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DBS in Dystonia
Targets, programming and therapeutic challenges

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Neurologische Klinik und Poliklinik
Direktor: Prof. Dr. J. Volkmann

Neurologie
Klinische Neurobiologie

Conflicts of interest

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- Consulting fees and speaker honoraria:
  - Boston Scientific
  - Medtronic
  - Brainlab
  - Head Instruments

Learning objectives

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Participants should know…

…the basic components and functions of a DBS system.

…the most common targets and the targeting of the Gpi.

…typical indications and subgroups of dystonias with typical outcomes.

…the initial clinical testing procedure.

…typical problems and side effects during follow-up and their management.

Question 1

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- What is your profession?

a. Neurologist
b. Neuropediatrician
c. Neurology resident
d. Psychiatrist
e. Nurse
f. Physiotherapist
g. Geneticist
h. Psychologist
i. Patient or patient representative
j. Other

Question 2

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- What is your connection to DBS in dystonia?

a. I never see patients with DBS.
b. I have some patients with DBS.
c. I have many patients with DBS but don’t program DBS.
d. I routinely program DBS patients.
e. I have a strong clinical and/or scientific focus ôn DBS for dystonia.

Lesioning procedures in Movement Disorders

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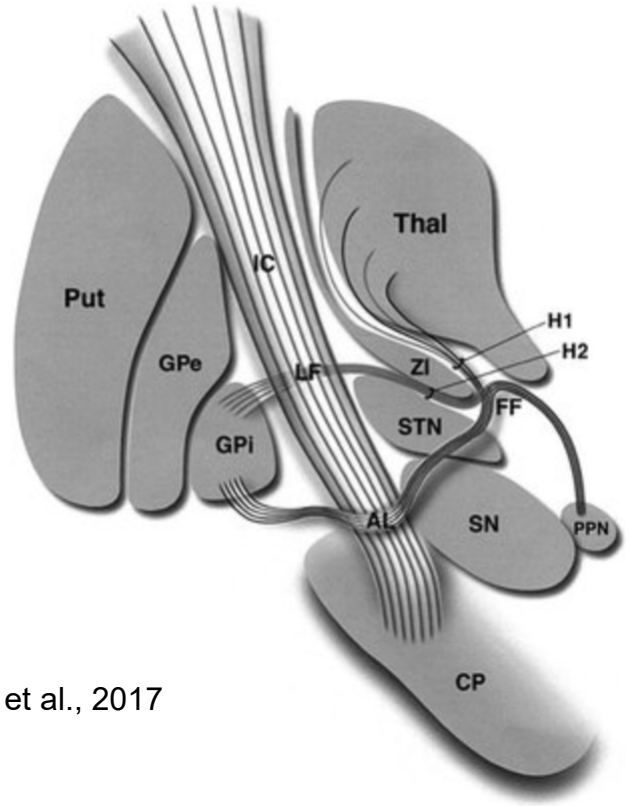
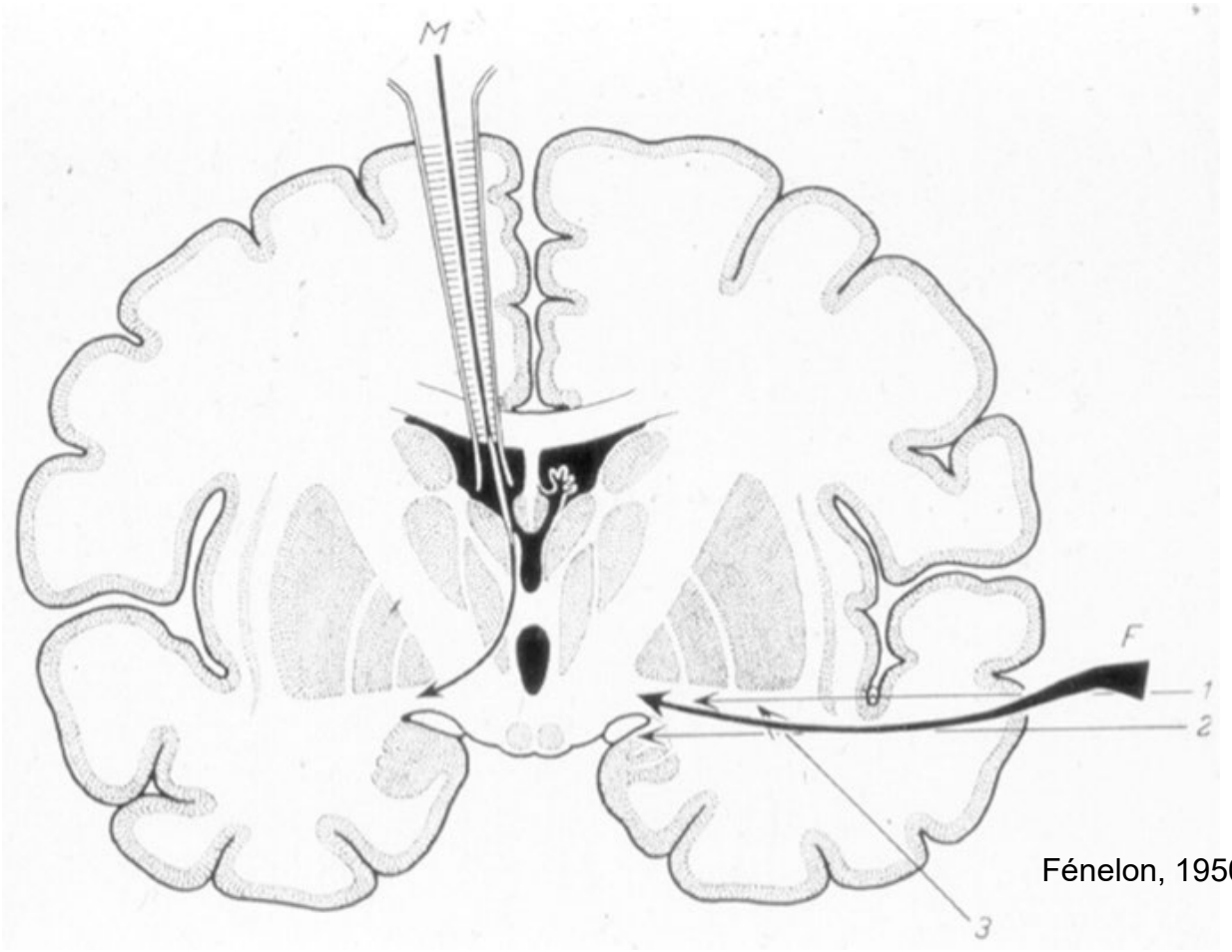
- The beginnings:
  - Open surgical techniques for relief in movement disorders
  - Dissection of pallido-fugal fibers
  - High morbidity and mortality



