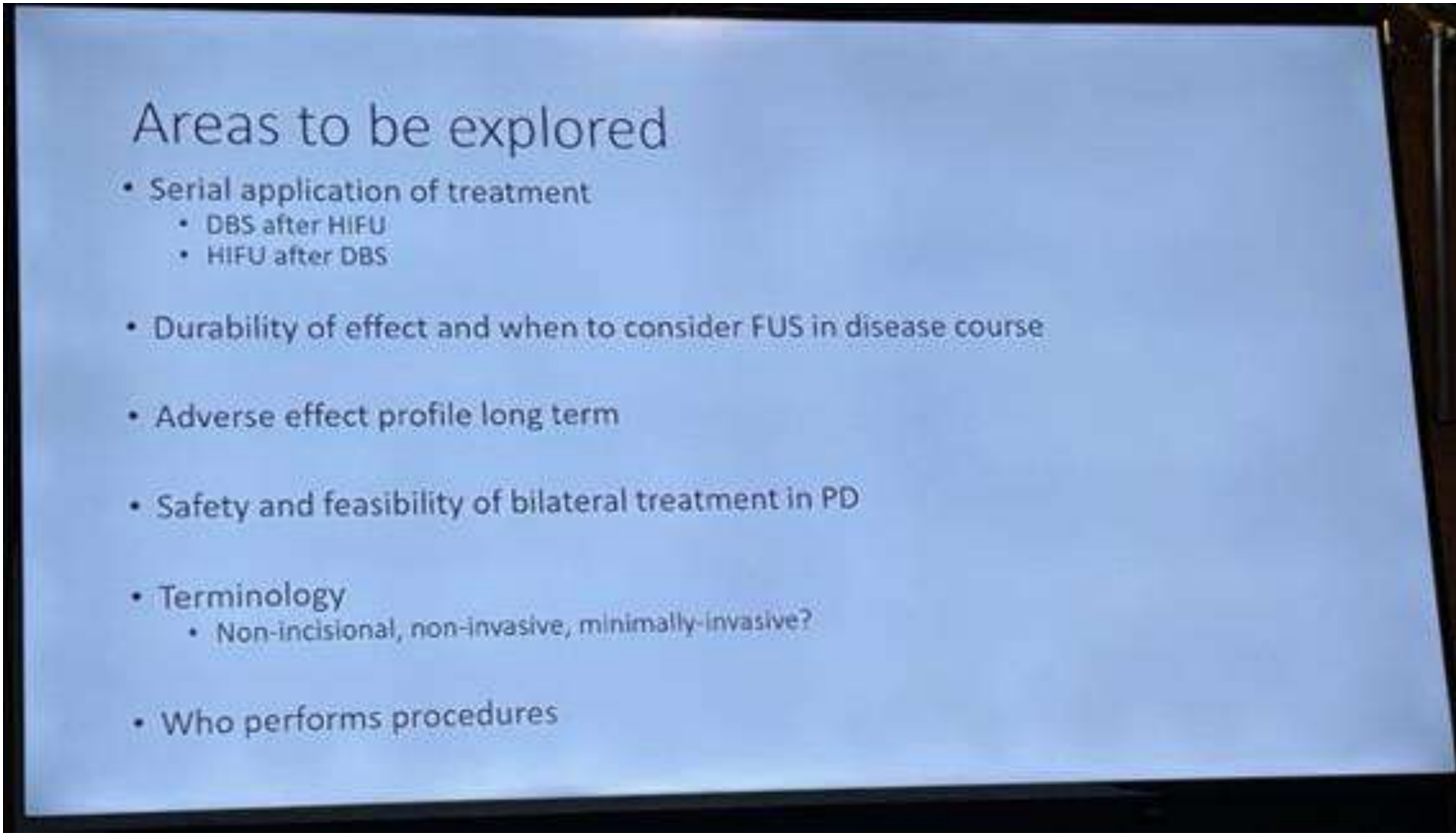
Table 2. Primary and Secondary Outcomes at 3 Months.

Outcome	FUSA of the Gl Pallidus Intern (N=65)
Primary outcome: response — no. (%)*	45 (69)
Secondary outcomes‡	
Mean improvement in MDS-UPDRS IV score (95% CI)	5.1 (4.2 to 6.
Mean improvement in total MDS-UPDRS III score in the off-medication state (95% CI)	6.0 (3.7 to 8.
Mean improvement in MDS-UPDRS II score (95% CI)	2.8 (1.4 to 4.



>30% no response FUS

Binit Shah 2023 World Parkinson Congress



Binit Shah 2023 World Parkinson Congress



Parkinson's Tremor

Tremor does not have to respond to dopaminergic medications

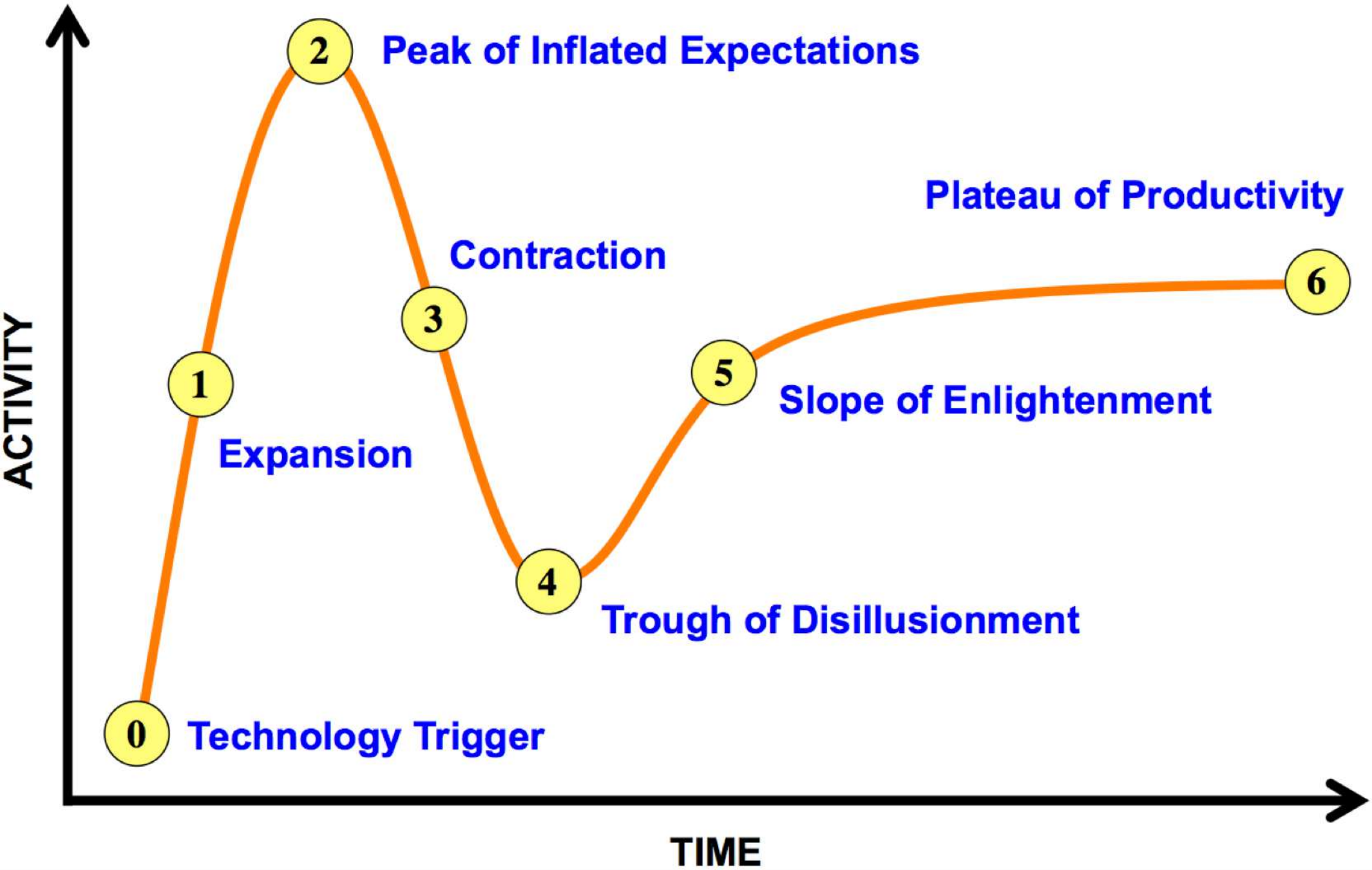


Parkinson Dyskinesia



GPi dyskinesia suppressor
STN (medication reduction, but…)




ACTIVITY
TIME
0
Technology Trigger
1
Expansion
2
Peak of Inflated Expectations
3
Contraction
4
Trough of Disillusionment
5
Slope of Enlightenment
6
Plateau of Productivity

PLOS ONE



RESEARCH ARTICLE

Interdisciplinary Parkinson's Disease Deep Brain Stimulation Screening and the Relationship to Unintended Hospitalizations and Quality of Life

Masa-aki Higuchi[1], Daniel Martinez-Ramirez[1], Hokuto Morita[1], Dan Topiol[1], Dawn Bowers[4], Herbert Ward[3], Lisa Warren[5], Meredith DeFranco[5], Julie A. Hicks[5], Karen W. Hegland[5], Michelle S. Troche[6], Shankar Kulkarni[4], Erin Hastings[1], Kelly D. Foote[2], Michael S. Okun[1,2]*

Interdisciplinary Screening Matters

Parkinsonism & Related Disorders
Available online 28 June 2017
In Press, Corrected Proof

Causes of failure of pallidal deep brain stimulation in cases with pre-operative diagnosis of isolated dystonia

K. Amende M. Paus [a,b,f], Joachim K. Krauss [b], Constanze E. Kämpfer [a], Andrea A. Kühn [c], Christoph Schrader [d], Martin Glücrepe [e], Nicla Allert [f], Rainer Boesche [g], Christian Blahak [h], Jana K. Baltar [a], Carsten R. Finke [a, i], Wolfgang Fiegel [j], Thomas Liebig [k], Fayçal El Majdoub [l, f], Philipp Mahlknecht [m], Josef Kessler [n], Joerg Mueller [m, o], Juergen Voges [m, p], ... Lars Timmermann [a]

Movement Disorders

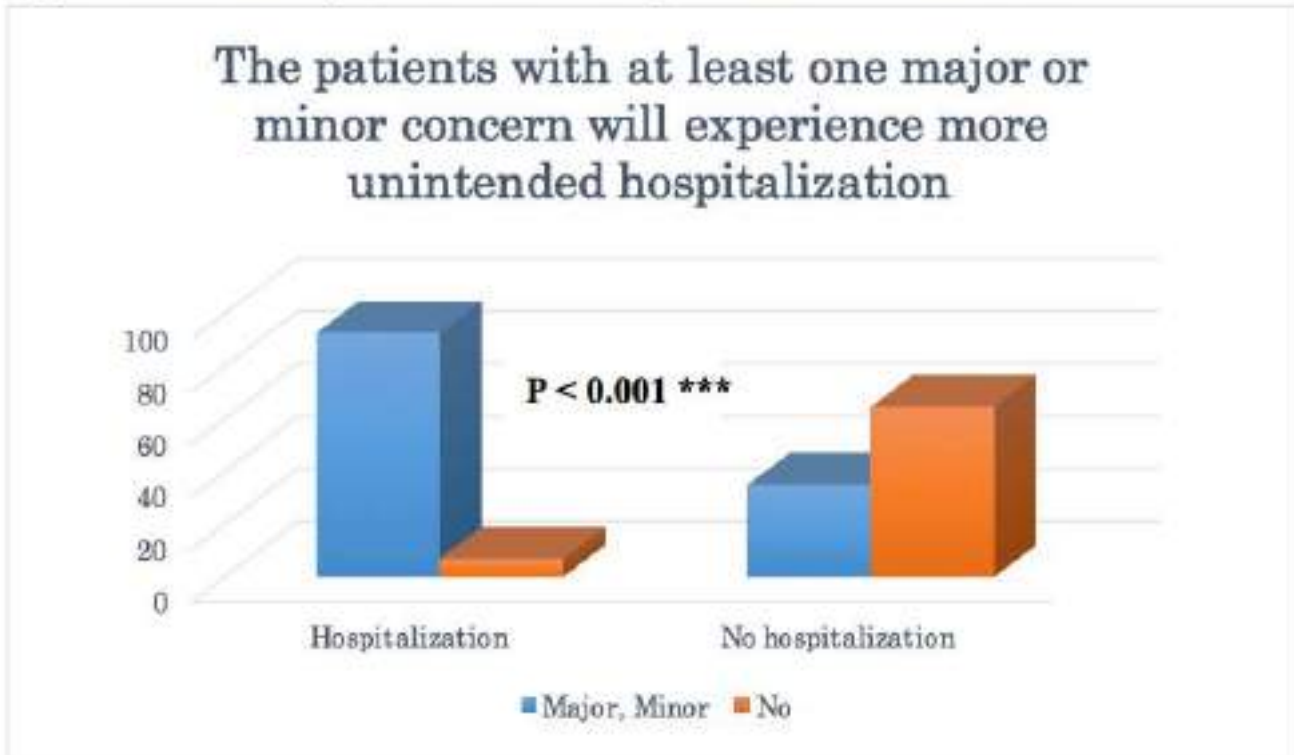
Global cognitive scores do not predict outcome after subthalamic nucleus deep brain stimulation

