

The background is a dark, abstract composition. A large, light-colored silhouette of a human head in profile, facing right, is the central element. Inside the head, there are intricate, wavy, and layered patterns in shades of grey and white, resembling a cross-section of a brain or a complex network of neural pathways. The overall color palette is dark, with deep purples, blues, and greys.

Updates in Deep Brain Stimulation (DBS)

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Outline

Brief intro to DBS (why, who, when)

Recent advances

- Improvements in devices and technology
- New directions of research

Why and
When to
consider
DBS



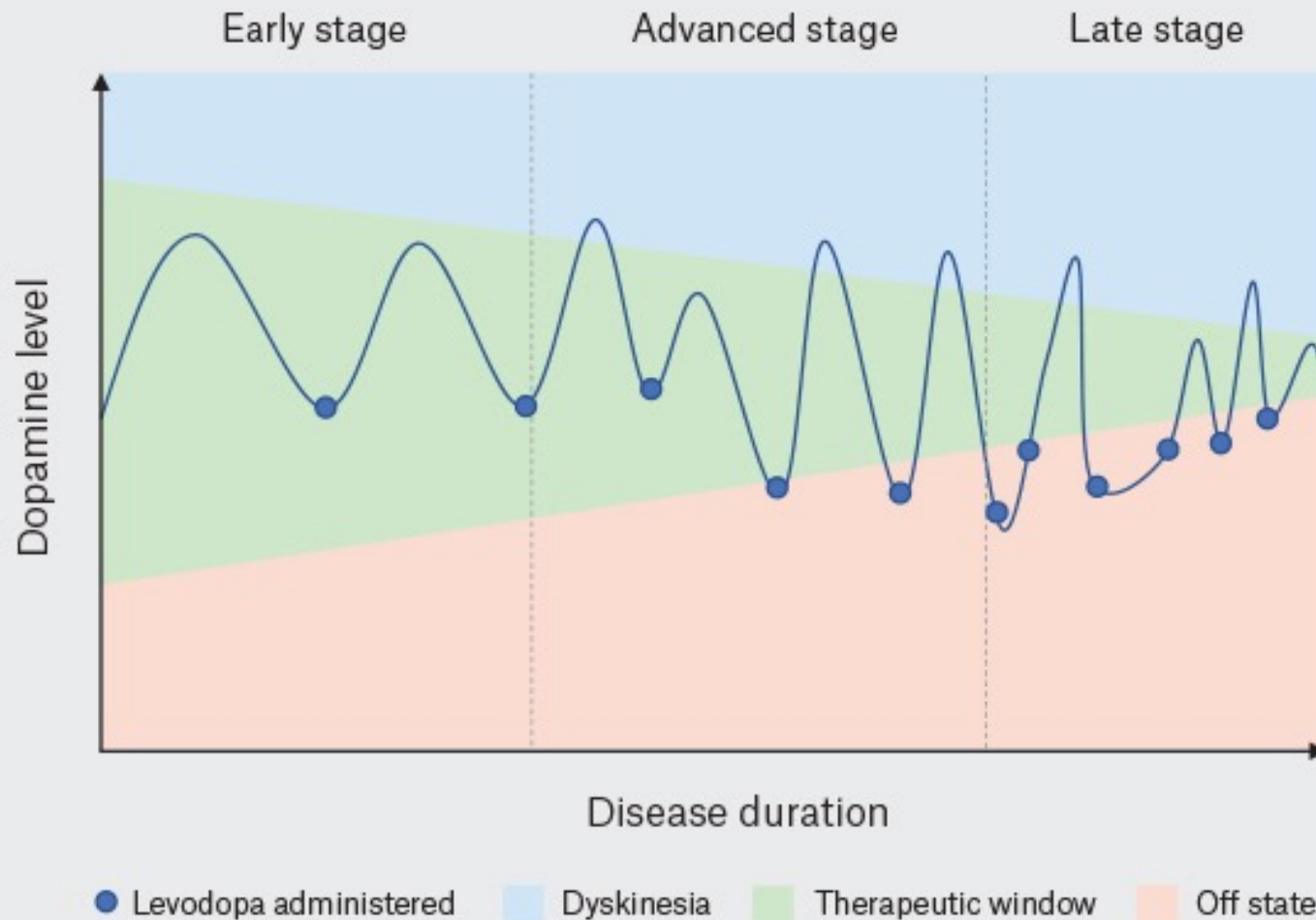
DBS is NOT ...

- A cure
- For everyone (due to certain risks)
- A treatment for all symptoms in PD

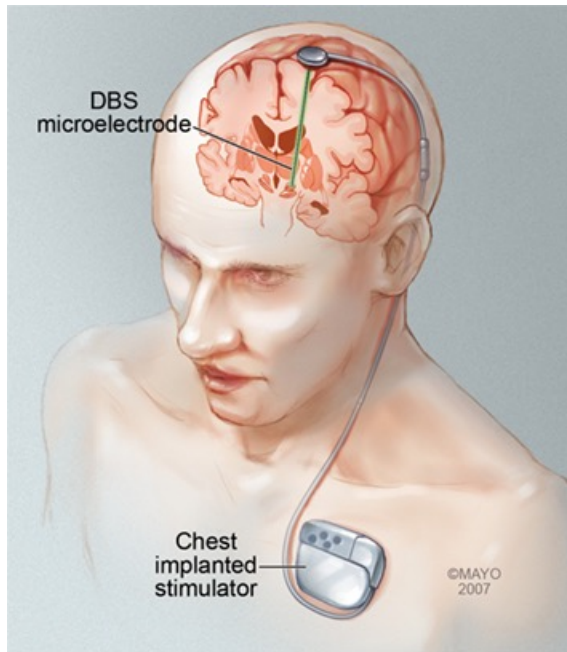
BUT, when properly selected it helps ...

- Reduce motor fluctuations
- Reduce medications
- Improve quality of life

When medications stop working well ...