Park et al., 2017



Fénelon, 1950

The road to stereotaxy

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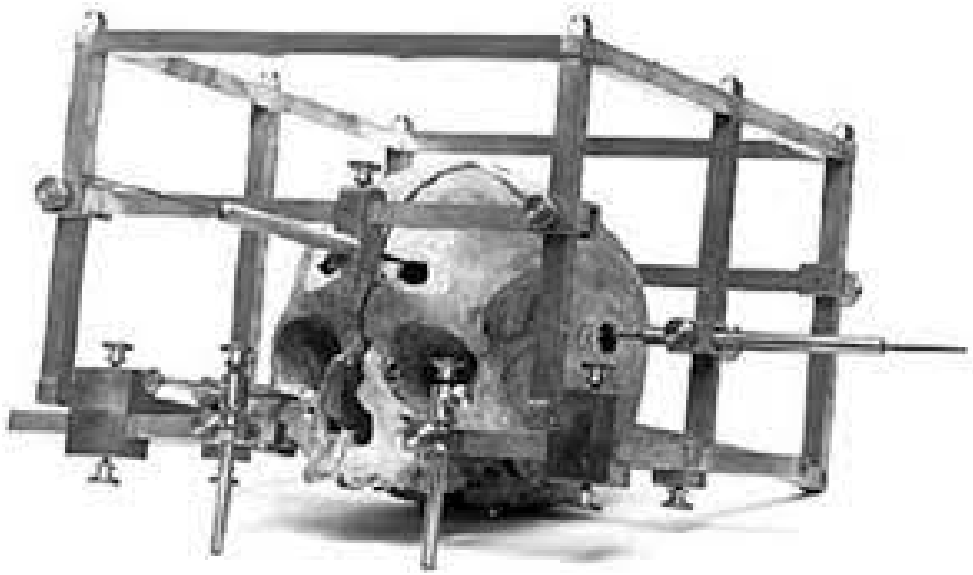
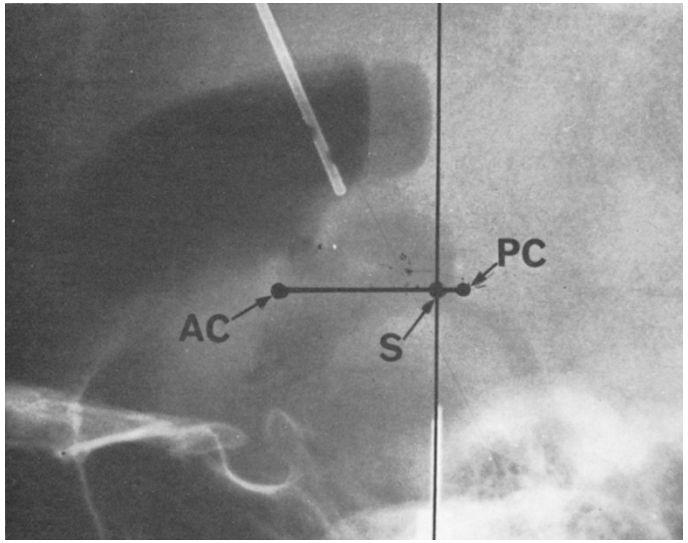
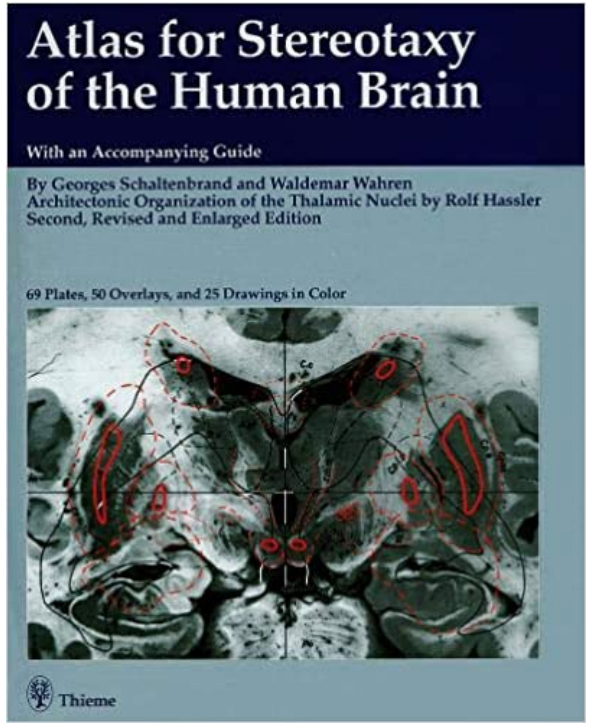
- The three requirements of steoreotactic procedures in the pre-CCT/MRI era:
  - Stereotactic apparatus
  - Intracranial imaging procedures for planning
  - Stereotactic atlas