Darlene Hacker PhD [1], Nolan M. Bush PhD, Scott E. Cooper MD, PhD, Cynthia S. Kubu PhD, Andre G. Machado MD, PhD

PLOS ONE

Interdisciplinary Parkinson's Disease Deep Brain Stimulation Screening and the Relationship to Unintended Hospitalizations and Quality of Life

Figure 2. The relationship between unintended hospitalization and level of concern



Received: 29 April 2021 | Revised: 23 November 2021 | Accepted: 2 January 2022

DOI: 10.1002/brb3.2503

Brain and Behavior Open Access WILEY

ORIGINAL ARTICLE

Subthalamic deep brain stimulation in Parkinson's disease with *SNCA* mutations: Based on the follow-up to 10 years

Jinyoung Youn[1,2] | Genko Oyama[3] | Nobutaka Hattori[3] | Yasushi Shimo[3] | Tomi Kuusimäki[4,5] | Valtteri Kaasinen[4,5] | Angelo Antonini[6] | Dongyeop Kim[1,2] | Jung-Il Lee[7] | Kyung Rae Cho[8] | Jin Whan Cho[1,2]



Microelectrode Recording



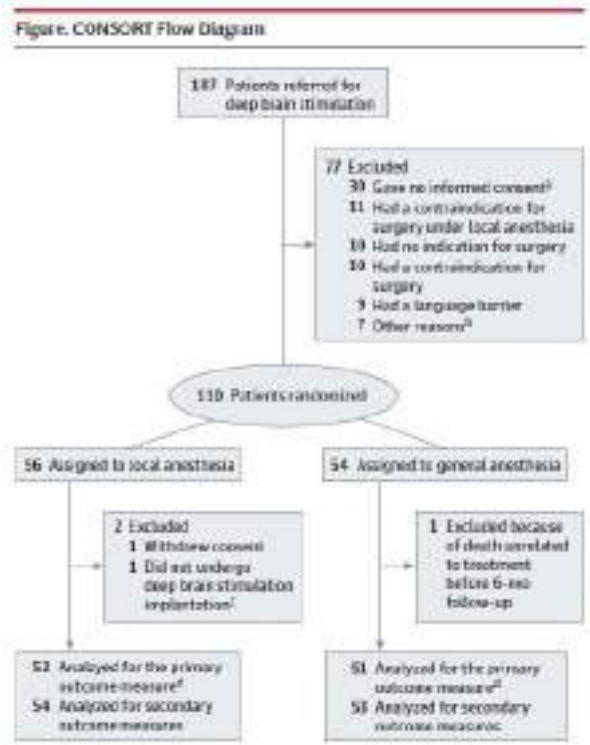


JAMA Neurology | Original Investigation

General Anesthesia vs Local Anesthesia in Microelectrode Recording–Guided Deep-Brain Stimulation for Parkinson Disease

The GALAXY Randomized Clinical Trial

Rozemarije A. Holewijn, MD; Dagmar Verbaan, PhD; Pepijn M. van den Munckhof, MD, PhD; Maarten Bot, MD, PhD; Gert J. Geurtsen, PhD; Joke M. Dijk, MD, PhD; Vincent J. Odekerken, MD, PhD; Martijn Beudel, MD, PhD; Rob M. A. de Bie, MD, PhD; P. Rick Schuurman, MD, PhD



- Single-center randomized; n= 110
- Frame-based microelectrode-guided asleep DBS.
- Similar cognitive, mood, and behavioral adverse effects compared with awake DBS.

Mode of delivery

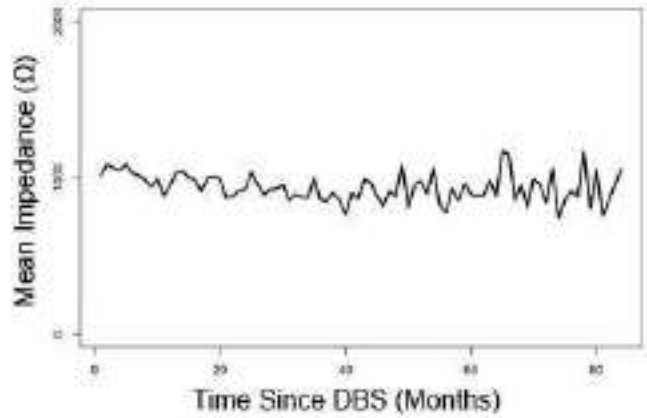
Physiologic Impedance

Current Stimulation Into Tissue

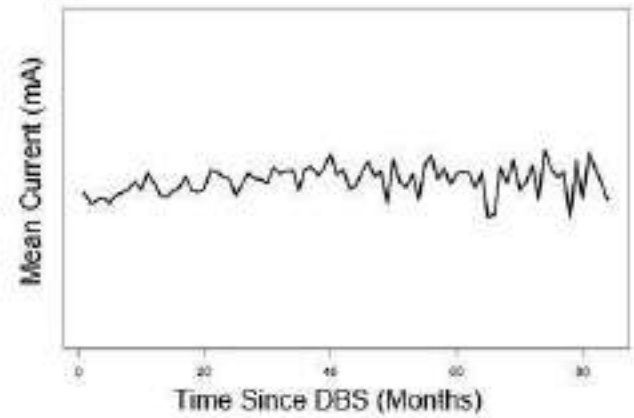
a

Constant Voltage

b



c

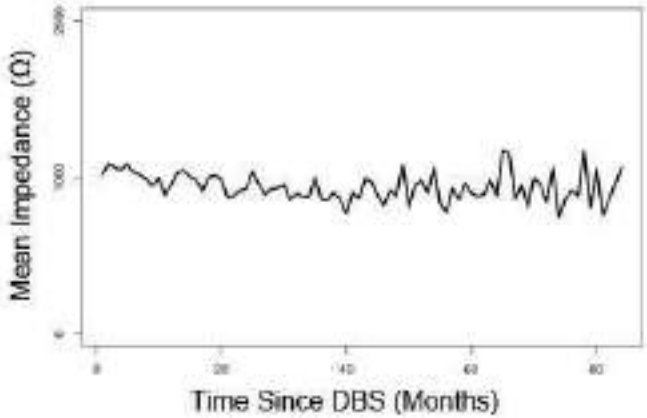


d

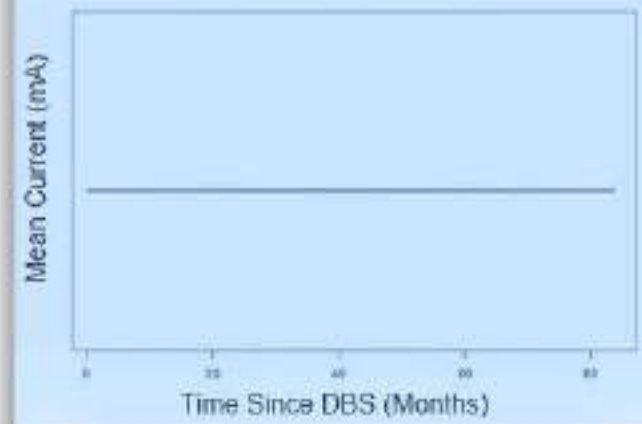
Constant Current



e



f



frontiers in Neuroscience

REVIEW
published: 03 April 2014
doi: 10.3389/fnins.2014.00137

Proceedings of the Third Annual Deep Brain Stimulation Think Tank: A Review of Emerging Issues and Technologies

P. Justin Rossi[1]*, Aysegul Gunduz[2], Jack Judy[3], Linda Wilson[4], Andre Machado[5], James J. Giordano[6], W. Jeff Elias[7], Marvin A. Rossi[8], Christopher L. Butson[9], Michael D. Fox[10], Cameron C. McIntyre[11], Nader Pouratian[12], Nicole C. Swann[13], Coralie de Hemptinne[13], Robert E. Gross[14], Howard J. Chizeck[15], Michele Tagliati[16], Andres M. Lozano[17], Wayne Goodman[18], Jean-Philippe Langevin[19], Ron L. Alterman[8],

OPEN ACCESS

Edited by:

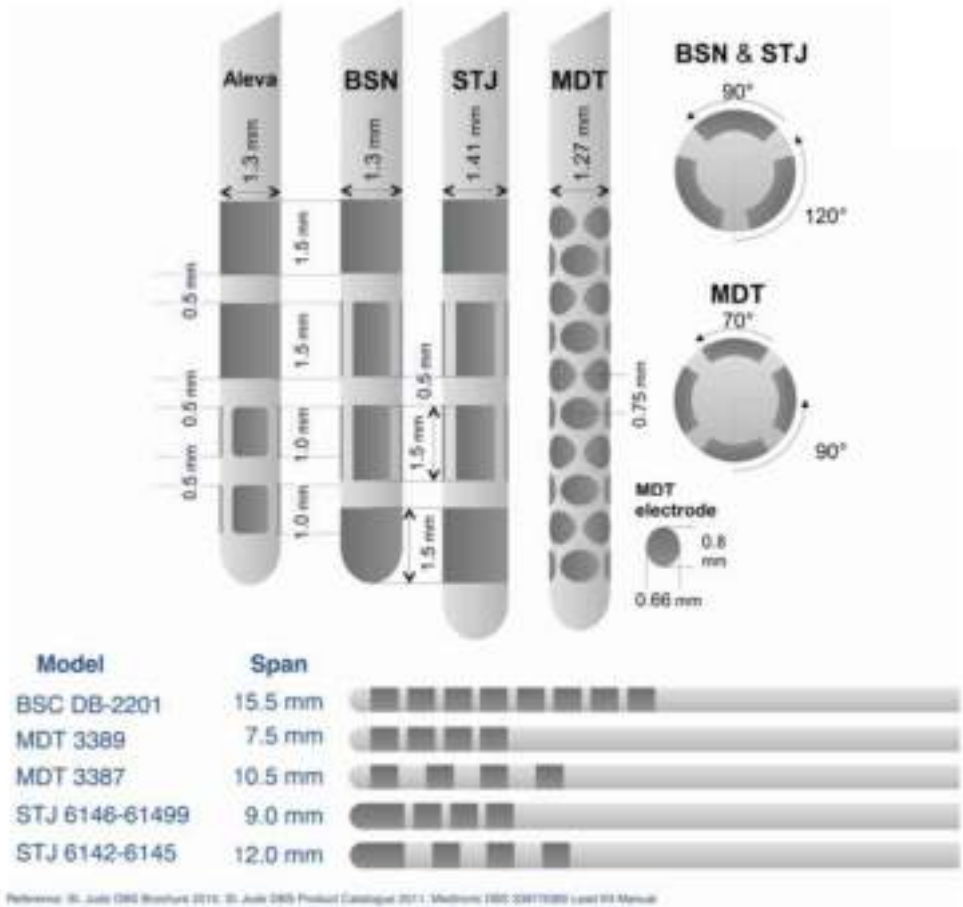
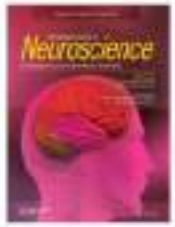


FIGURE 3 | Comparison of emerging DBS electrode lead technology. BSN, Boston Scientific Neuromodulation; STJ, St. Jude Medical; MDT, Medtronic. Reference: St. Jude DBS Brochure 2010, St. Jude DBS Product Catalog 2011, Medtronic DBS 3387/3389 Lead Kit Manual.