Deep brain Stimulation (DBS) Therapy

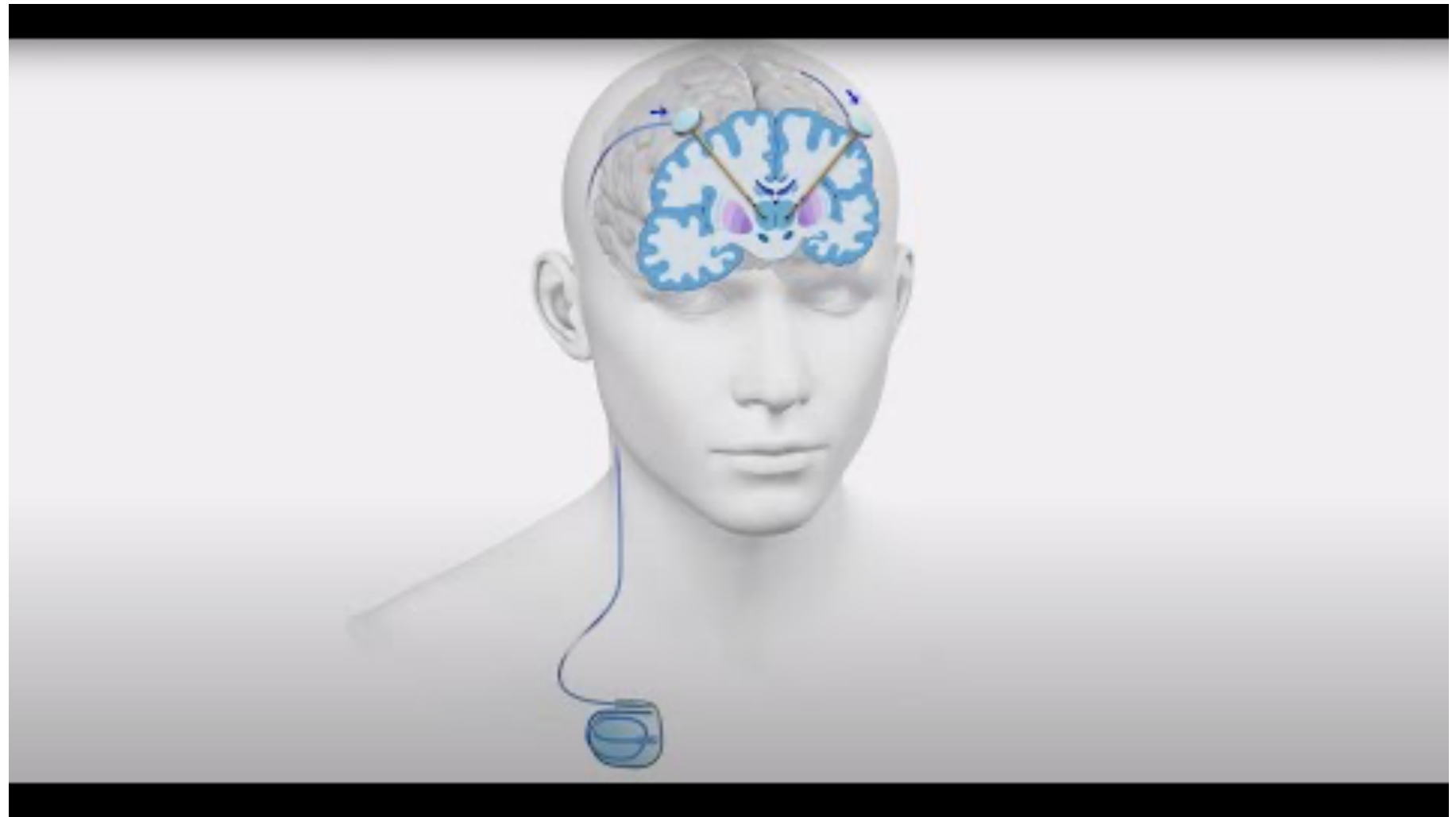


Components:

- Electrode lead
- Extension wire
- Implantable pulse generator (IPG)

http://www.frontiersin.org/files/Articles/14206/fnint-05-00069-r2/image_m/fnint-05-00069-g001.jpg

<http://www.reuters.com/article/2007/08/01/uk-brain-stimulation-idUKN0135742320070801>



DBS surgery

<https://youtu.be/xLgEcb447gA?feature=shared>



**Before
Deep Brain Stimulation**



**After
Deep Brain Stimulation**

DBS can be helpful for tremor, slowness,
stiffness, dyskinesia, dystonia



Recent Advances

Advances to improve programming (*already available in routine clinical practice*)

Directional DBS leads (all available systems)

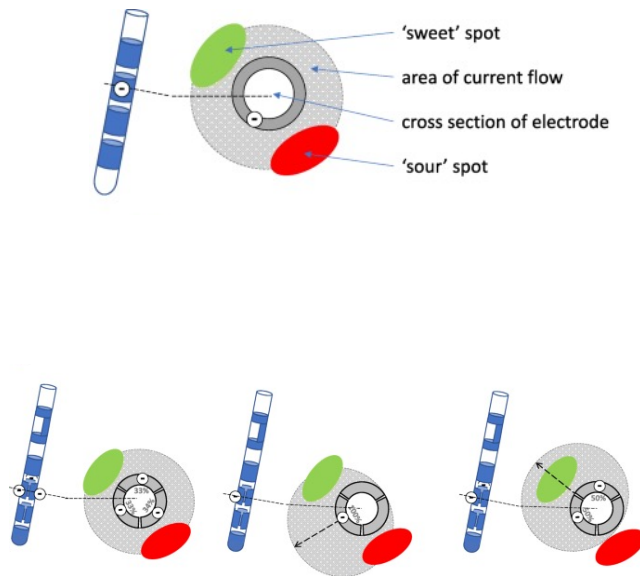
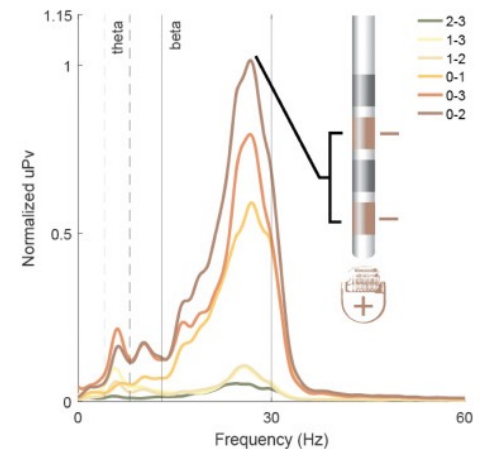


Image-guided programming (Boston Devices)

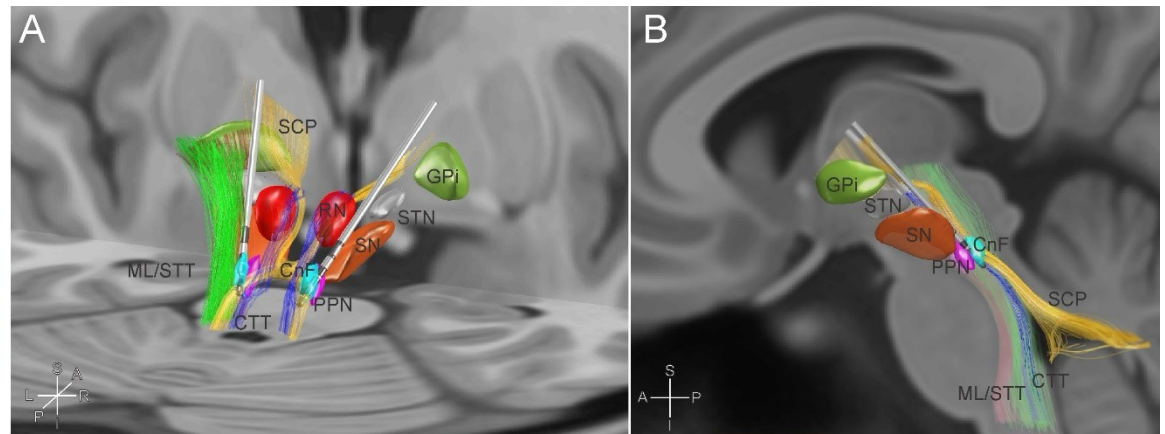
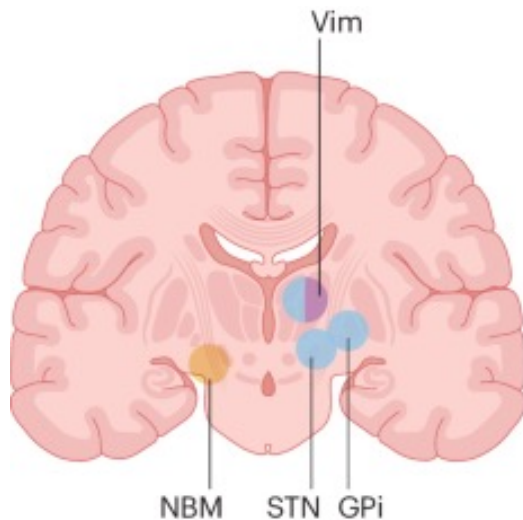


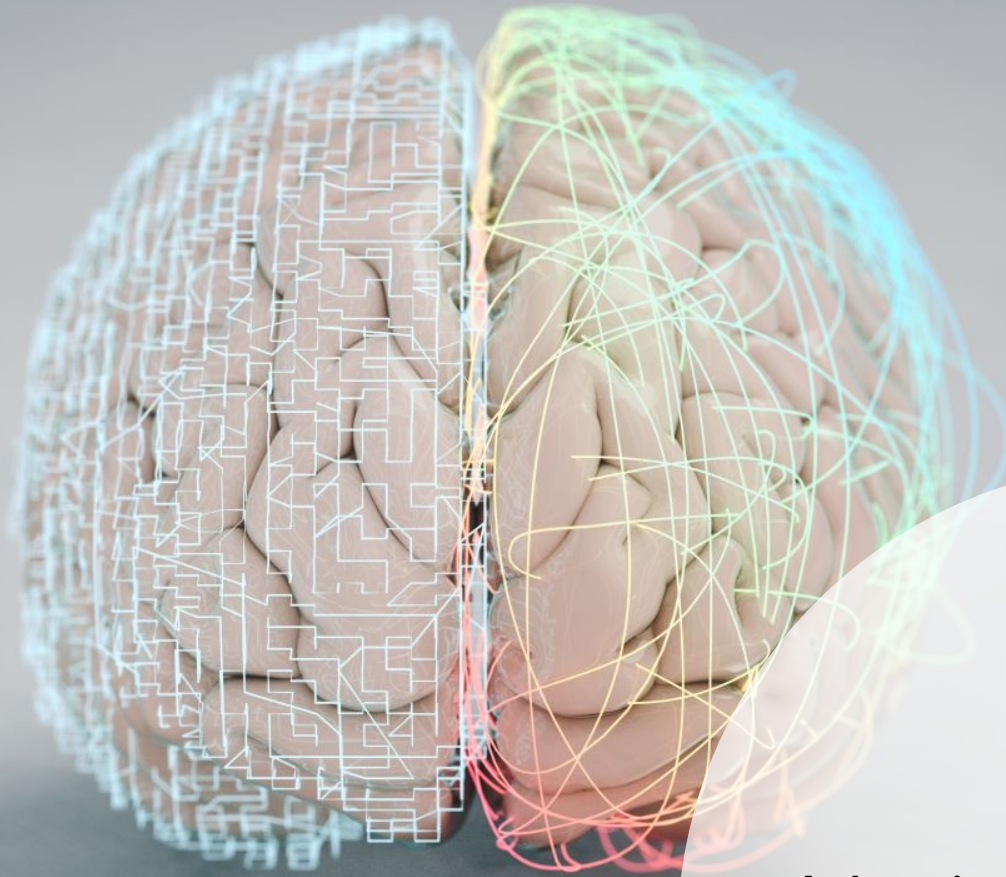
Sensing-guided Programming (Medtronic Devices)