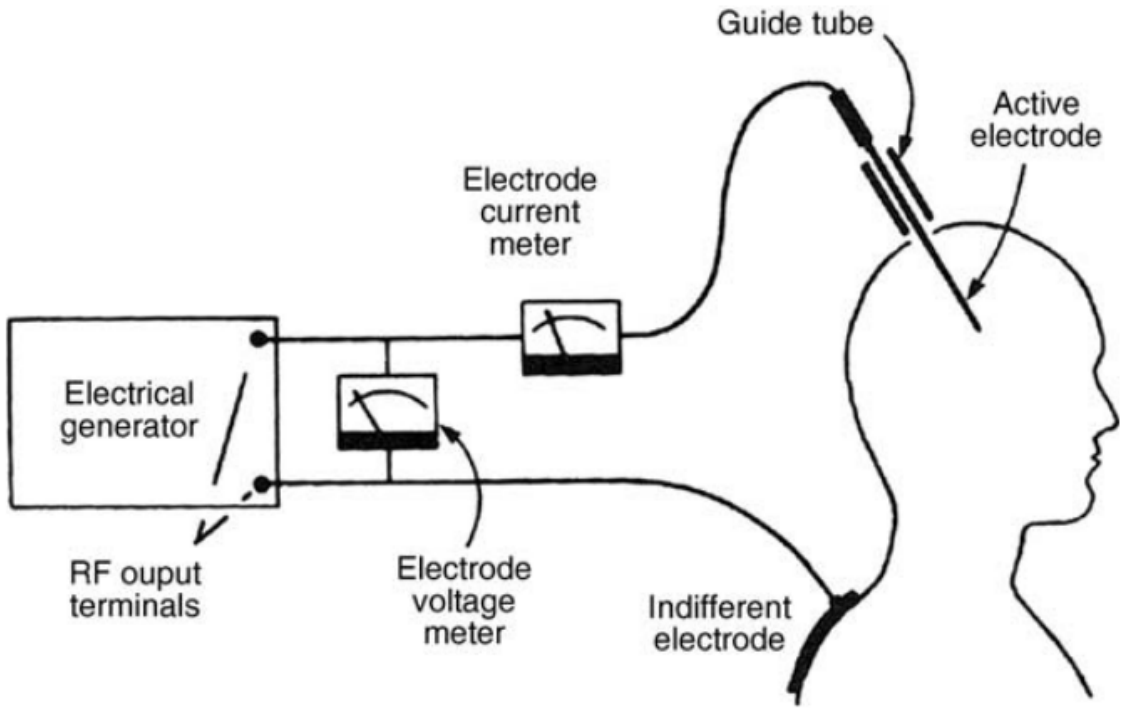






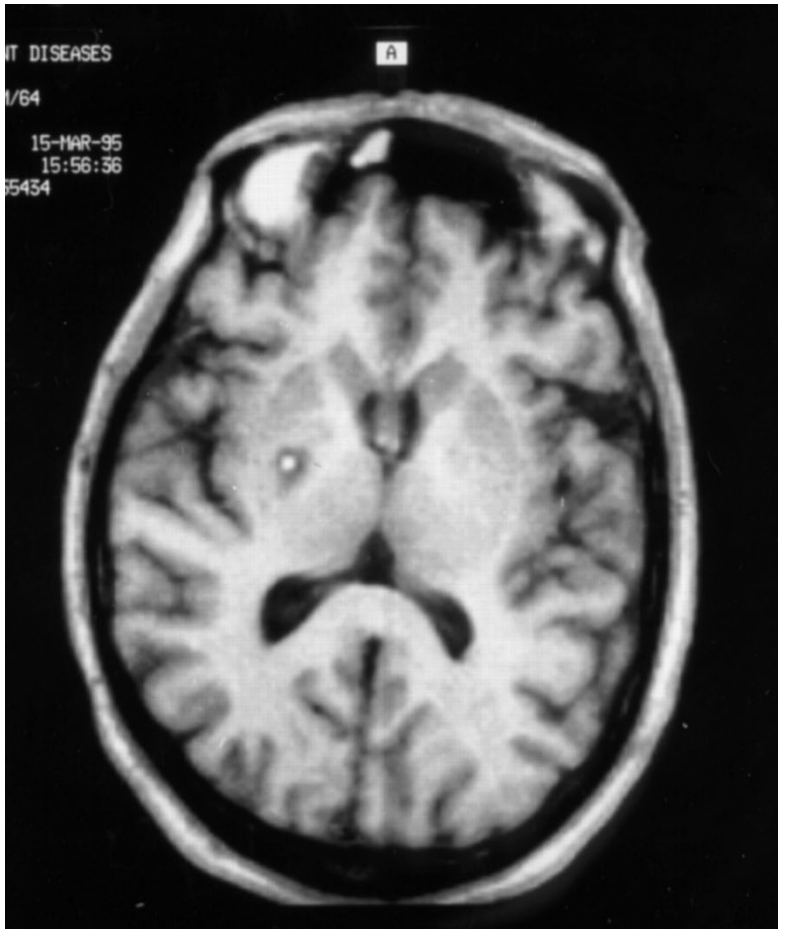
High frequency lesions

- Lesioning procedures by high frequency current



Textbook of Stereotactic Neurosuregery, 2009

Perrine, et al.