International Journal of Neuroscience

ISSN: 0020-7454 (Print) 1543-5245 (Online) Journal homepage: http://www.tandfonline.com/loi/ines20

Proceedings of the Second Annual Deep Brain Stimulation Think Tank: What's in the Pipeline

Aysegul Gunduz, Hokuto Morita, P. Justin Rossi, William L. Allen, Ron L. Alterman, Helen Bronte-Stewart, Christopher R. Butson, David Charles, Sjaak Deckers, Coralie de Hemptinne, Mahlon DeLong, Darin Dougherty, Jens Ellrich, Kelly D. Foote, James Giordano, Wayne Goodman, Benjamin D. Greenberg, David Greene, Robert Gross, Jack W. Judy, Edward Karst, Alexander Kent, Brian Kopell, Anthony Lang, Andres Lozano, Codrin Lungu, Kelly E. Lyons, Andre Machado, Hubert Martens, Cameron McIntyre, Hoon-Ki Min, Joseph Neimat, Jill Ostrem, Sat Pannu, Francisco Ponce, Nader Pouratian, Donnie Reymers, Lauren Schrock, Sameer Sheth, Ludy Shih, Scott Stanslaski, G. Karl Steinke, Paul Stypulkowski, Alexander I. Tröster, Leo Verhagen, Harrison Walker & Michael S. Okun



Stereotactic and Functional Neurosurgery

Clinical Study

Stereotact Funct Neurosurg 2021;99:305–312
DOI: 10.1159/000512231

Received: November 16, 2019
Accepted: August 31, 2020
Published online: January 5, 2021

Directional Leads for Deep Brain Stimulation: Technical Notes and Experiences

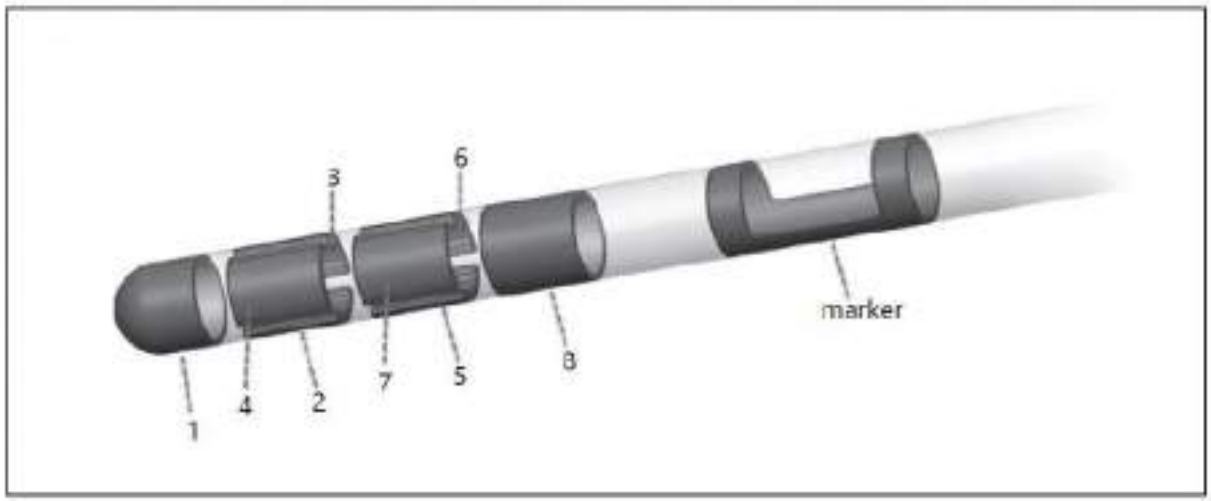
Patrick Fricke[a] Robert Nickl[a] Maria Breun[a] Jens Volkmann[b] Dalal Kirsch[b]
R.-I. Ernestus[a] Frank Steigerwald[b] Cordula Matthies[a]

[a]Department of Neurosurgery, Würzburg University Hospital, Würzburg, Germany; [b]Department of Neurology, Würzburg University Hospital, Würzburg, Germany

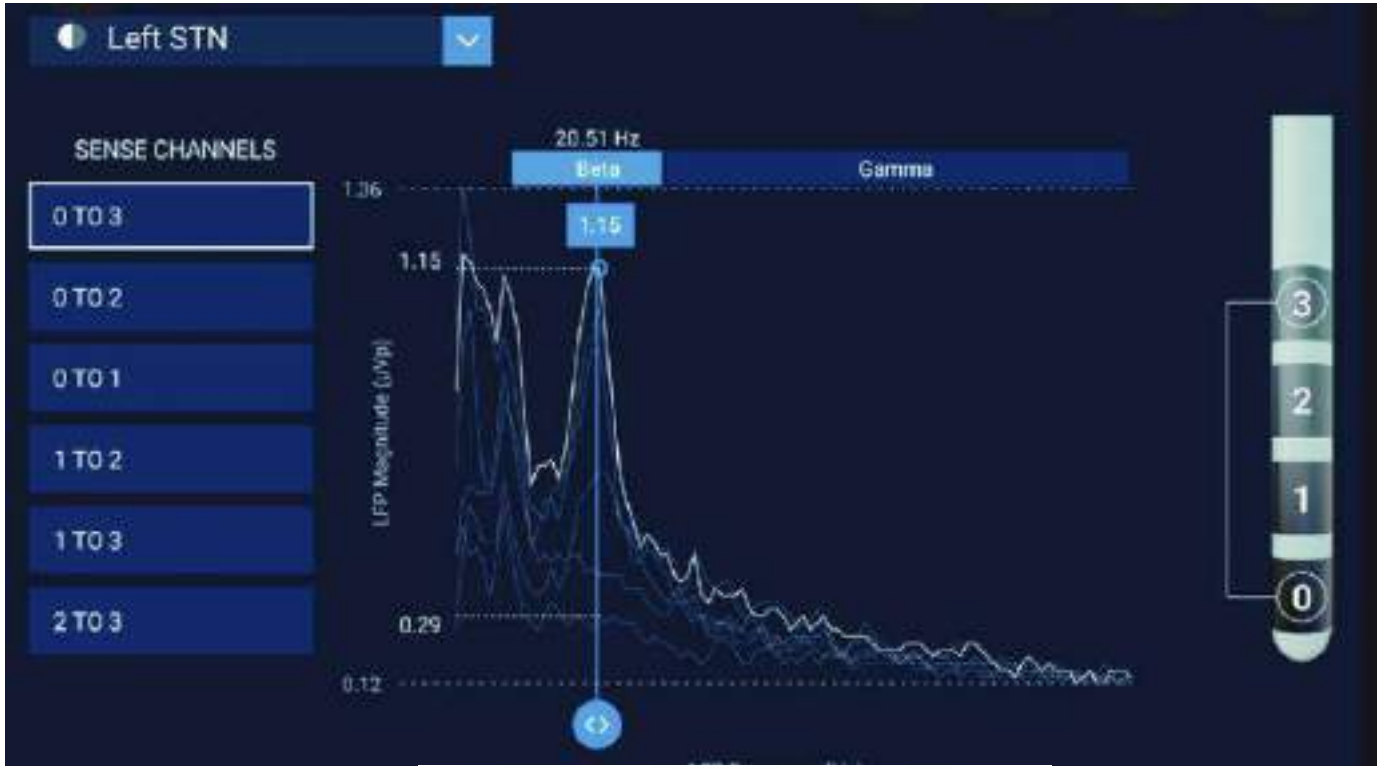


- Higher X-ray dose compared to conventional lead implantations

  415.53 vs. 328.96 Gy cm2; p = 0.09







Physiology



Remote Programming

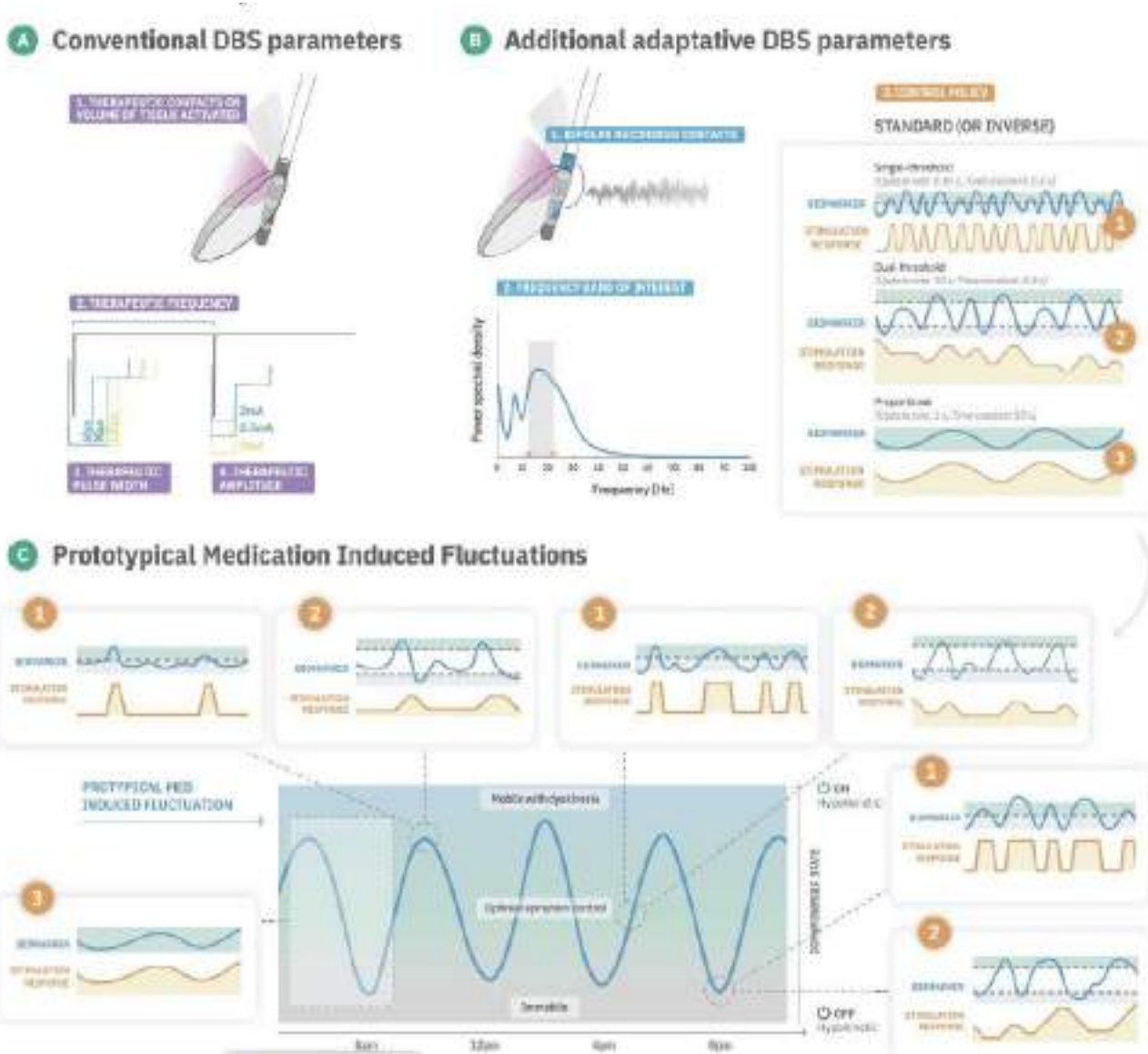
REVIEW

Adaptive Deep Brain Stimulation: From Experimental Evidence Toward Practical Implementation

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

Wolf-Julian Neumann, MD,[1] Rosa Gilron, PhD,[2] Simon Little, MD, PhD,[3] and Gerd Tinkhauser, MD, PhD[4]*

[1]Movement Disorder and Neuromodulation Unit, Department of Neurology, Charité-Universitätsmedizin Berlin, Berlin, Germany
[2]Rune Labs, San Francisco, California, USA
[3]Movement Disorders and Neuromodulation Centre, University of California San Francisco, San Francisco, California, USA
[4]Department of Neurology, Bern University Hospital and University of Bern, Bern, Switzerland





BMJ Open

Double-blind cross-over pilot trial protocol to evaluate the safety and preliminary efficacy of long-term adaptive deep brain stimulation in patients with Parkinson's disease

Sara Marceglia ,[1,2] Costanza Conti,[3] Oleg Svanidze,[3] Guglielmo Foffani,[4,5] Andres M Lozano,[6,7] Elena Moro,[8] Jens Volkmann,[9] Mattia Arlotti,[3] Lorenzo Rossi,[3] Alberto Priori[10,11]