Exploring New electrode locations (early in research)

- Cuneiform Nucleus (CnF) to treat walking problems
 - ClinicalTrials.gov ID NCT04218526 (U Miami)
- Nucleus basalis of Meynert (NMB) for cognition
 - ClinicalTrials.gov ID NCT05968703 (Stanford)



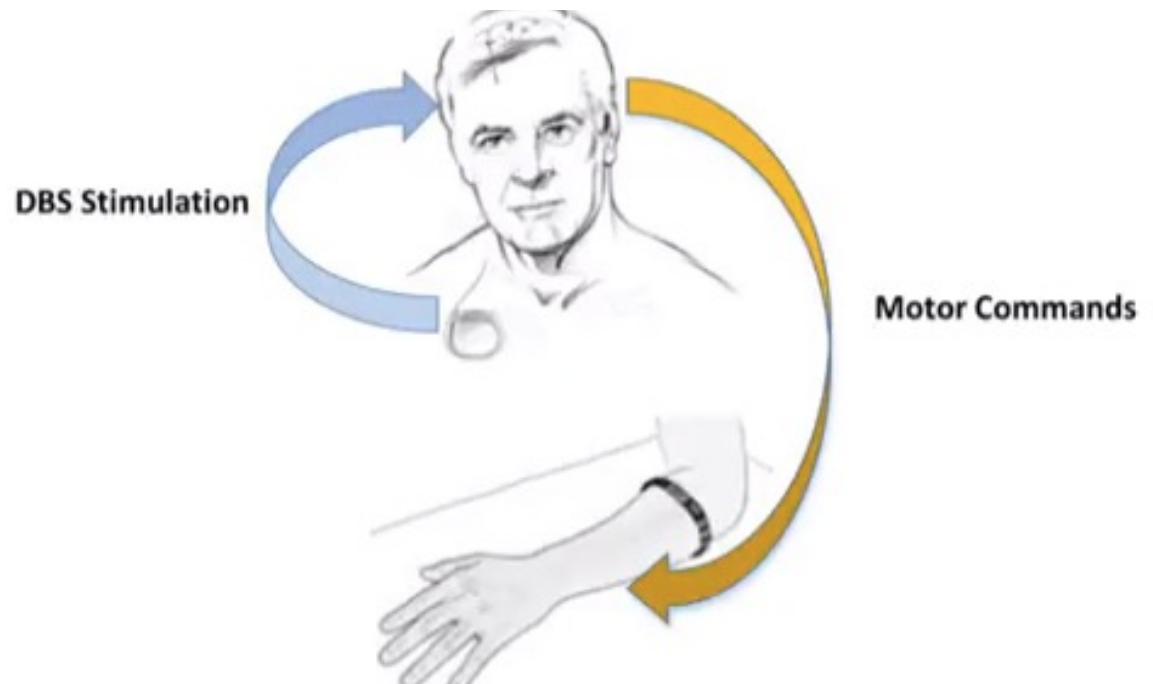


Adaptive Closed-Loop DBS

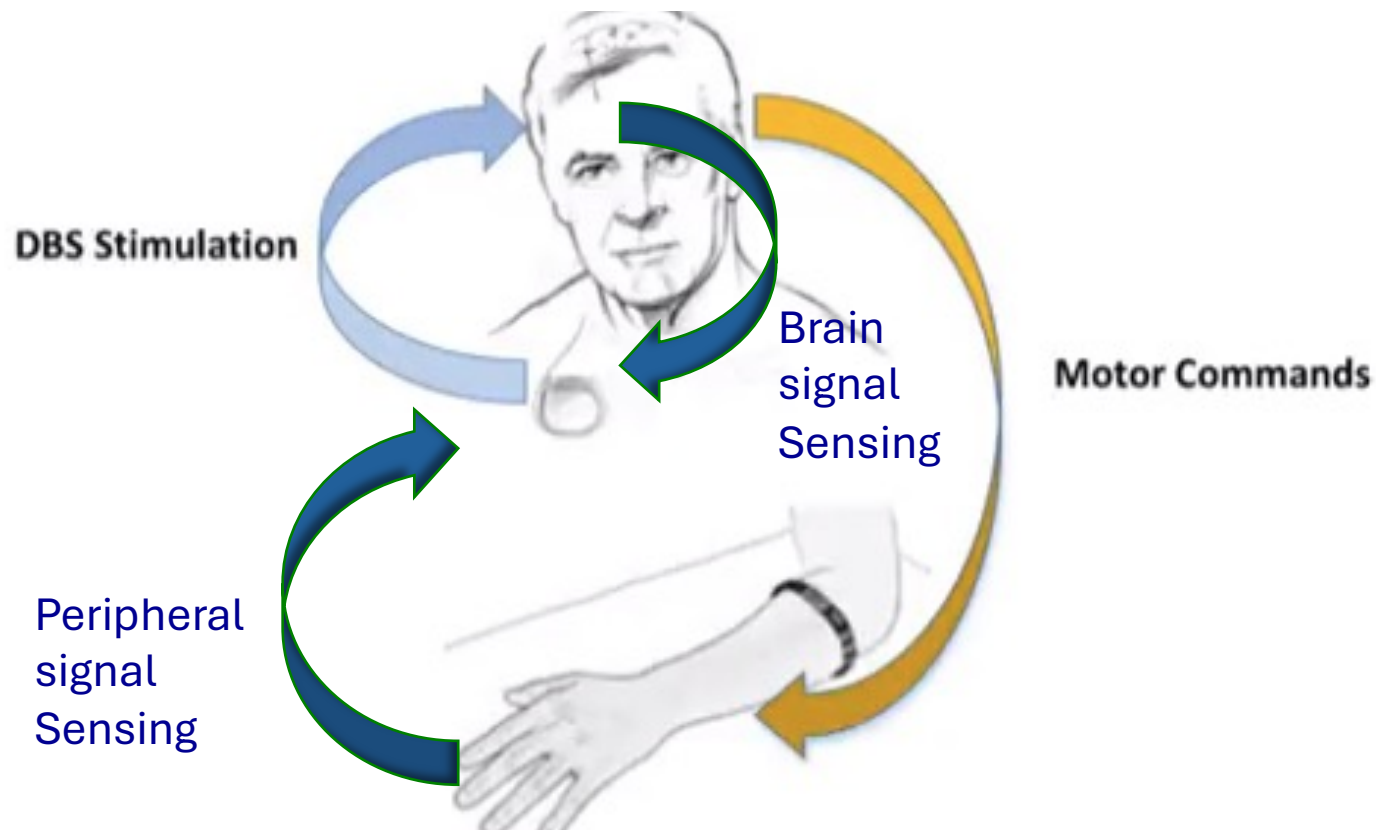
What's the hype?