The posteroventral Pallidotomy

Deep brain stimulation – the „hardware“

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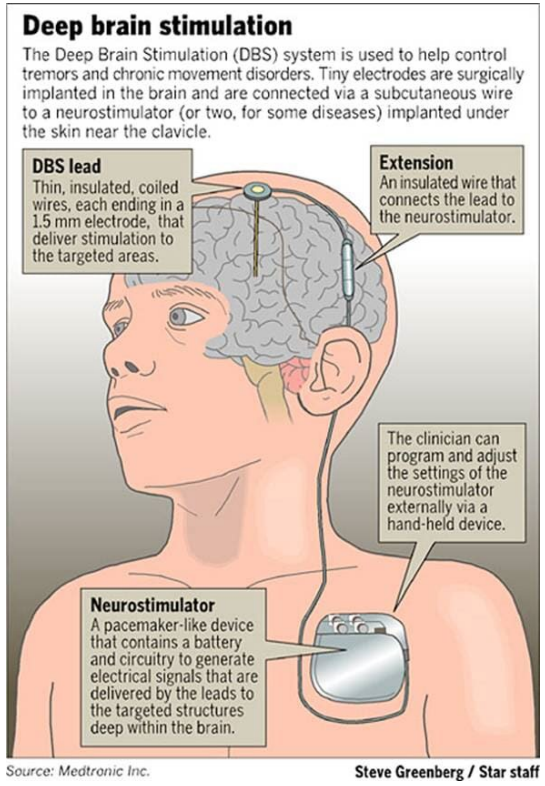
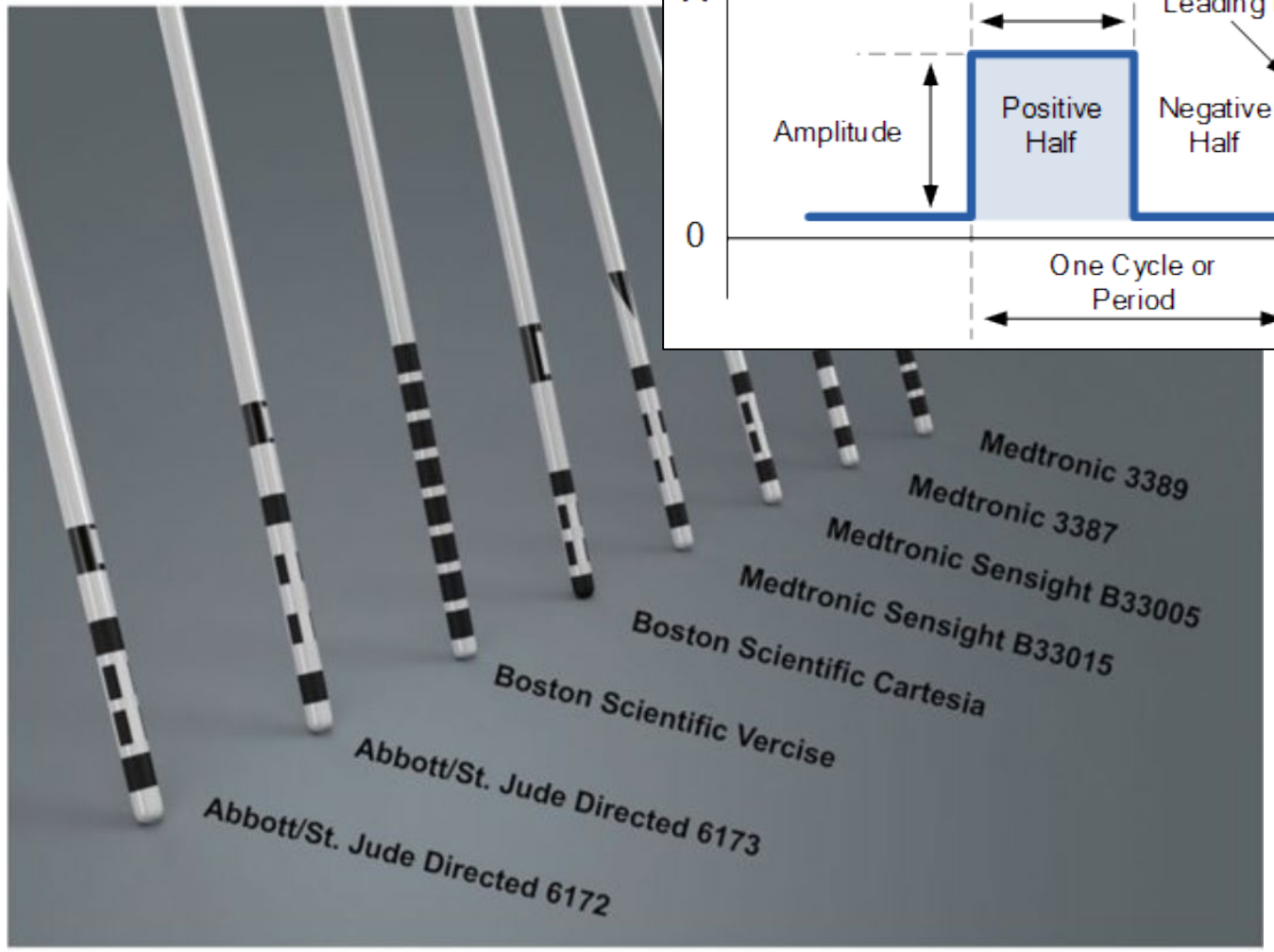
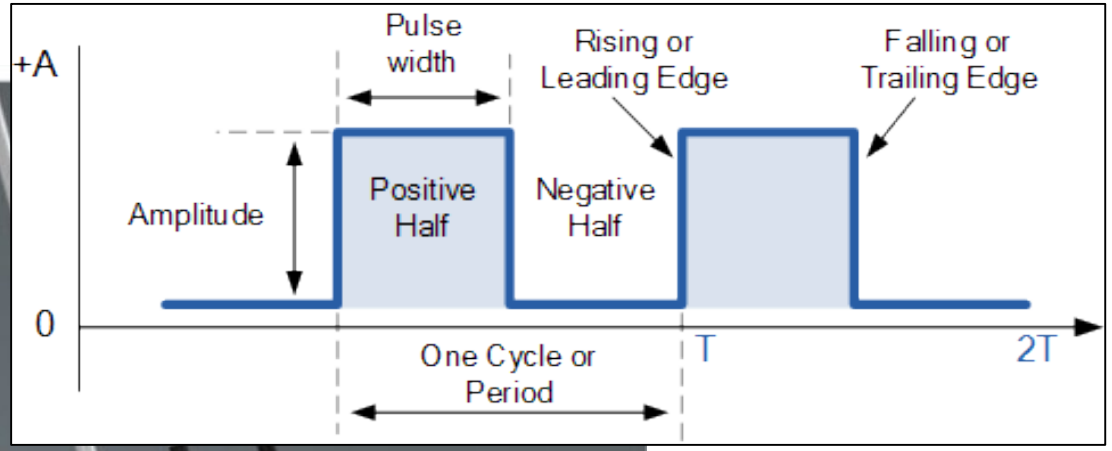
- Lead(s)
- Extensions
- Stimulator