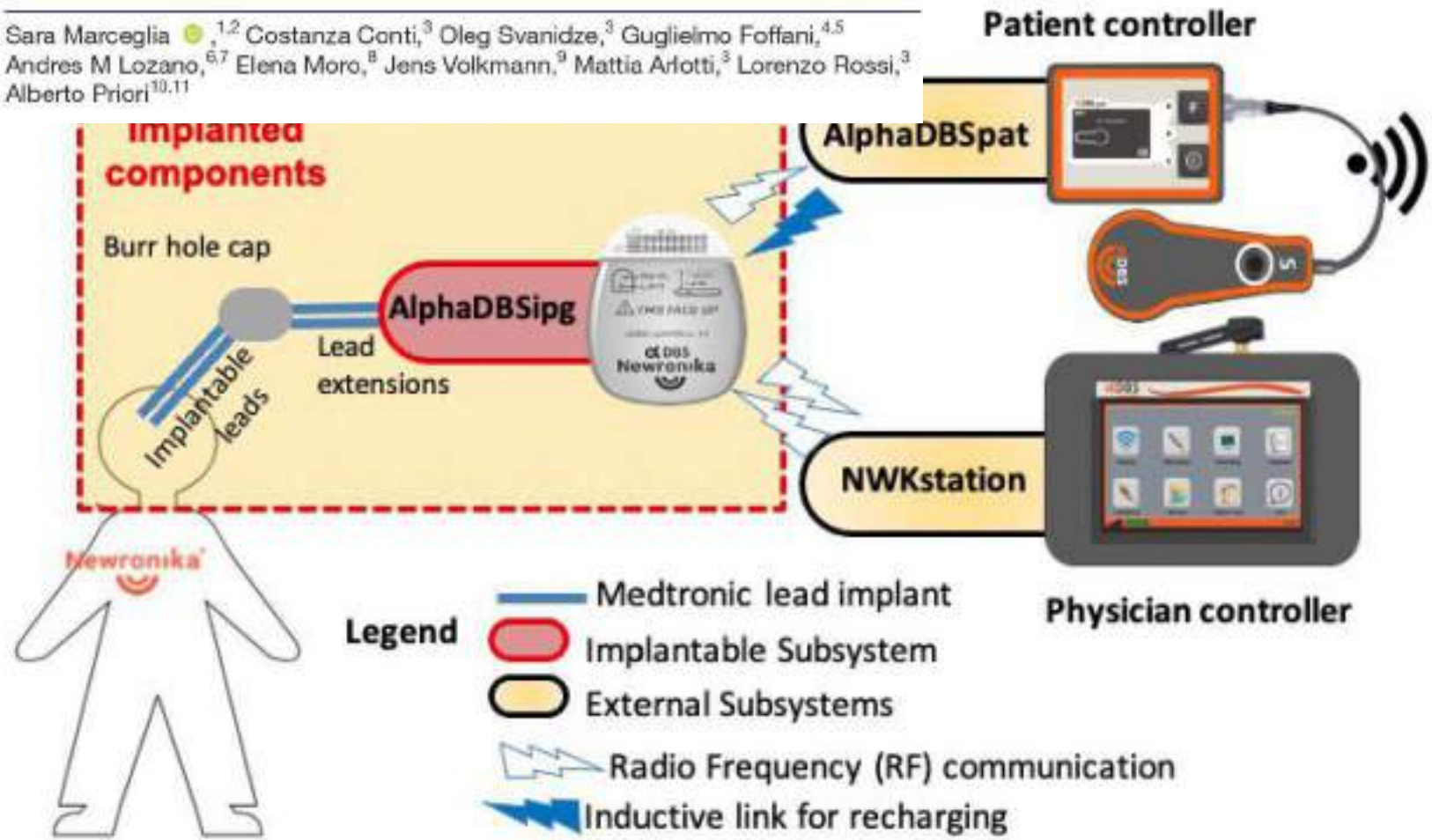
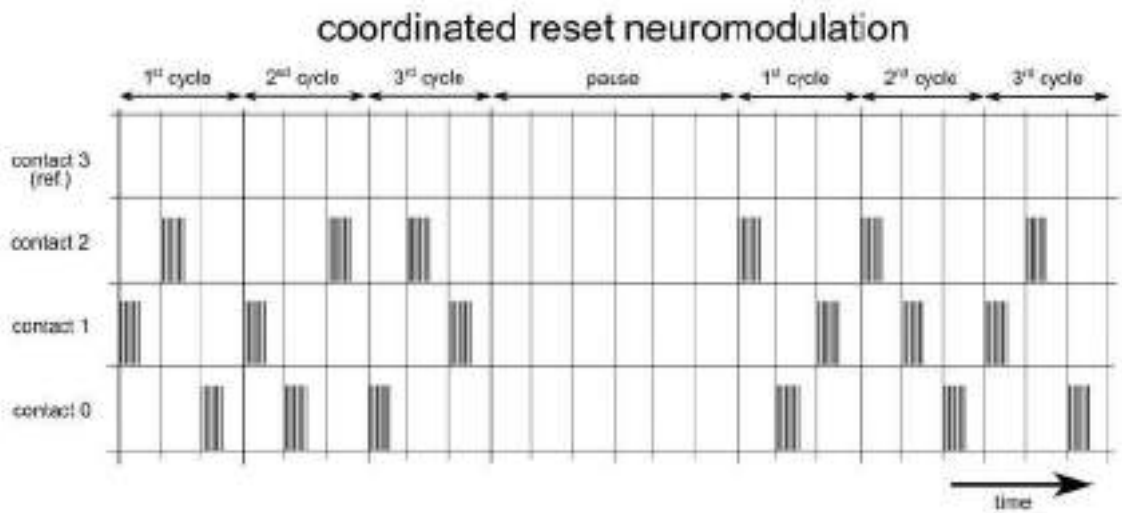


Figure 2 AlphaDBS system overview. AlphaDBS, alpha deep brain stimulation; RF, radiofrequency.

Novel Neuromodulation Paradigms

- <u>Coordinated reset DBS</u>– delivers brief HF pulse trains through different stimulation contacts on implanted lead to “reset” the pathological synaptic neuronal synchrony within the circuit

  - Primate model, HFS vs coordinated rest neuromodulation- CRN worked better and lasted longer up to 90 min (Tass PA, el al. *Ann Neurol* 2012;72:812-820.
  - PD (N=6) proof of concept study, externalized leads for 3 days. Reduction of beta band activity and improvement in motor function (Adamchic I, et al. *Movement Dis* 2014;29 (13).



In CR neuromodulation, brief high-frequency pulse trains are delivered through different sites at different, equally spaced times. The 3-2 ON-OFF pattern[2,6] and the random variation of the pulse train sequences[7] optimize the desynchronizing CR effect. The pattern is repeated periodically.

Coordinated Reset Neuromodulation for Parkinson's Disease: Proof-of-Concept Study

Ilya Adamchic, MD,[1] Christian Hauptmann, PhD,[1]
Utako Brigit Barnikol, MD,[1,2,3,4] Norbert Pawelczyk,[1]
Oleksandr Popovych, PhD,[1] Thomas Theo Barnikol, MD,[1]
Alexander Silchenko, PhD,[1] Jens Volkmann, MD,[5]
Günter Deuschl, MD,[6]
Wassilios G. Meissner, MD, PhD,[7,8,9,10]
Mohammad Maarouf, MD,[4] Volker Sturm, MD,[4,5]
Hans-Joachim Freund, MD,[1]
and Peter Alexander Tass, MD, PhD[1,2,4*]

Courtesy Jill Ostrem, UCSF

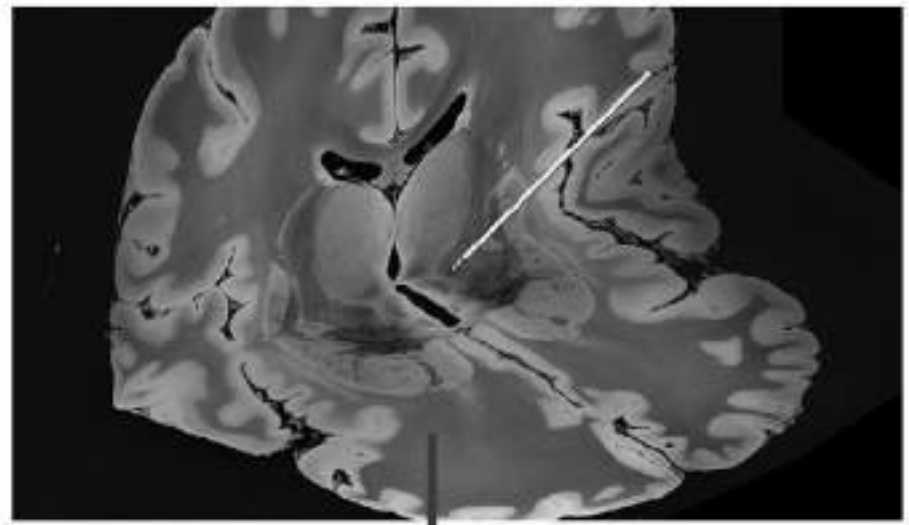
REVIEW

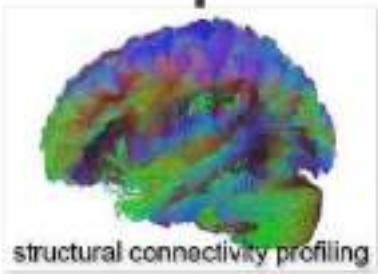
A Comprehensive Review of Brain Connectomics and Imaging to Improve Deep Brain Stimulation Outcomes

Joshua K. Wong, MD,[1*] Erik H. Middlebrooks, MD,[2] Sanjeet S. Grewal, MD,[3] Leonardo Almeida, MD,[1] Christopher W. Hess, MD,[1] and Michael S. Okun, MD[1]