DBS currently is an open-loop brain pacemaker

- Constant stimulation delivered, set by clinician in clinic
- lacks dynamic response to changing clinical states of the patient

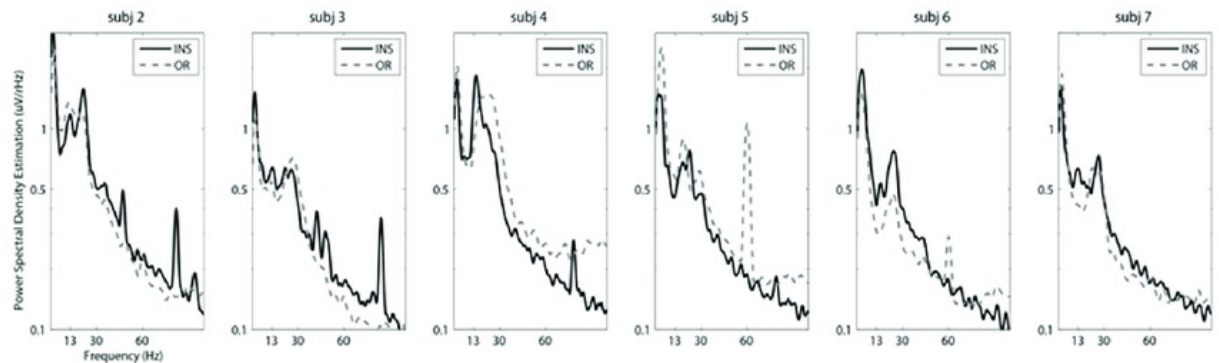
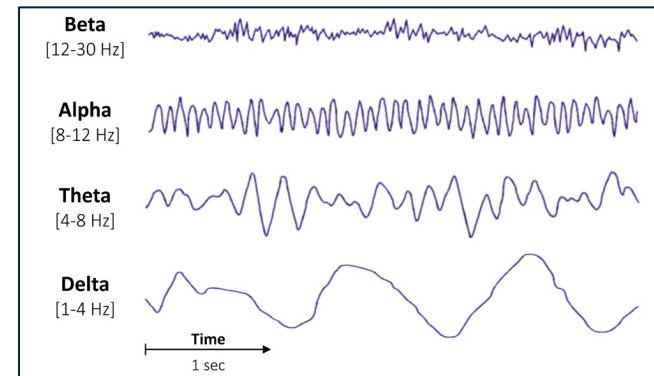
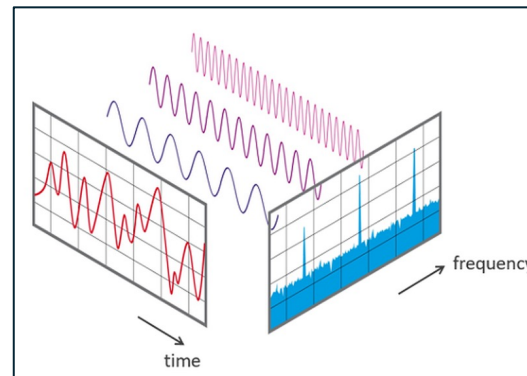
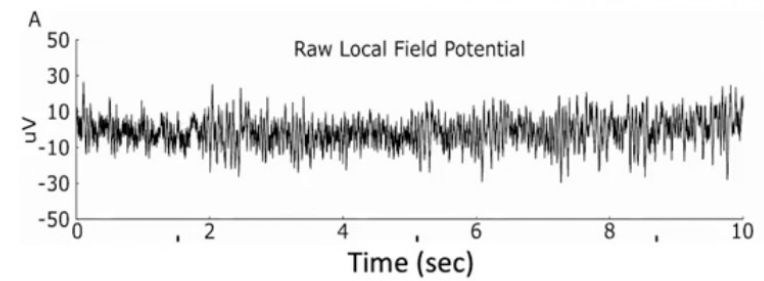
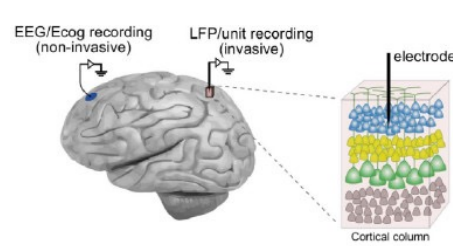


Working towards a closed-loop DBS system

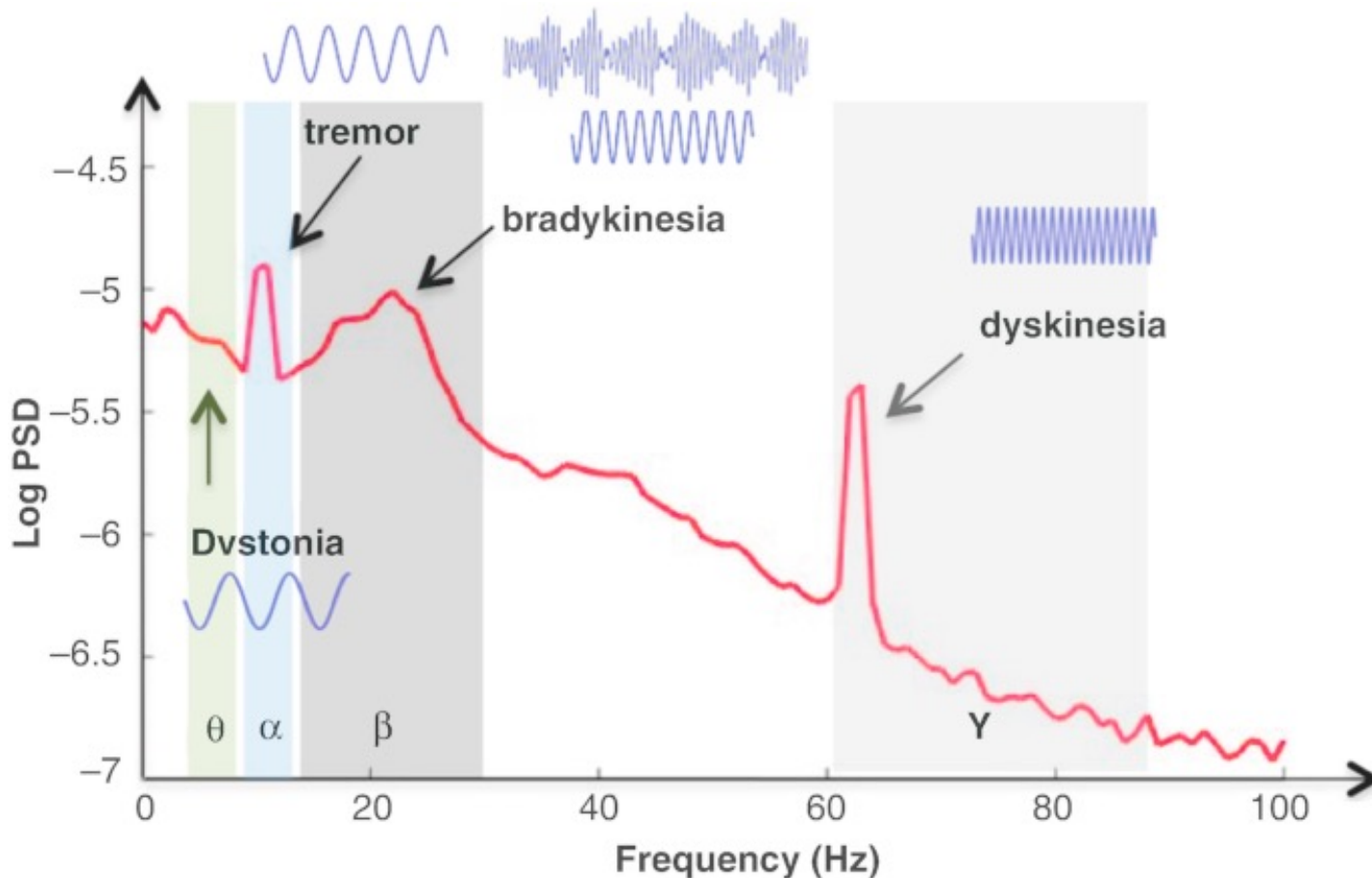


Sensing Brain Signals

Local Field Potentials (LFP)



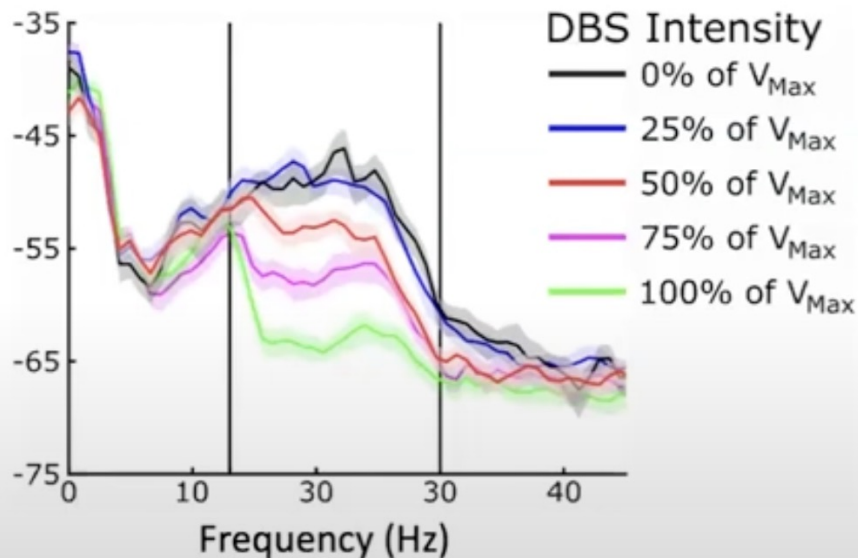
In PD, oscillations in different frequencies seem to correlate with different symptoms/states