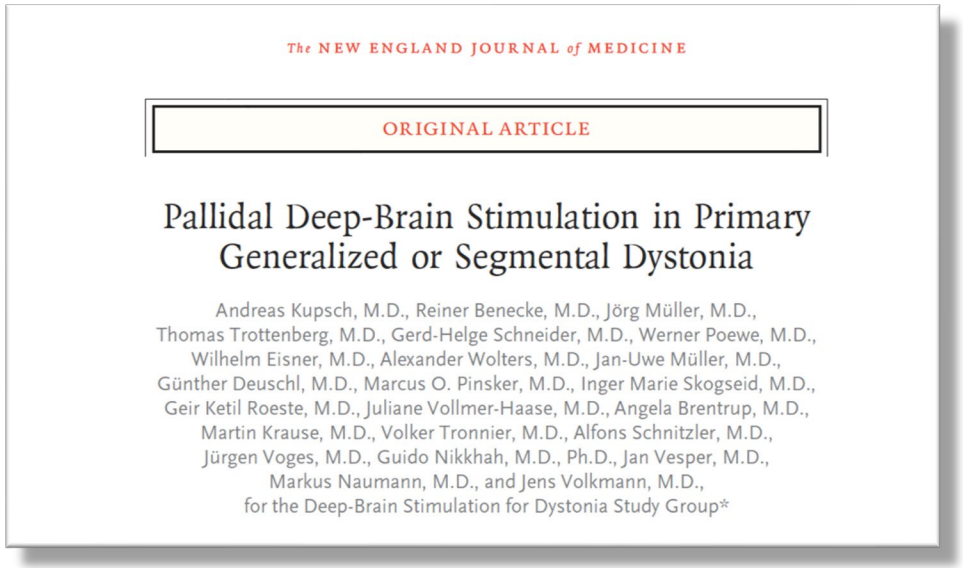


Frey, et al. 2022



Electronics Tutorials

Design of the German dystonia trial

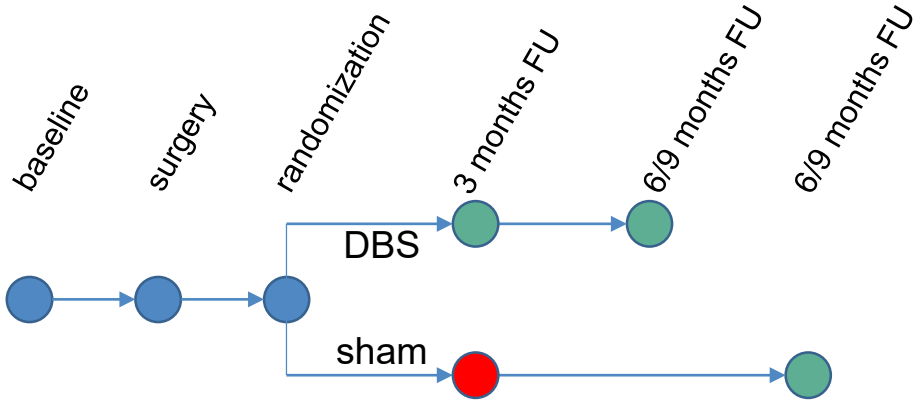


The NEW ENGLAND JOURNAL of MEDICINE

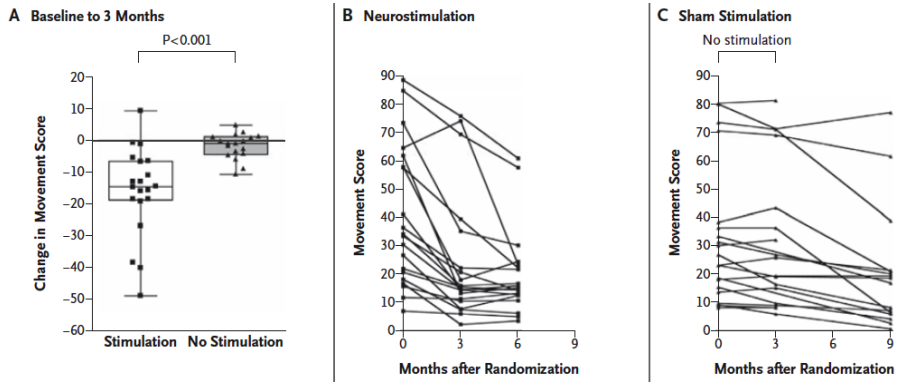
ORIGINAL ARTICLE

Pallidal Deep-Brain Stimulation in Primary Generalized or Segmental Dystonia

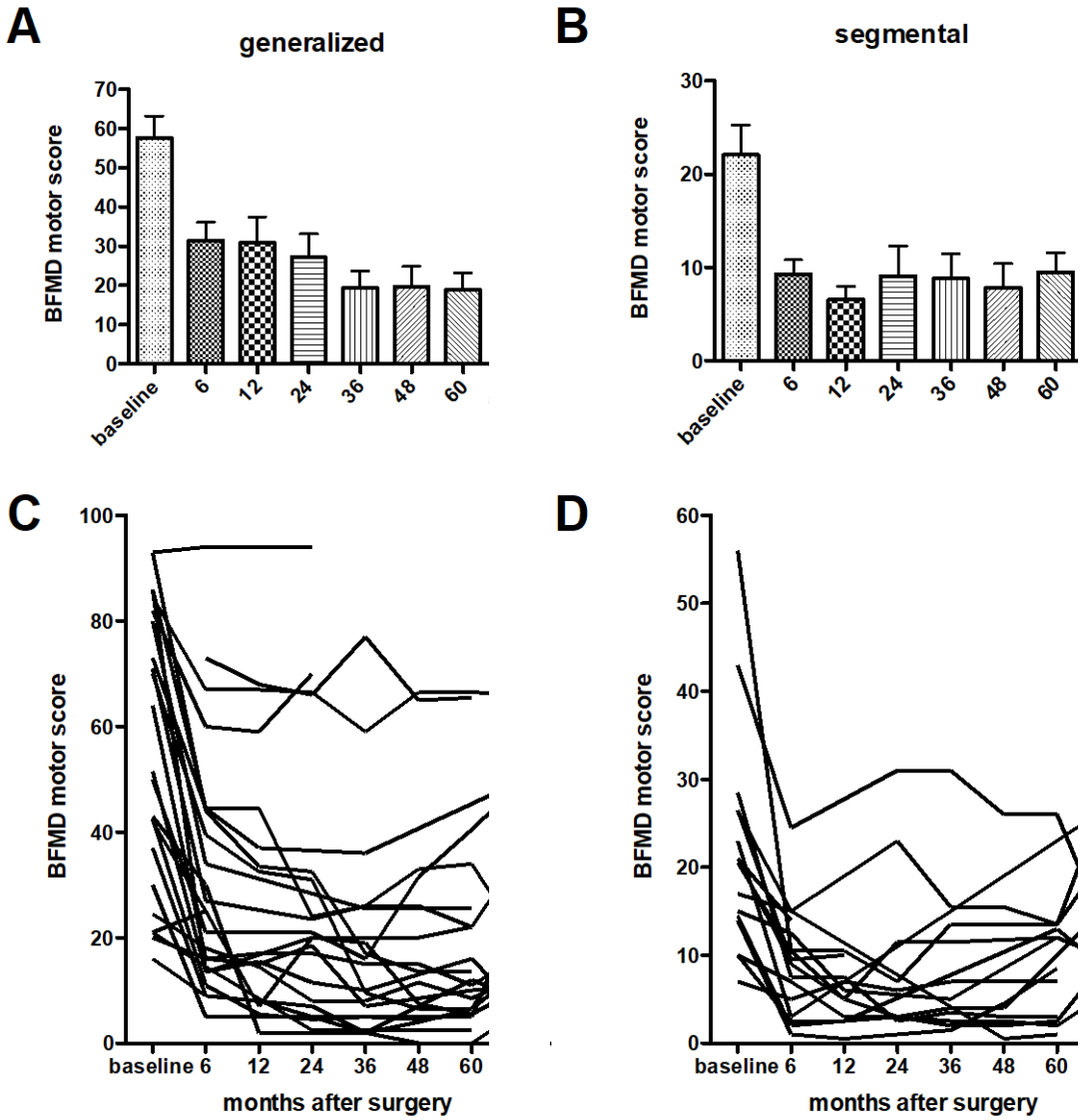
Andreas Kupsch, M.D., Reiner Benecke, M.D., Jörg Müller, M.D., Thomas Trottenberg, M.D., Gerd-Helge Schneider, M.D., Werner Poewe, M.D., Wilhelm Eisner, M.D., Alexander Wolters, M.D., Jan-Uwe Müller, M.D., Günther Deuschl, M.D., Marcus O. Pinsker, M.D., Inger Marie Skogseid, M.D., Geir Ketil Roeste, M.D., Juliane Vollmer-Haase, M.D., Angela Brentrup, M.D., Martin Krause, M.D., Volker Tronnier, M.D., Alfons Schnitzler, M.D., Jürgen Voges, M.D., Guido Nikkhah, M.D., Ph.D., Jan Vesper, M.D., Markus Naumann, M.D., and Jens Volkmann, M.D., for the Deep-Brain Stimulation for Dystonia Study Group*