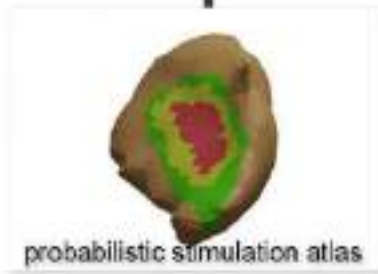
BRAIN CONNECTOMICS IN DBS

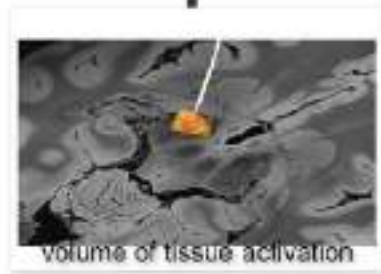












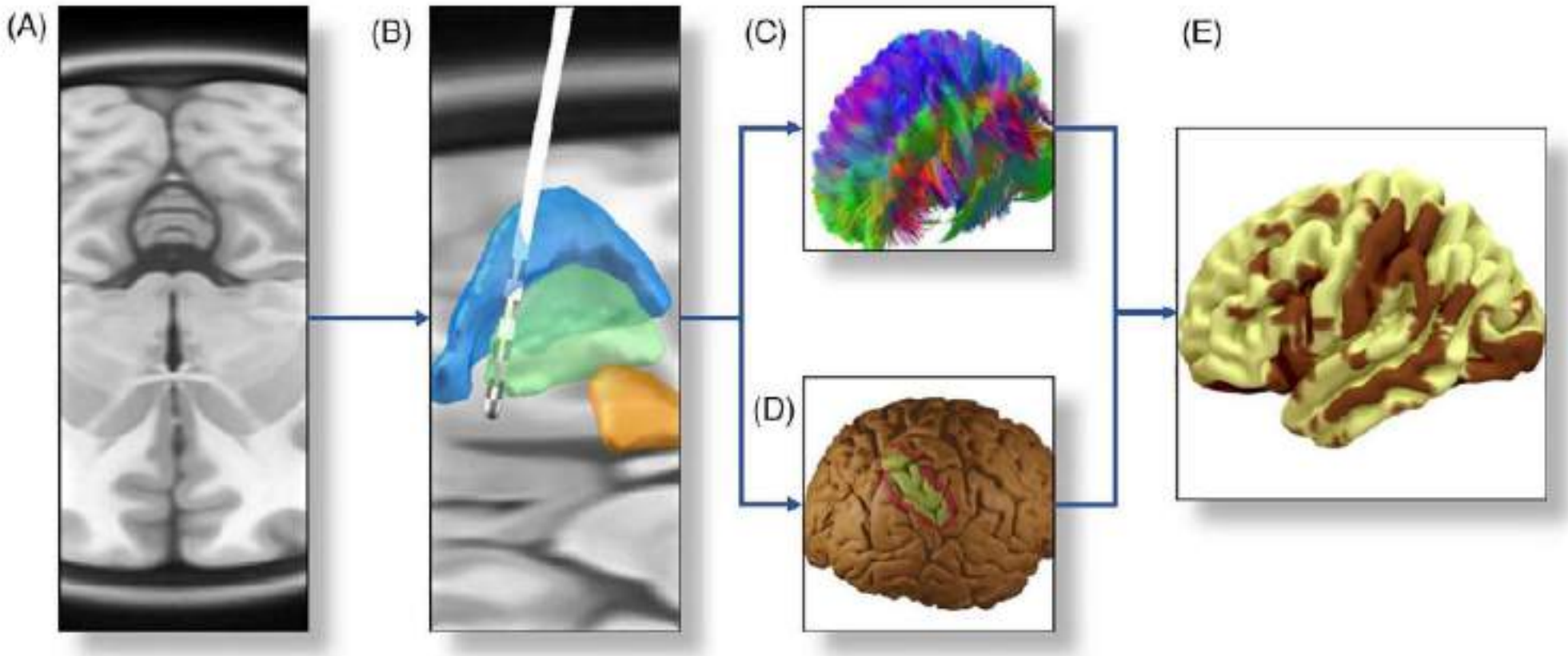


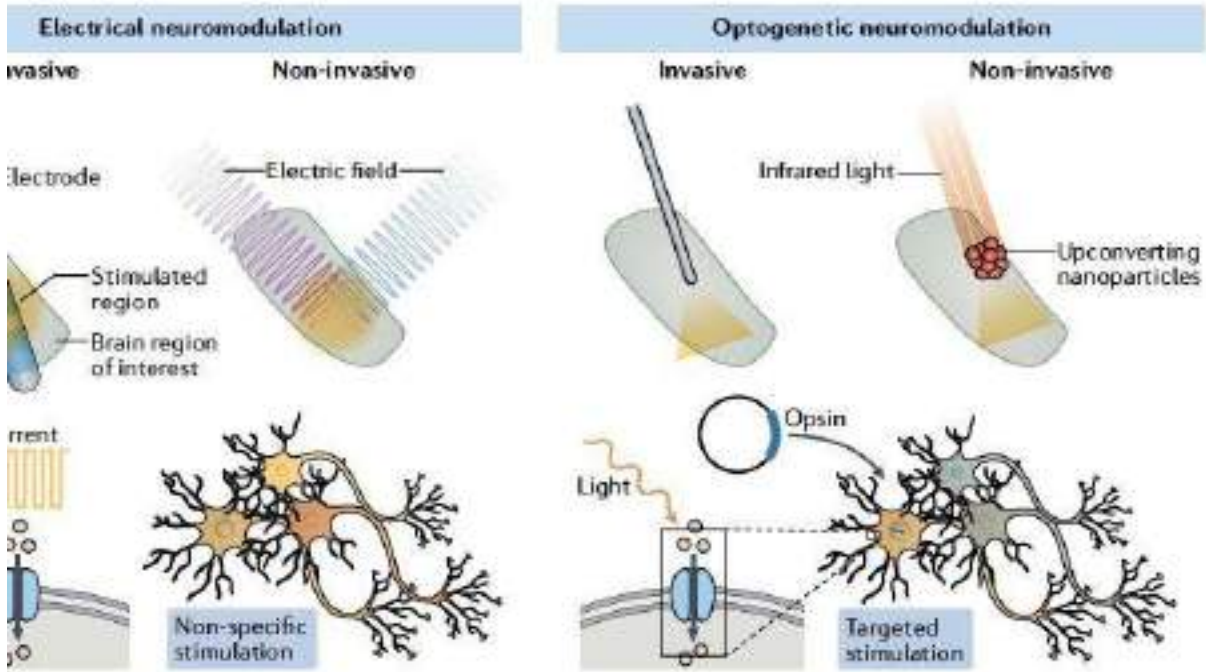
FIG. 3. Application of structural and functional connectivity in DBS. DBS analysis begins with postoperative imaging (A) and lead localization (B). Neuroimaging techniques can then be used to compute patient-specific structural (C) and functional (D) connectivity. These data can be combined with clinical outcome data to create statistical brain-mapping images (E) to guide DBS optimization strategies. Images were rendered using the Lead-DBS advanced processing pipeline and DSI Studio.[39,78,79] [Color figure can be viewed at wileyonlinelibrary.com]

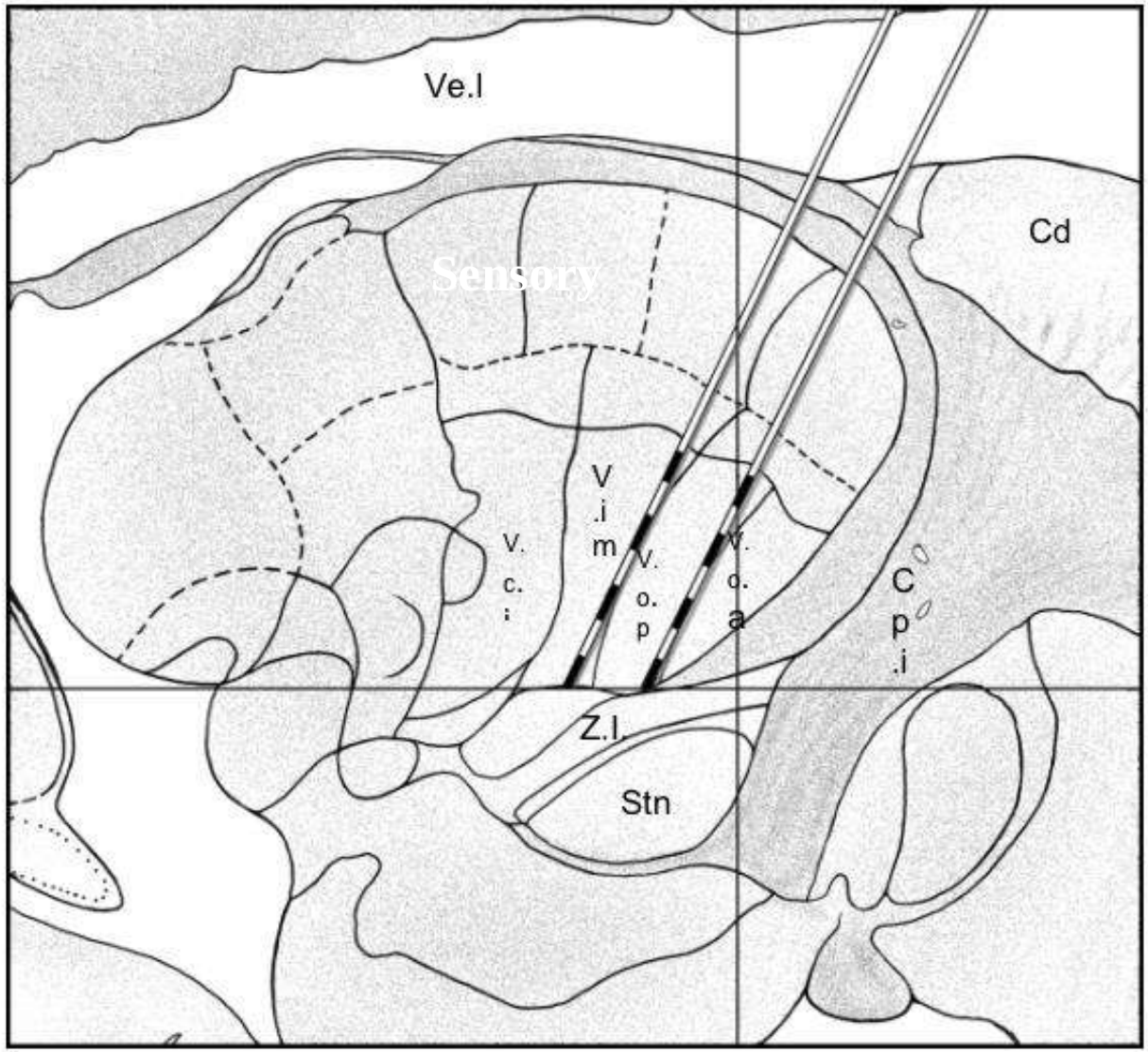




Emerging therapies in Parkinson disease — repurposed drugs and new approaches

Ahmad Elkouzi[1,3], Vinata Vedam-Mai[1,2,3], Robert S. Eisinger[1] and Michael S. Okun[1,2]*







May Use more than one lead

Adapted from Foote and Okun, Neurosurg, 2005

Sub-optimal Outcomes in DBS

Factors to Consider

- Incorrect diagnosis
- Surgical complication
- Suboptimal lead placement
- Hardware malfunction
- Improper programming or medication adjustment
- Poor access to programming
- Lack of multidisciplinary team
- Unrealistic patient expectation
- Disease progression



Okun M, et al Management of Referred DBS Stimulation Failures, Arch Neurol 2005.

Jill Ostrem 2023 World Parkinson Congress

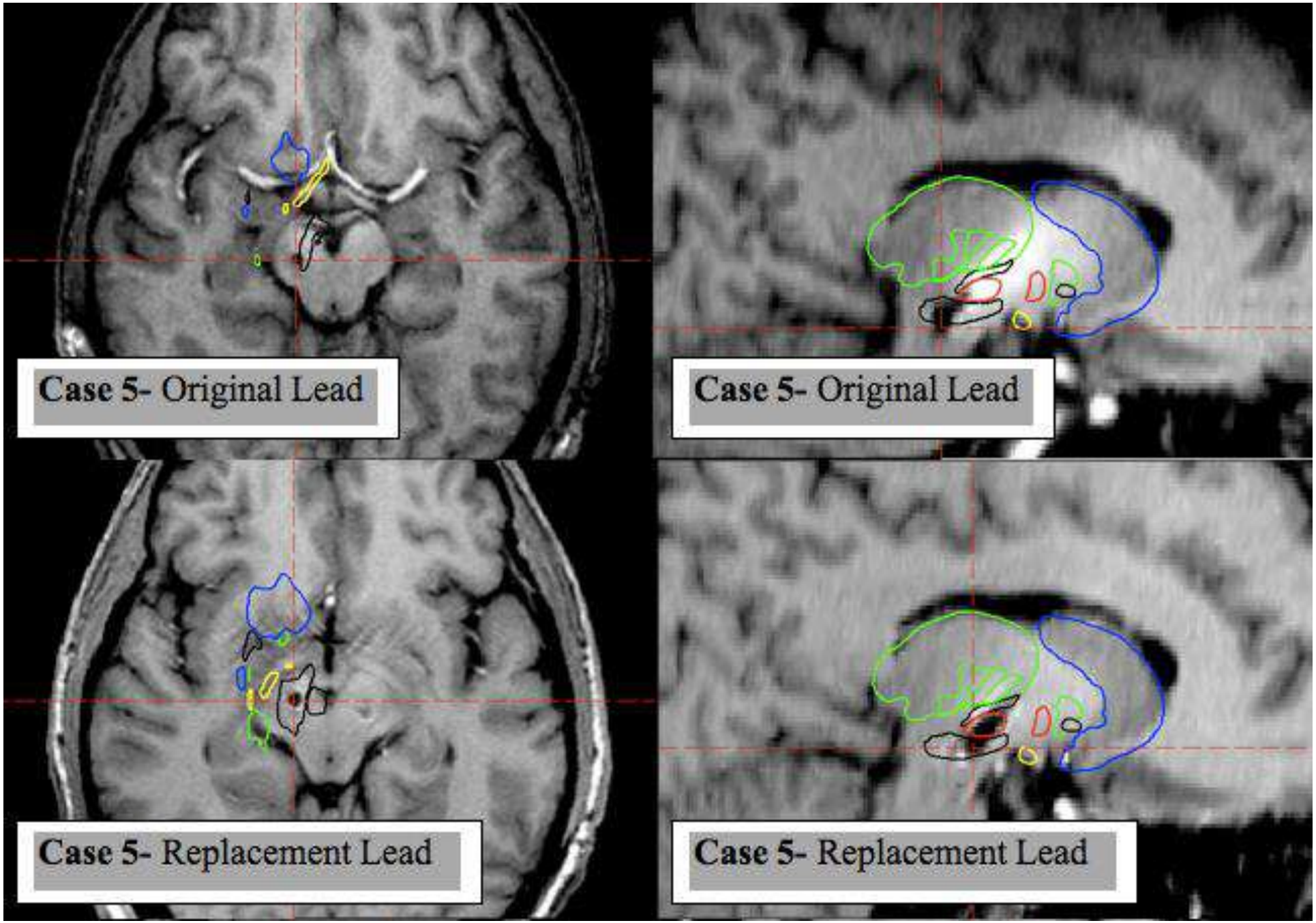
Cerebral venous infarction following DBS