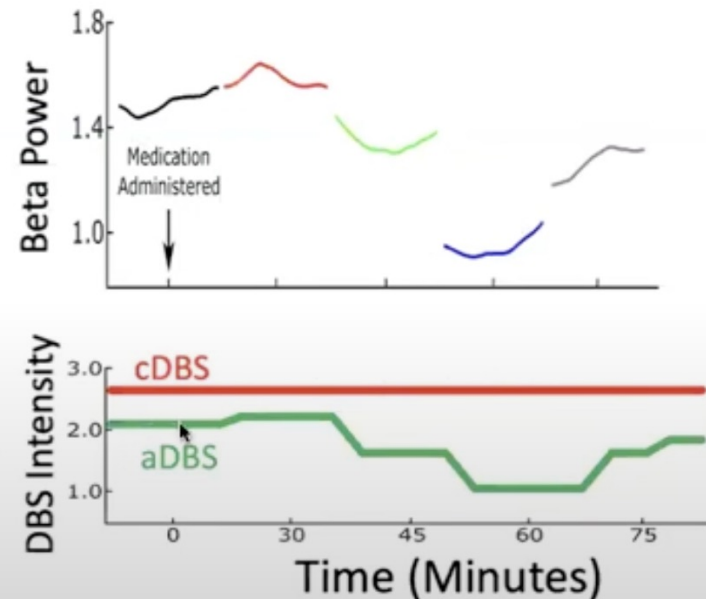
Wang et al. *Stereotactic and functional Neurosurgery*. 2020.

Beta band power as a relevant input signal for adaptive DBS

STN DBS attenuates beta power in a dose dependent manner

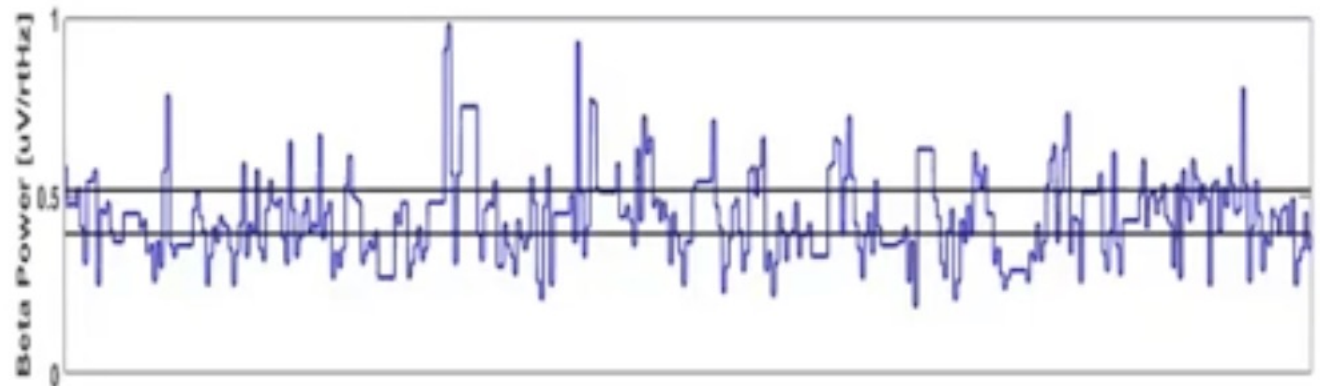


Beta power responds to onset and offset of levodopa dose

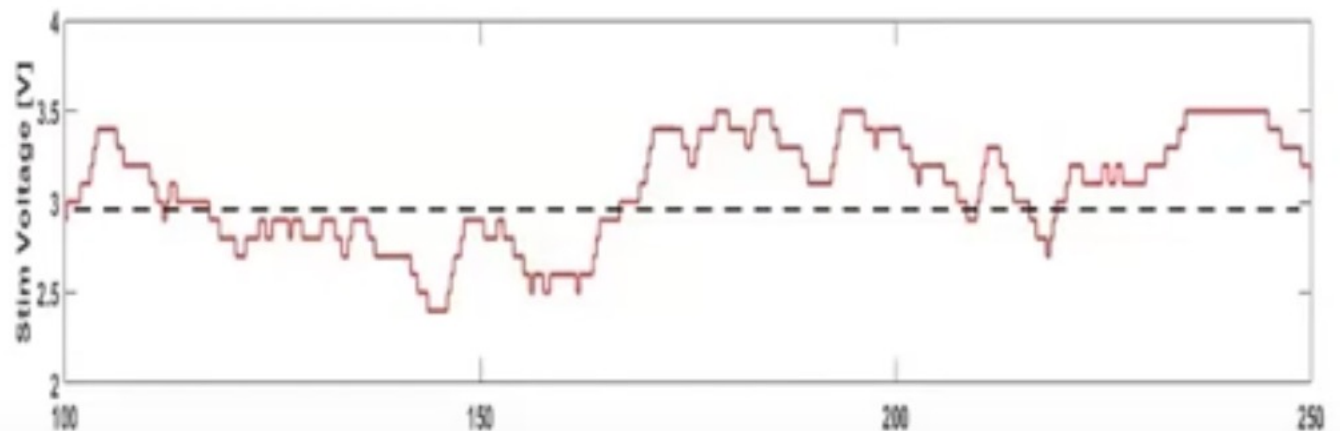


Two modes of adaptation

Dual threshold
(slower timescale)



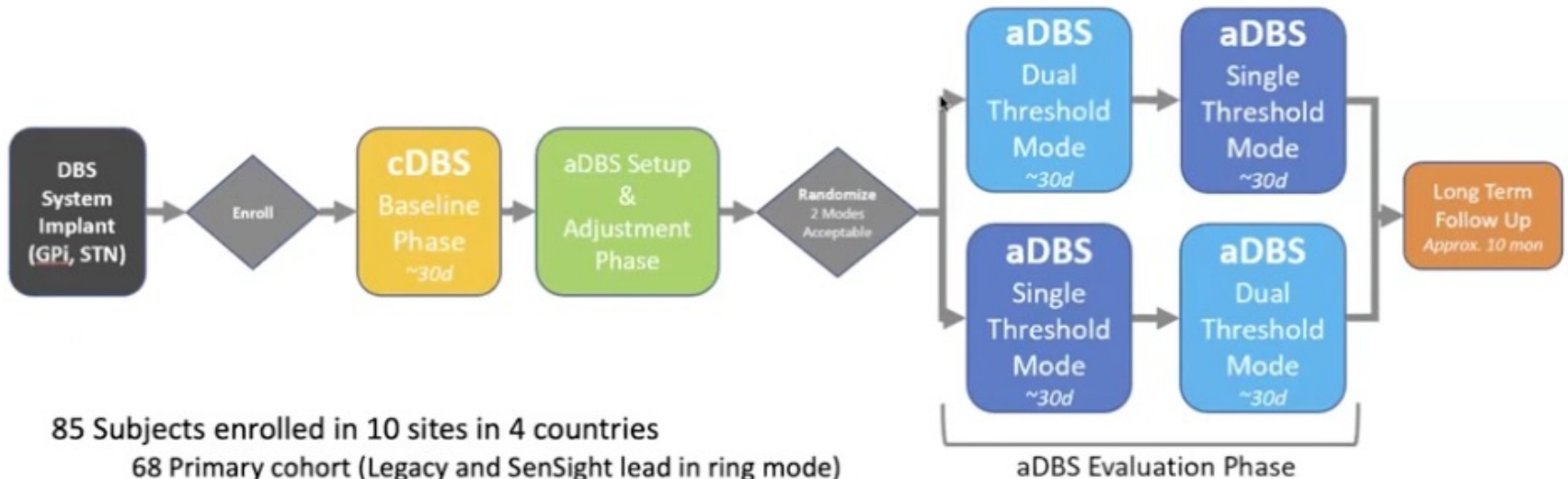
Single threshold
(faster timescale)



Adaptive DBS Algorithm for Personalized Therapy in Parkinson's Disease

International Multicenter Pivotal Trial – sponsor Medtronic PLC

Primary outcome: equivalence to open loop DBS in % time ON without dyskinesia



85 Subjects enrolled in 10 sites in 4 countries

68 Primary cohort (Legacy and SenSight lead in ring mode)

17 Directional cohort (SenSight lead directional stimulation)

Medtronic ADAPT-PD trial

Completed with
encouraging results

Under review by the FDA

The New York Times



A Personalized Brain Pacemaker for Parkinson's

In a new frontier for deep brain stimulation, researchers used A.I. to develop individualized algorithms, which helped a skateboarder and other patients with Parkinson's disease.