Delayed clinical syndrome





Characteristic flame shaped hemorrhage


Case 5- Original Lead
Case 5- Original Lead
Case 5- Replacement Lead
Case 5- Replacement Lead

Pre-op

Post-op





Parkinson's Disease

Tremor

Dyskinesia

On-off fluctuations

Levodopa responsive symptoms

Shortcomings

Gait

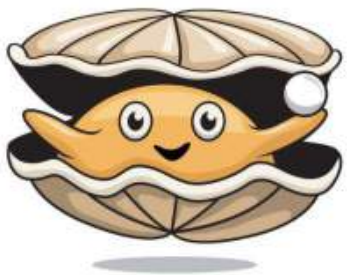
Freezing

Balance

Speech

Cognition

The NEW ENGLAND JOURNAL of MEDICINE



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Correction Has Been Published

A Randomized Trial of Deep-Brain Stimulation for Parkinson's Disease

Günther Deuschl, M.D., Ph.D., Carmen Schade-Brittinger, Paul Krack, M.D., Ph.D., Jens Volkmann, M.D., Ph.D., Helmut Schäfer, Ph.D., Kai Bötzel, M.D., Ph.D., Christine Daniels, M.D., Angela Deutschländer, M.D., Ulrich Dillmann, M.D., Ph.D., Wilhelm Eisner, M.D., Ph.D., Doreen Gruber, M.D., Wolfgang Hamel, M.D., Jan Herzog, M.D., Rüdiger Hilker, M.D., Ph.D., Stephan Klebe, M.D., Manja Kloß, M.D., Jan Koy, M.D., Martin Krause, M.D., Andreas Kupsch, M.D., Ph.D., Delia Lorenz, M.D., Stefan Lorenzl, M.D., Ph.D., H. Maximilian Mehdorn, M.D., Ph.D., Jean Richard Moringlane, M.D., Ph.D., Wolfgang Oertel, M.D., Ph.D., Marcus O. Pinsker, M.D., Heinz Reichmann, M.D., Ph.D., Alexander Reuß, M.S., Gerd-Helge Schneider, M.D., Alfons Schnitzler, M.D., Ph.D., Ulrich Steude, M.D., Ph.D., Volker Sturm, M.D., Ph.D., Lars Timmermann, M.D., Volker Tronnier, M.D., Ph.D., Thomas Trottenberg, M.D., Lars Wojtecki, M.D., Elisabeth Wolf, M.D., Werner Poewe, M.D., Ph.D., and Jürgen Voges, M.D., Ph.D. for the German Parkinson Study Group, Neurostimulation Section

N Engl J Med 2006; 355:896-908 | August 31, 2006 | DOI: 10.1056/NEJMoa060281

- Quality of Life and motor function improved vs. medication group (paired)
- Mobility, activities of daily living, emotional well-being, stigma, and bodily discomfort improved
- Serious adverse events were more common in DBS (13 percent vs. 4 percent)

JAMA The Journal of the American Medical Association



Bilateral Deep Brain Stimulation vs Best Medical Therapy for Patients With Advanced Parkinson Disease

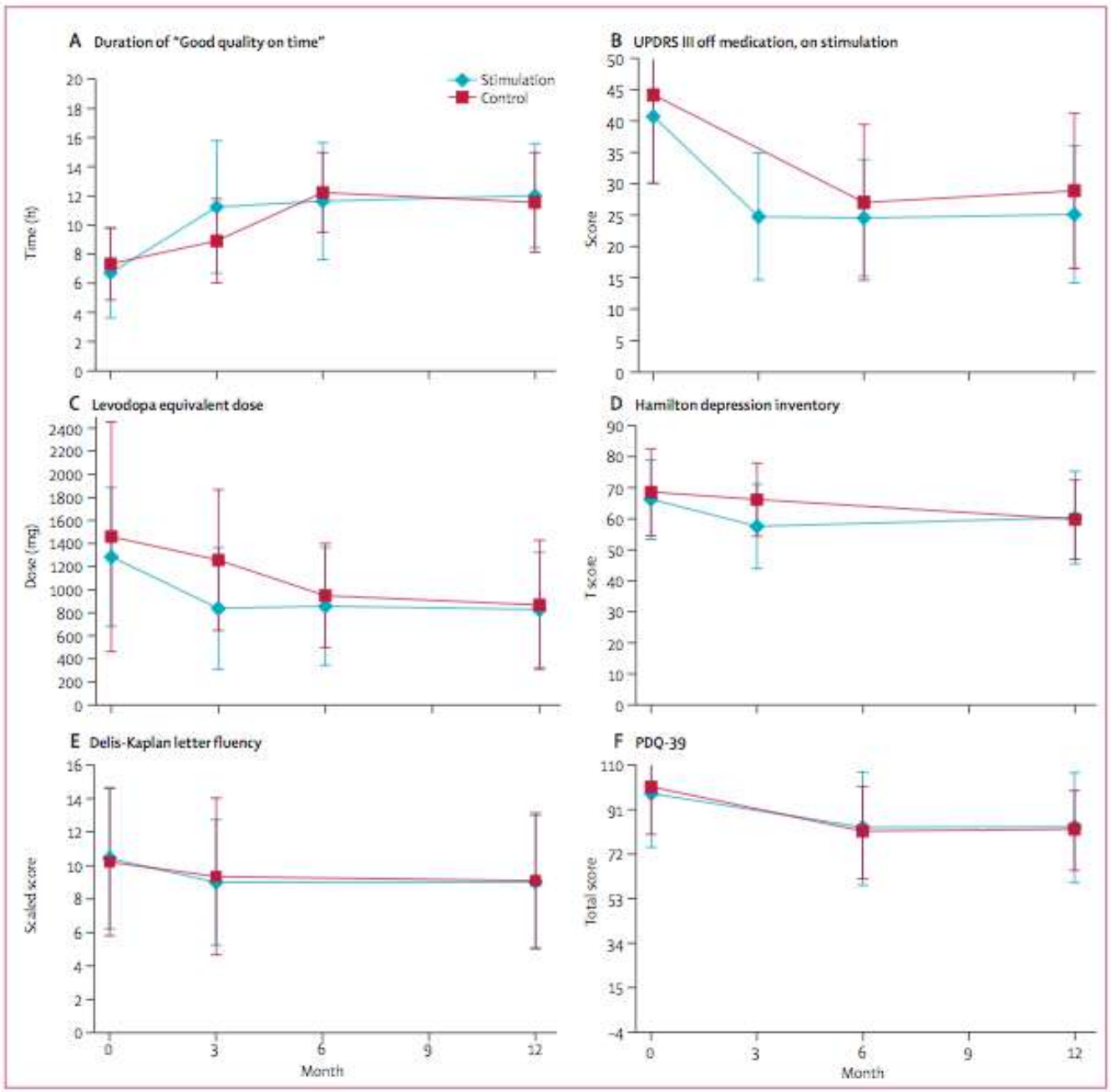
A Randomized Controlled Trial FREE

Frances M. Weaver, PhD; Kenneth Follett, MD, PhD; Matthew Stern, MD; Kwan Hur, PhD; Crystal Harris, PharmD; William J. Marks, MD; Johannes Rothlind, PhD; Oren Sagher, MD; Domenic Reda, PhD; Claudia S. Moy, PhD; Rajesh Pahwa, MD; Kim Burchiel, MD; Penelope Hogarth, MD; Eugene C. Lai, MD, PhD; John E. Duda, MD; Kathryn Holloway, MD; Ali Samii, MD; Stacy Horn, DO; Jeff Bronstein, MD, PhD; Gatana Stoner, RN, CCRC; Jill Heemskerk, PhD; Grant D. Huang, PhD; for the CSP 468 Study Group

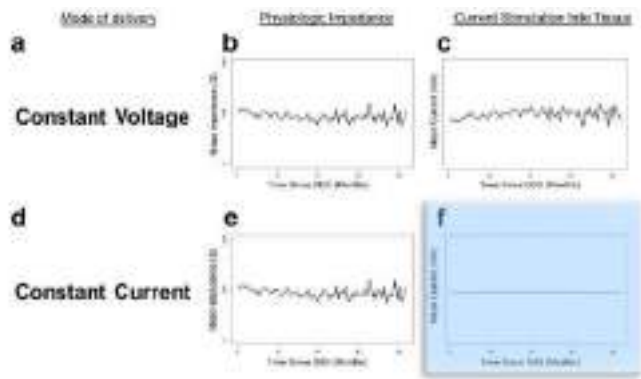
[+] Author Affiliations

PD DBS Constant Current Study

25% Patients Implanted
Not Activated for 90 days

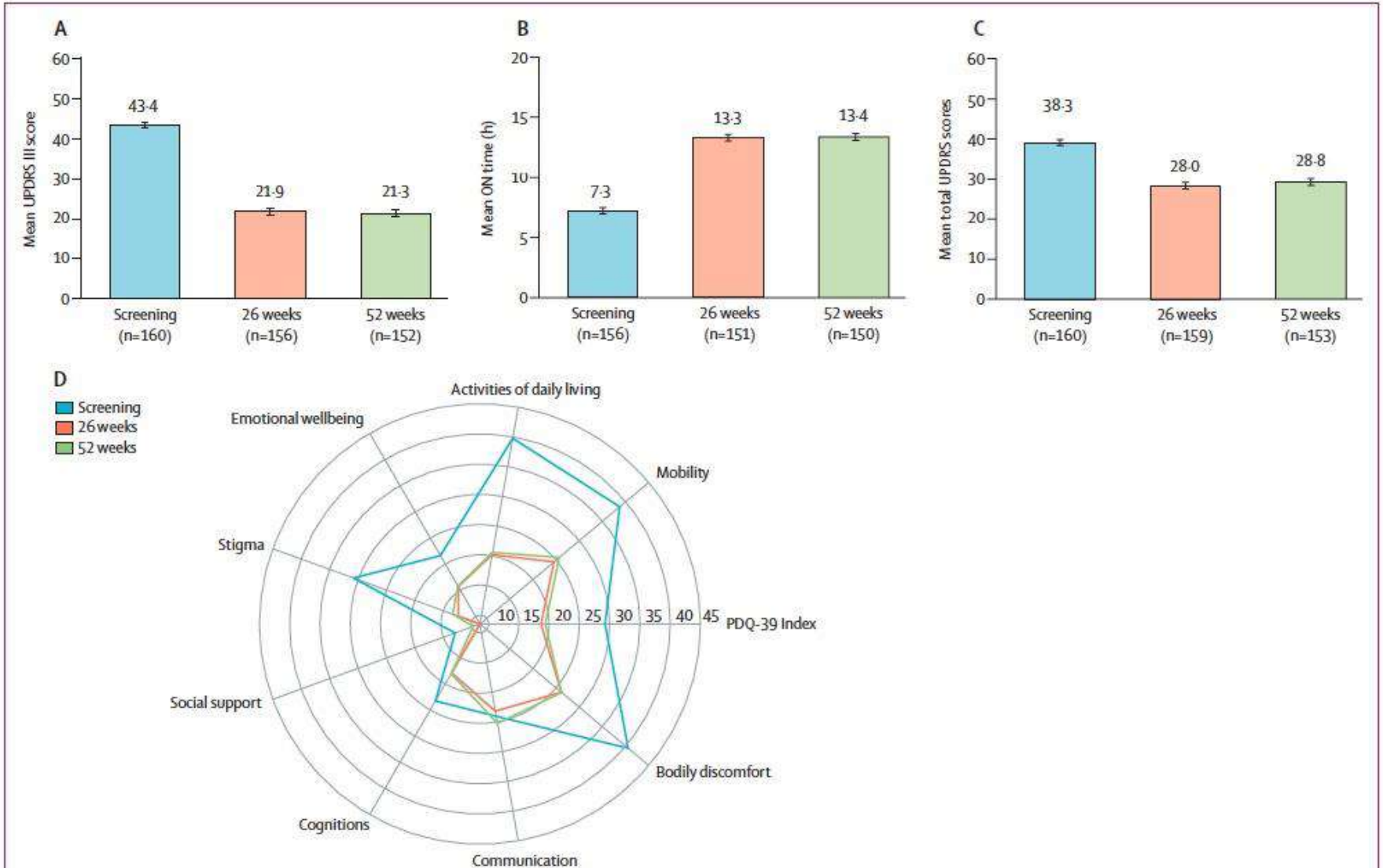






Subthalamic nucleus deep brain stimulation with a multiple independent constant current-controlled device in Parkinson's disease (INTREPID): a multicentre, double-blind, randomised, sham-controlled study