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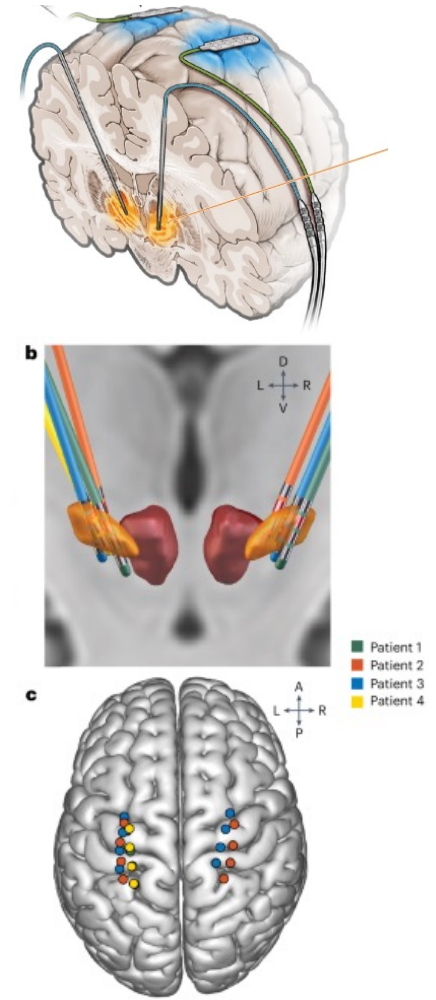


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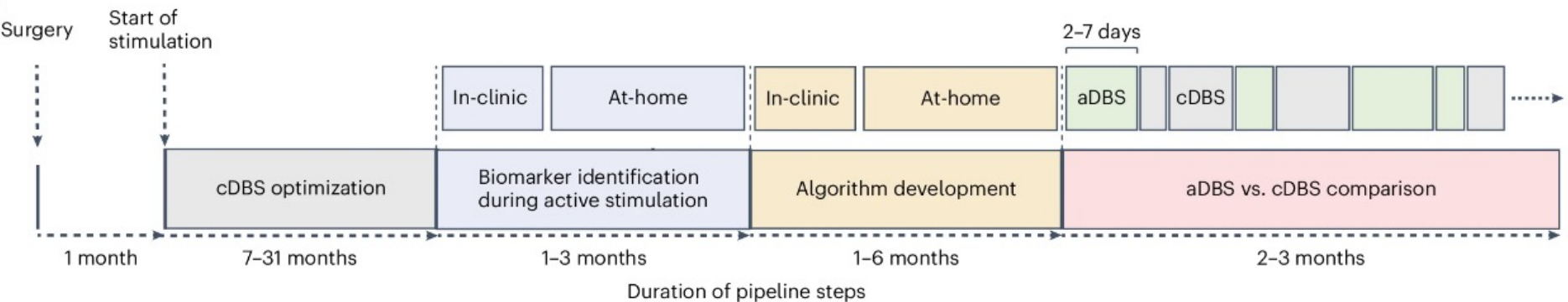
Study Design

- blinded randomized cross-over **pilot (feasibility) trial**
- **4 male patients** with DBS for motor fluctuations who had persistent fluctuations on optimized continuous DBS (cDBS)
- DBS leads into the **STN** + **paddles over the sensorimotor cortex**
- Did NOT preselect frequency bands for adaptation
- Compared 1mo in each condition (aDBS vs. cDBS)



Patient Selection and Study Flow

Patient demographics							Residual motor symptoms on cDBS		
Patient	Age	Sex	Disease duration (yrs)	MDS-UPDRS III off-medication	LEDD (mg) pre-surgery	LEDD (mg) post-surgery	Body side	Most bothersome	Opposite
Pat-1	61	M	15	44	2,100	1,050	Right	Bradykinesia	Dyskinesia
Pat-2	68	M	10	30	2,220	1,050	Bilateral	Off-medication dystonia	Dysarthria
Pat-3	58	M	11	49	1,425	800	Bilateral	Bradykinesia	Dyskinesia
Pat-4	47	M	13	32	1,091	884	Right	Bradykinesia	Dyskinesia



Identifying Neural Signals for Adaptation

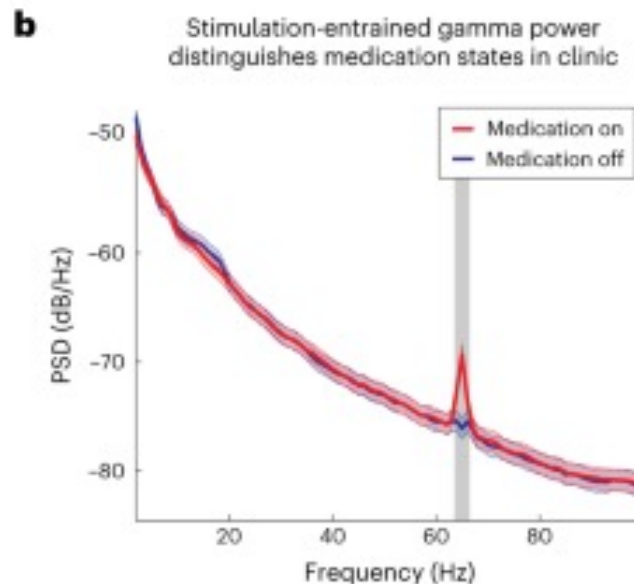
- Movement disorders neurologist set the acceptable upper and lower limits of stimulation
- In clinic monitoring – using standard clinical motor tests
- At home monitoring – using the PKG watch
- Integrated non-parametric statistics and machine learning to identify individualized neural biomarkers



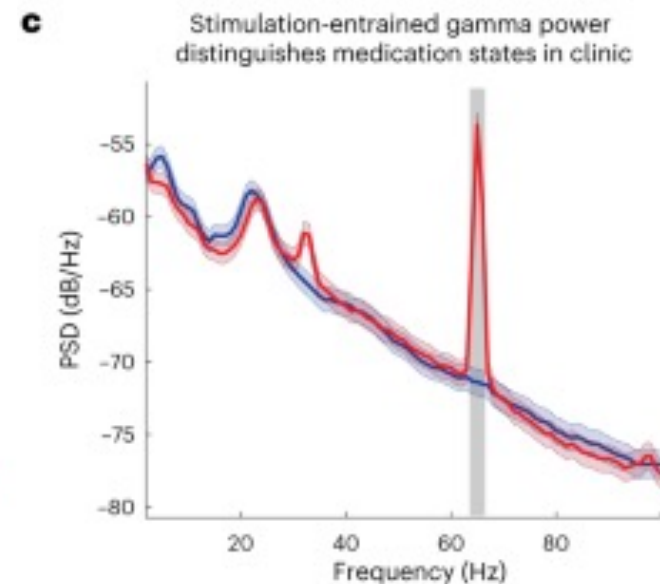
Stimulation-entrained gamma oscillations as optimal markers of medication-related symptom state

- centered at about half the stimulation rate (~65 Hz)
- in the STN or motor cortex
- Not just a marker of dyskinesia

Example neural recordings from the STN (pat-2L)