Jerrold L. Vitek, Roshini Jain, Lilly Chen, Alexander I. Tröster, Lauren E. Schrock, Paul A. House, Monique L. Giroux, Adam O. Hebb, Sierra M. Form, Donald M. Whiting, Timothy A. Leichliter, Jill L. Ostrem, Marta San Luciano, Nicholas Galifianakis, Leo Verhagen Metman, Sepehr Sani, Jessica A. Karl, Mustafa S. Siddiqui, Stephen B. Tatter, Ishtiaq ul Haq, Andre G. Machado, Michal Gostkowski, Michele Tagliati, Adam N. Mamelak, Michael S. Okun, Kelly D. Foote, Guillermo Moguel-Cobos, Francisco A. Ponce, Rajesh Pahwa, Jules M. Nazzaro, Cathrin M. Buetefisch, Robert E. Gross, Cornelia C. Luca, Jonathan R. Jagid, Gonzalo J. Revuelta, Istvan Takacs, Michael H. Pourfar, Alon Y. Mogilner, Andrew P. Duker, George T. Mandybur, Joshua M. Rosenow, Scott E. Cooper, Michael C. Park, Suketu M. Khandhar, Mark Sethuk, Fenna T. Phillips, Julie G. Pilitsis, Ryan J. Uitti, Philip A. Starr



Randomized Target Comparisons

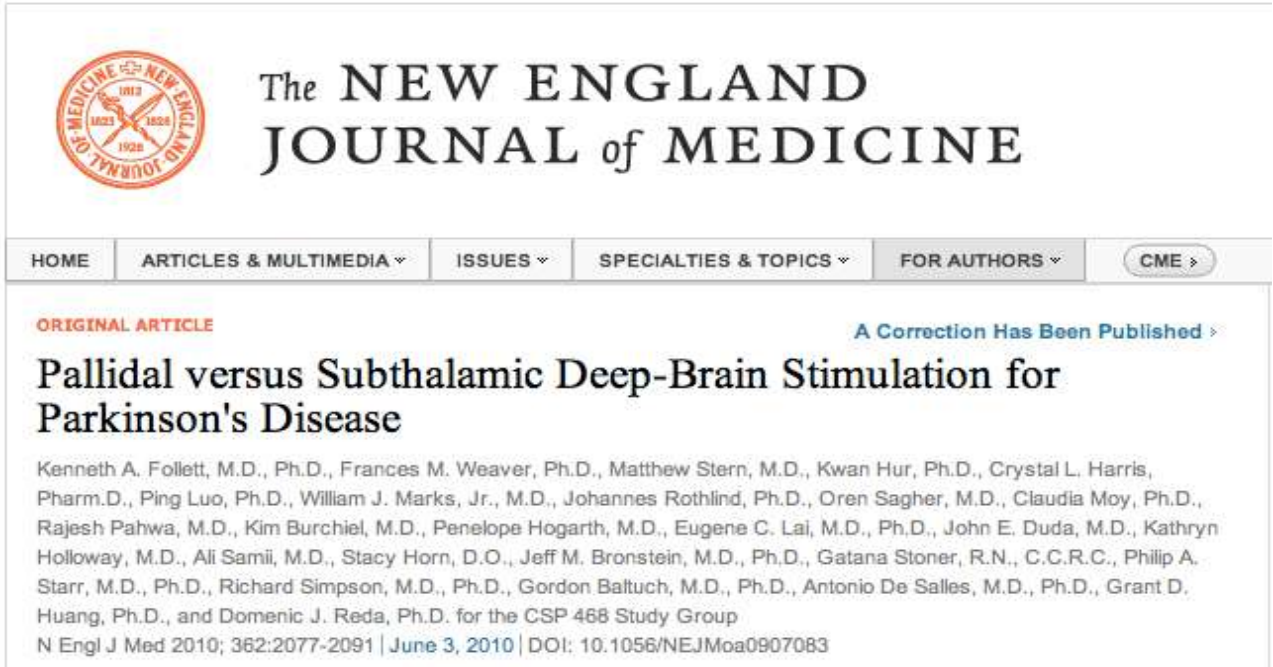


Cognition and Mood in Parkinson's Disease in Subthalamic Nucleus versus Globus Pallidus Interna Deep Brain Stimulation: The COMPARE Trial

Michael S. Okun, MD, Hubert H. Fernandez, MD, Samuel S. Wu, PhD, Lindsey Kirsch-Darrow, MS, Dawn Bowers, PhD, Frank Bova, PhD, Michele Suelter, BS, Charles E. Jacobson IV, BS, Xinping Wang, PhD, Clifford W. Gordon, Jr., BS, Pam Zeilman, ARNP, Janet Romrell, PA-C, Pam Martin, RN, Herbert Ward, MD, Ramon L. Rodriguez, MD, and Kelly D. Foote, MD

- Unilateral GPi and unilateral STN both effective for motor
- Trended toward more medication reduction in STN
- Similar mood and cognitive outcome





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ORIGINAL ARTICLE

A Correction Has Been Published

Pallidal versus Subthalamic Deep-Brain Stimulation for Parkinson's Disease

Kenneth A. Follett, M.D., Ph.D., Frances M. Weaver, Ph.D., Matthew Stern, M.D., Kwan Hur, Ph.D., Crystal L. Harris, Pharm.D., Ping Luo, Ph.D., William J. Marks, Jr., M.D., Johannes Rothlind, Ph.D., Oren Sagher, M.D., Claudia Moy, Ph.D., Rajesh Pahwa, M.D., Kim Burchiel, M.D., Penelope Hogarth, M.D., Eugene C. Lai, M.D., Ph.D., John E. Duda, M.D., Kathryn Holloway, M.D., Ali Samii, M.D., Stacy Horn, D.O., Jeff M. Bronstein, M.D., Ph.D., Gatana Stoner, R.N., C.C.R.C., Philip A. Starr, M.D., Ph.D., Richard Simpson, M.D., Ph.D., Gordon Baltuch, M.D., Ph.D., Antonio De Salles, M.D., Ph.D., Grant D. Huang, Ph.D., and Domenic J. Reda, Ph.D. for the CSP 468 Study Group

N Engl J Med 2010; 362:2077-2091 | June 3, 2010 | DOI: 10.1056/NEJMoa0907083

- Bilateral STN and GPi both effective at addressing motor symptoms
- More medication reduction in STN
- May be advantage for GPi in cognition and medication adjustment flexibility at 36 month follow-up



THE LANCET Neurology

Volume 12, Issue 1, January 2013, Pages 37–44

Articles

Subthalamic nucleus versus globus pallidus bilateral deep brain stimulation for advanced Parkinson's disease (NSTAPS study): a randomised controlled trial

Vincent J.J. Odekerken, MD[a], Teus van Laar, MD[b], Michiel J Staal, MD[c], Arne Mosch, MD[d], Carel FE Hoffmann, MD[e], Peter CG Nijssen, MD[f], Guus N Beute, MD, Jeroen PP van Vugt, MD, Mathieu WPM Lenders, MD[a], M Fiorella Contarino, MD[a], Marieke SJ Mink, MSc[a], Lo J Bour, PhD[a], Pepijn van den

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GPi vs STN deep brain stimulation for Parkinson disease

Three-year follow-up

Vincent J.J. Odekerken, MD*, Judith A. Boel, MSc*, Ben A. Schmand, PhD, Rob J. de Haan, PhD, M. Figee, MD, PhD, Pepijn van den Munckhof, MD, PhD, P. Richard Schuurman, MD, PhD, Rob M.A. de Bie, MD, PhD; For the NSTAPS study group

+ SHOW AFFILIATIONS | + SHOW FULL DISCLOSURES
Correspondence to Dr. Odekerken: v.j.odekerken@amc.uva.nl

Published online before print January 27, 2016, doi: http://dx.doi.org/10.1212/WNL.0000000000002401
Neurology February 23, 2016 vol. 86 no. 8 755-761

- Bilateral STN and GPi both performed well for motor function (maybe better STN); 3 years slight advantage off motor STN (UPDRS)
- Academic Medical Center Linear Disability Scale (ALDS- time spent in the off phase and on phase
- Composite score for cognitive, mood, and behavioural effects
- Medication reduction favored STN

More Equal than the Field Assumed

ANNALS OF NEUROLOGY

Cognition and Mood in Parkinson's Disease in Subthalamic Nucleus versus Globus Pallidus Interna Deep Brain Stimulation: The COMPARE Trial

Michael S. Okun, MD, Hubert H. Fernandez, MD, Samuel S. Wu, PhD, Lindsey Kirsch-Darrow, MS, Dawn Bowers, PhD, Frank Bova, PhD, Michele Suelter, BS, Charles E. Jacobson IV, BS, Xinping Wang, PhD, Clifford W. Gordon, Jr., BS, Pam Zeilman, ARNP, Janet Romrell, PA-C, Pam Martin, RN, Herbert Ward, MD, Ramon L. Rodriguez, MD, and Kelly D. Foote, MD

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Parkinsonism and Related Disorders 75 (2020) 7–13

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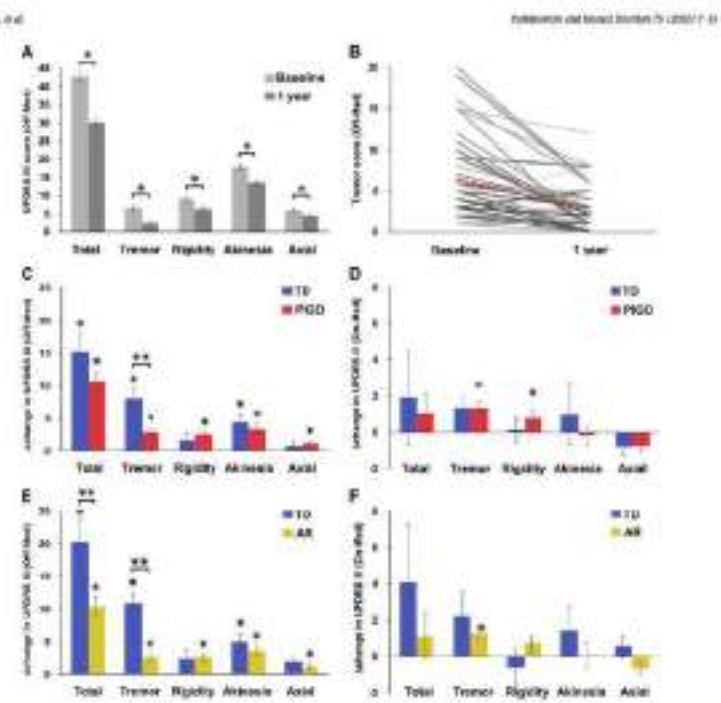
Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

Parkinson's disease motor subtypes and bilateral GPi deep brain stimulation: One-year outcomes

Takashi Tsuboi[a,b,*], Janine Lemos Melo Lobo Jofili Lopes[a], Bhavana Patel[a], Joseph Legacy[a], Kathryn Moore[a], Robert S. Eisinger[a], Leonardo Almeida[a], Kelly D. Foote[c], Michael S. Okun[a], Adolfo Ramirez-Zamora[a]

[a] Department of Neurology, Norman Fixel Institute for Neurological Diseases, University of Florida, Gainesville, FL, USA
[b] Department of Neurology, Nagoya University Graduate School of Medicine, Nagoya, Japan
[c] Department of Neurosurgery, University of Florida, Gainesville, FL, USA



- Bilateral GPi DBS was effective regardless of motor subtypes.
- Greater tremor improvement in the Tremor Dominant patients accounted for greater Off-medication motor improvement.

Table 1. Baseline Characteristics of the Study Population.*

Characteristic	Neurostimulation (N = 124)	Medical Therapy (N = 127)
Age — yr	52.9±6.6	52.2±6.1
Sex — no. (%)		
Male	94 (75.8)	85 (66.9)
Female	30 (24.2)	42 (33.1)
Duration of Parkinson's disease — yr	7.3±3.1	7.7±2.7
Dyskinesia†		
No. of patients	84	94
Duration — yr	1.4±0.8	1.5±0.8
Motor fluctuations†		
No. of patients	121	124
Duration — yr	1.6±0.8	1.8±0.8
Treatment with levodopa		
No. of patients	111	115
Duration — yr	4.8±3.3	5.0±3.3
Treatment with dopamine agonist		
No. of patients	118	115
Duration — yr	5.9±3.0	6.1±3.0
Levodopa-equivalent daily dose — mg	918.8±412.5	966.9±416.5

* Plus–minus values are means ±SD. There were no significant between-group differences.

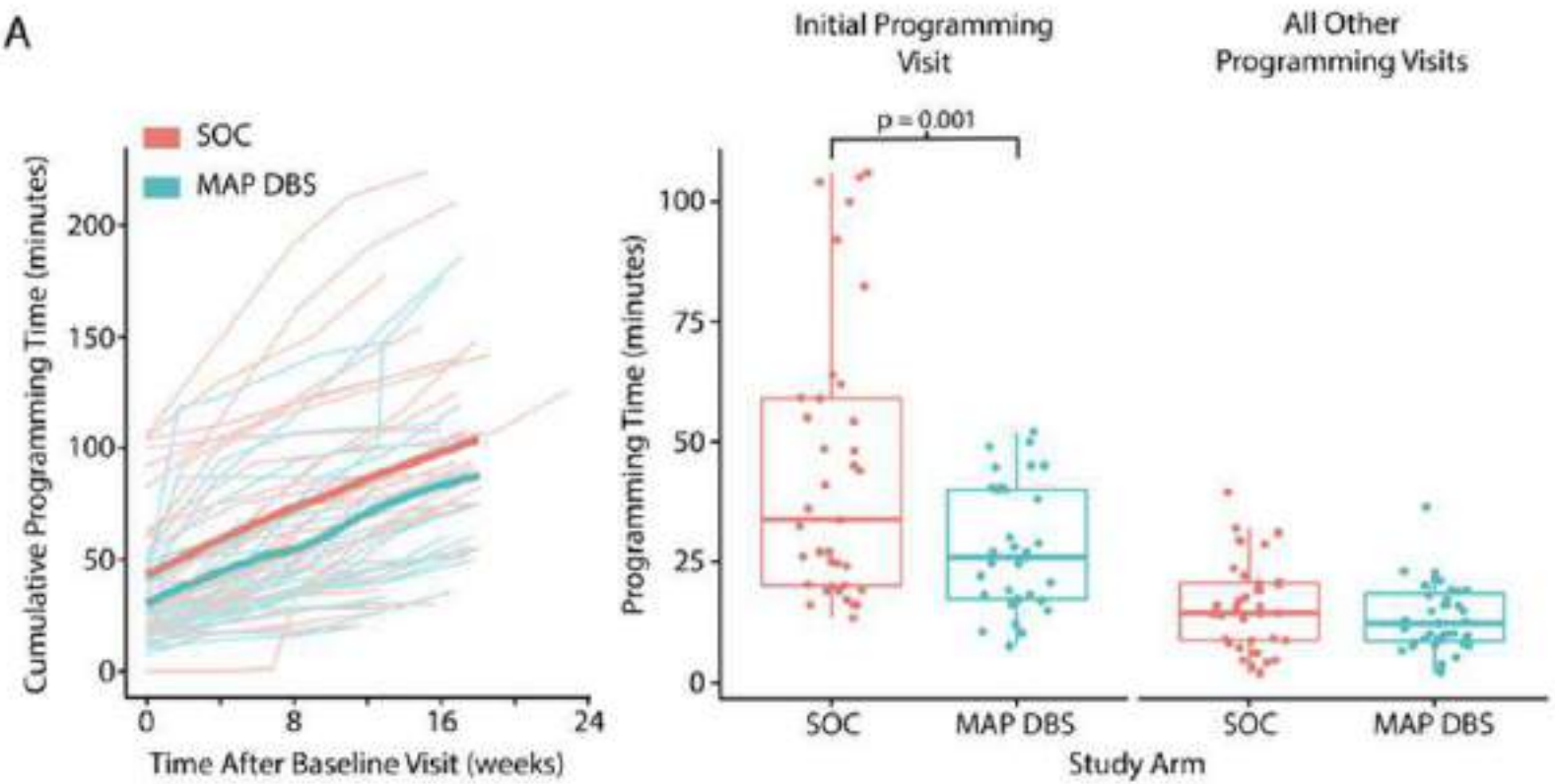
† The presence of dyskinesias or fluctuations for 3 years or less was an eligibility criterion.

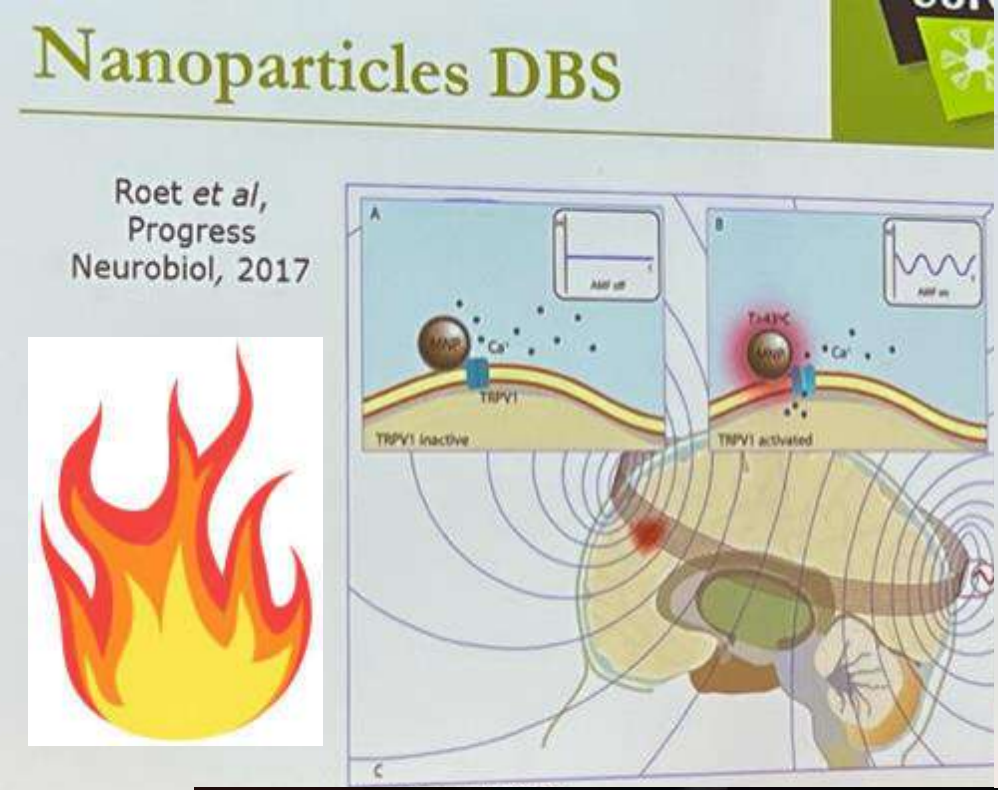
DBS Programming MAP-DBS vs. Standard Care

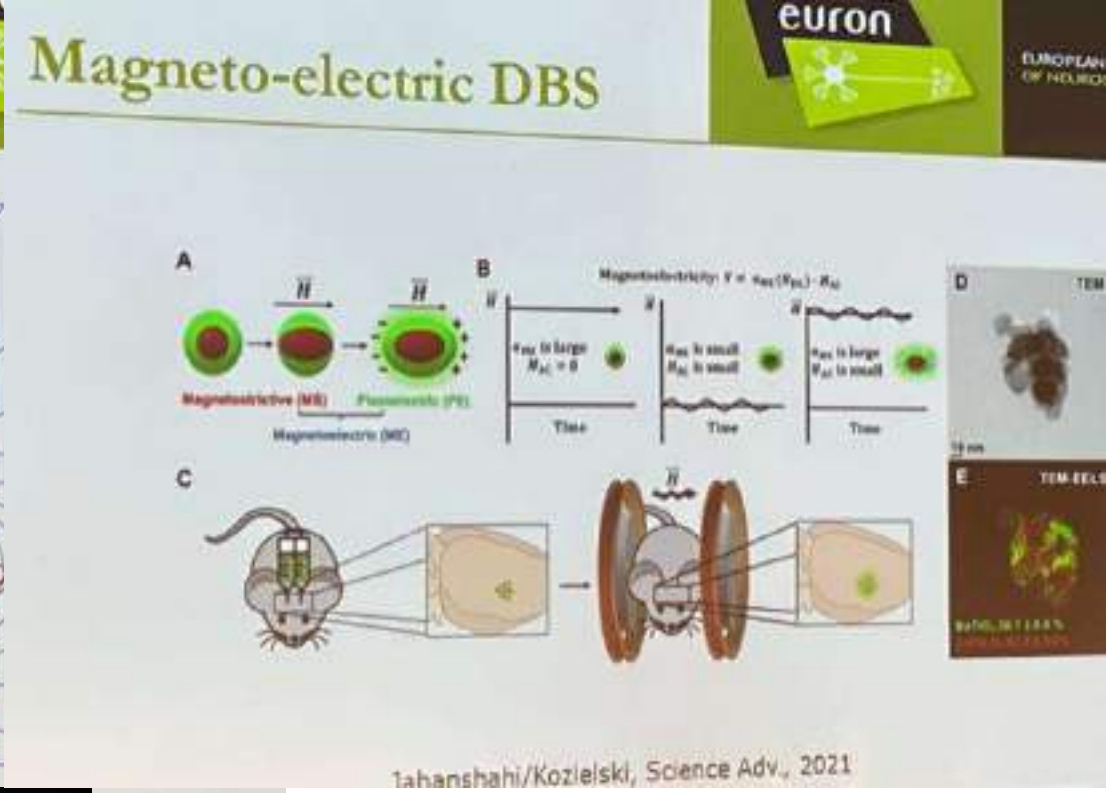


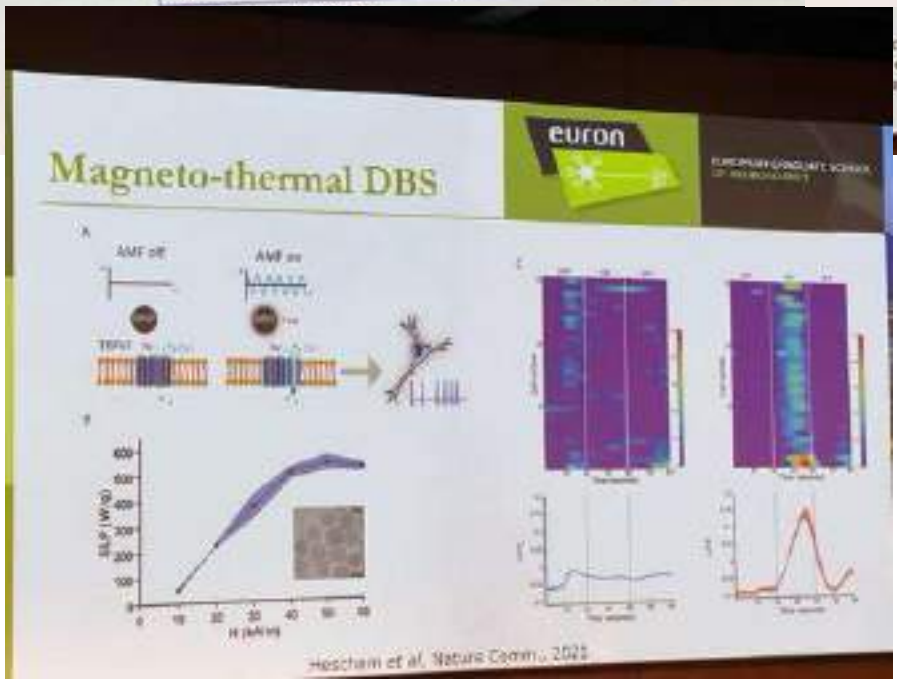
Parkinsonism and Related Disorders

Interactive mobile application for Parkinson's disease deep brain stimulation (MAP DBS): An open-label, multicenter, randomized, controlled clinical trial









Next Generation DBS

Nanoparticles

Magneto-electric

Magneto-thermal

DBS Society Meeting, Grenoble, 2023



nature biomedical engineering

Article | Published: 01 December 2022

Deep brain stimulation by blood–brain-barrier-crossing piezoelectric nanoparticles generating current and nitric oxide under focused ultrasound

Taejeong Kim, Hyun Jin Kim, Wonseok Choi, Yeong Mi Lee, Jung Hyun Pyo, Junseok Lee, Jeesu Kim, Jihoon Kim, Joung-Hun Kim, Chulhong Kim & Won Jong Kim ✉

Nature Biomedical Engineering **7**, 149–163 (2023) | Cite this article

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