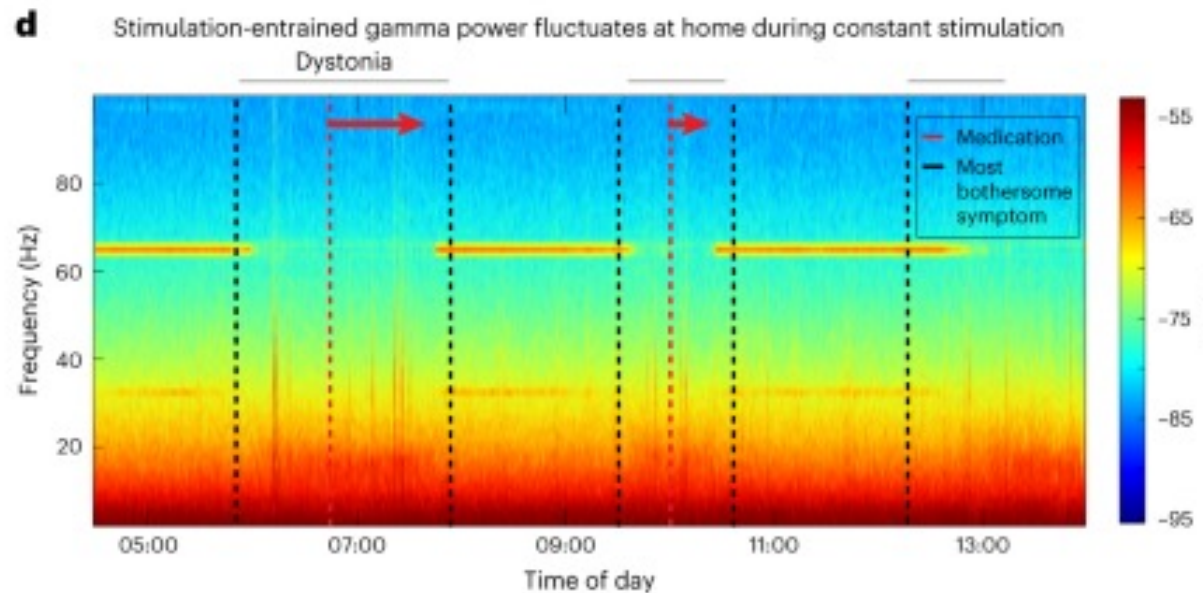
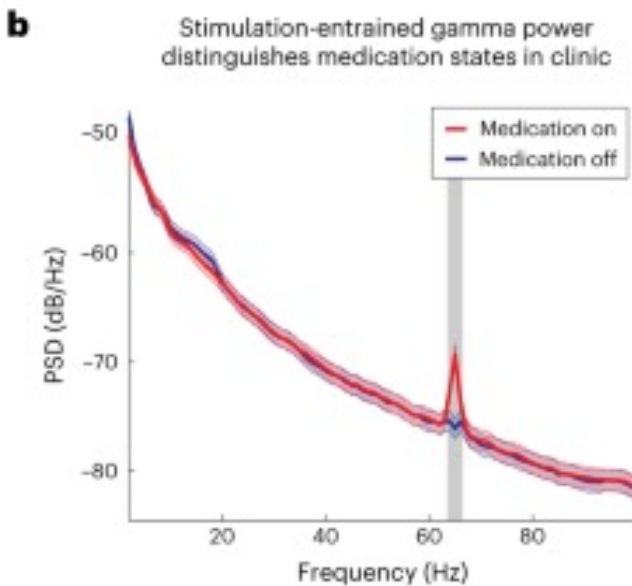


Example neural recordings from the motor cortex (pat-1)



Stimulation-entrained gamma oscillations fluctuate during constant stimulation and correlate with residual symptoms

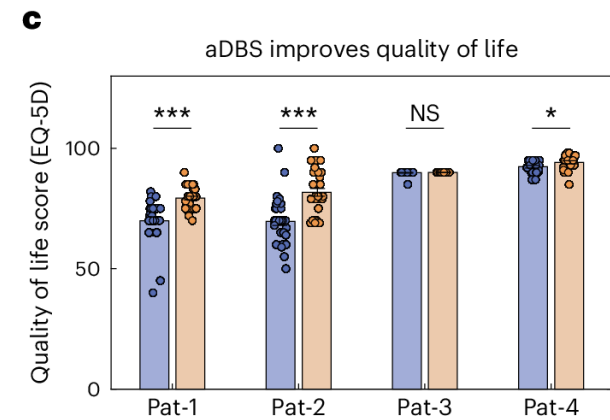
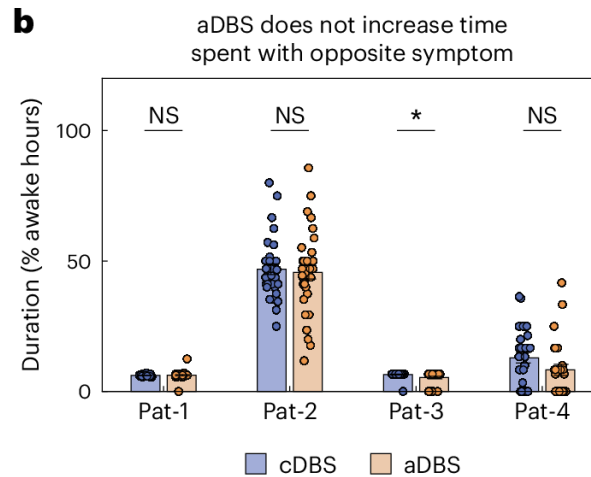
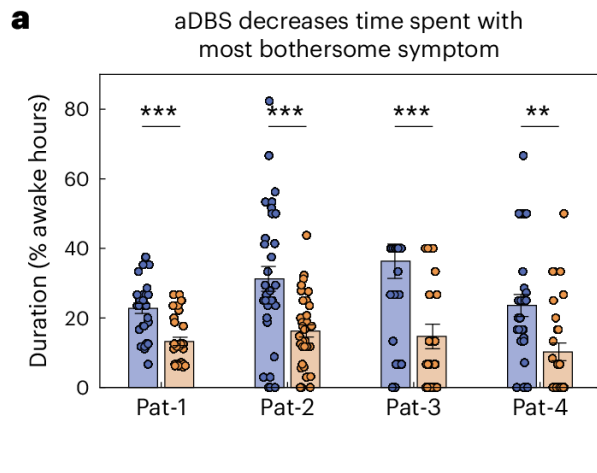
Example neural recordings from the STN (pat-2L)



Final control
signal for DBS
adaptation
differed in region
between the
patients

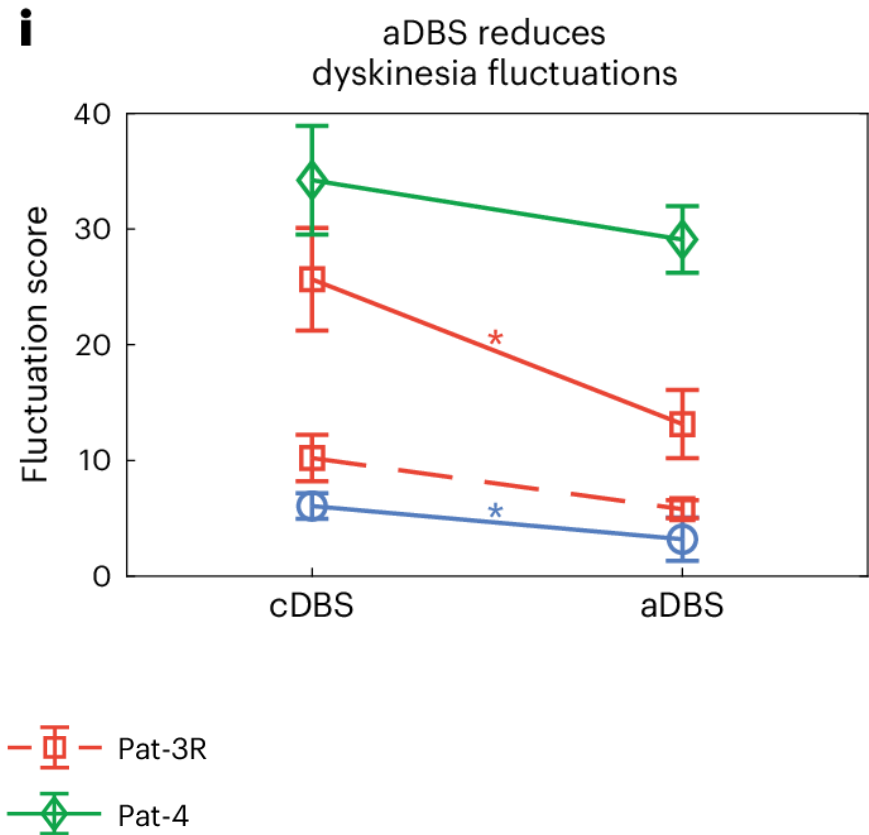
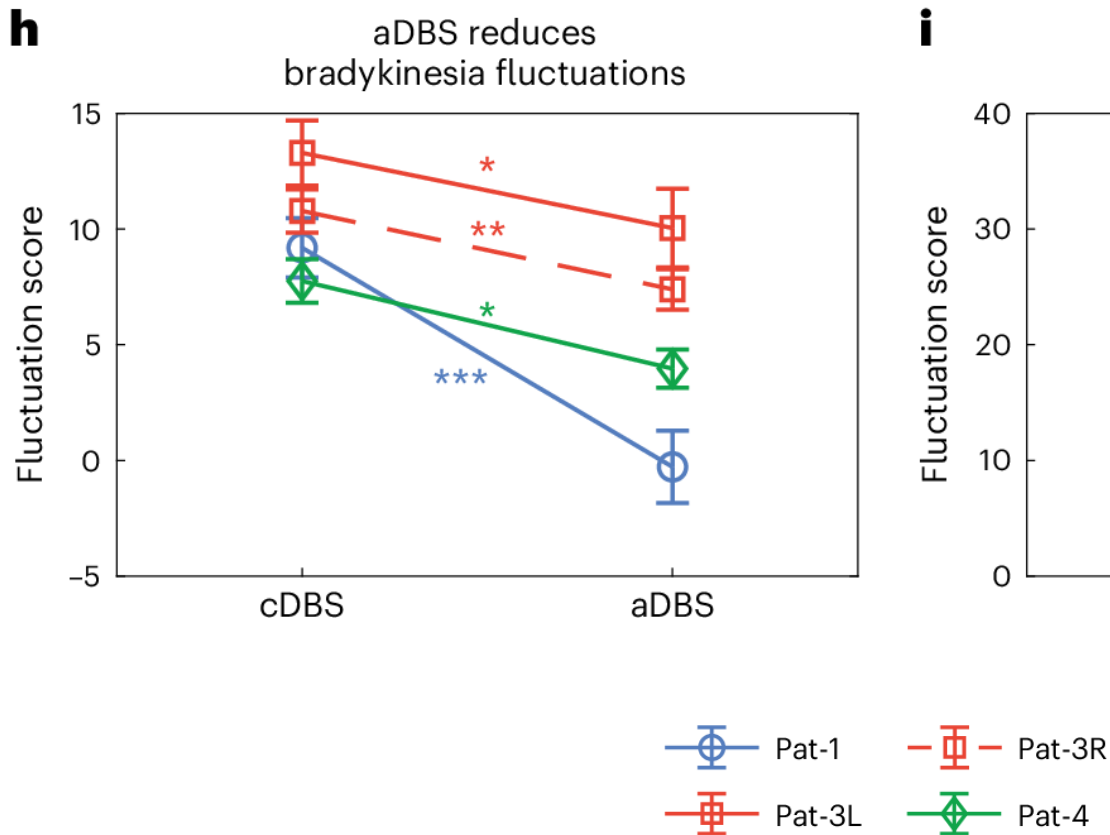
Parameters of individual adaptive DBS algorithms

Patient	Number of testing days (iterations)		Number of testing days with wearables		Control signal			Stimulation amplitudes (mA)			Other stimulation parameters		
	aDBS	cDBS	aDBS	cDBS	Hemi sphere	Brain region	Frequency (Hz)	cDBS	Low	High	Contact	Frequency (Hz)	Pulse width
Pat-1	37 (15)	32 (12)	14	13	L	Anterior cortical montage	64–66	3.2	2.0	4.5	2-C+	130	60
Pat-2	35 (10)	32 (9)	NA	NA	R	STN	64–66	3.1	1.8	3.7	2-C+	130	60
Pat-2	35 (10)	32 (9)	NA	NA	L	STN	64–66	2.5	1.8	2.8	2-C+	130	60
Pat-3	35 (12)	36 (14)	17	18	R	Posterior cortical montage	64–69	3.1	2.8	3.4	1-C+	130	60
Pat-3	35 (12)	36 (14)	17	19	L	Posterior cortical montage	64–69	2.4	1.7	2.5	2-C+	130	60
Pat-4	30 (9)	30 (9)	20	18	L	Anterior cortical montage	64–66	2.6	2.4	3.3	2-C+	130	60

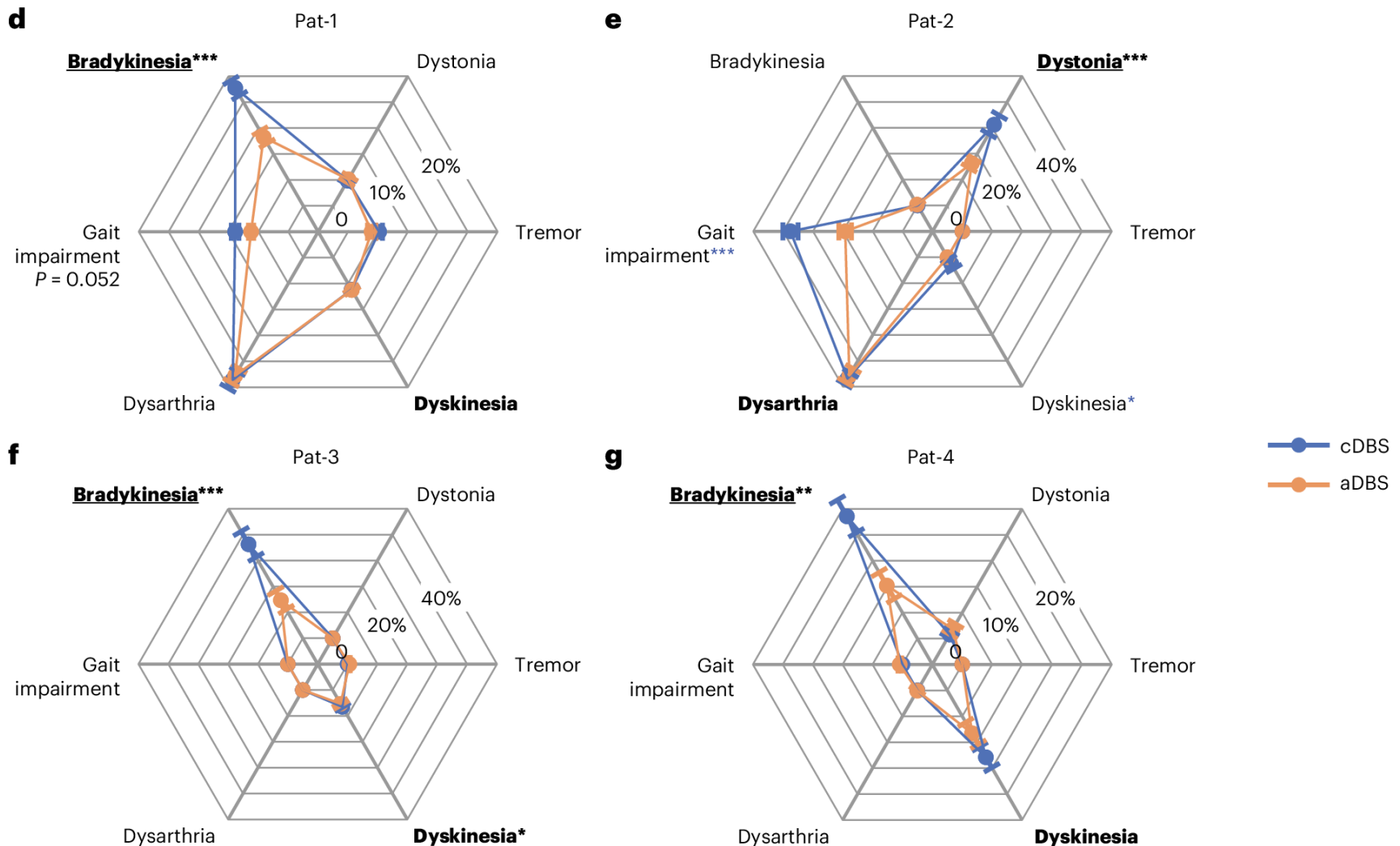


aDBS compared to cDBS reduced time with bothersome symptoms and improved quality of life (based on patient questionnaire)

aDBS also reduced motor fluctuations measured by wearable monitors



aDBS provided improvement in tracked symptom, without worsening other symptoms



Symmary



In select patients DBS can be an important part of their overall PD management



Advances in technology have led to improved programming of DBS devices



New targets for DBS lead implantation are being looked at to target some challenging symptoms in PD (cognition and gait)



Adaptive DBS is an exciting emerging area of research, but remains complex and will undoubtedly evolve in the coming years



Questions?