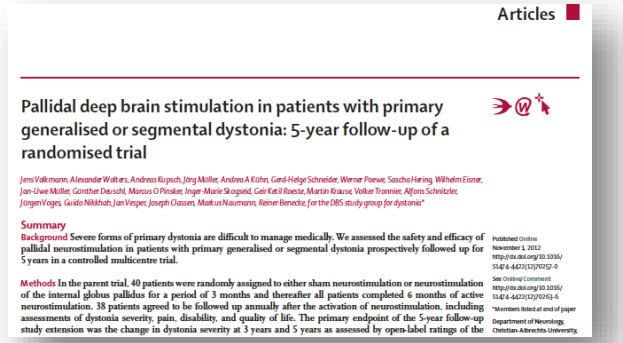


- Designed by R. Benecke and J. Volkmann 2001
- First randomized, sham controlled DBS trial
- Prospective, sham-controlled; open label longitudinal follow-up
  - *3 months randomized sham-controlled period*
  - *6 months open-label DBS compared to baseline*
- Annual FU visits for 5 years
- Need to standardize DBS programming across centers



Long-term follow-up





Articles

Pallidal deep brain stimulation in patients with primary generalised or segmental dystonia: 5-year follow-up of a randomised trial

Jens Volkmann, Alexandar Wolters, Andreas Kupsch, Jörg Müller, Andrea A Kühn, Gerd-Helge Schneider, Werner Poewe, Sascha Hering, Wilhelm Eisner, Jan-Uwe Müller, Günther Deuschl, Marcus O Pinsker, Inger-Marie Skogseid, Geir Kåtil Roeste, Martin Krause, Volker Tronnier, Alfons Schnitzler, Jürgen Voges, Guido Nikkhah, Jan Vesper, Joseph Classen, Markus Naumann, Reiner Benecke, for the DBS study group for dystonia*

Summary

Background Severe forms of primary dystonia are difficult to manage medically. We assessed the safety and efficacy of pallidal neurostimulation in patients with primary generalised or segmental dystonia prospectively followed up for 5 years in a controlled multicentre trial.

Methods In the parent trial, 40 patients were randomly assigned to either sham neurostimulation or neurostimulation of the internal globus pallidus for a period of 3 months and thereafter all patients completed 6 months of active neurostimulation. 38 patients agreed to be followed up annually after the activation of neurostimulation, including assessments of dystonia severity, pain, disability, and quality of life. The primary endpoint of the 5-year follow-up study extension was the change in dystonia severity at 3 years and 5 years as assessed by open-label ratings of the

Published Online November 1, 2012 http://dx.doi.org/10.1016/S1474-4422(12)70252-0

See Online/Comment http://dx.doi.org/10.1016/S1474-4422(12)70263-6

*Members listed at end of paper

Department of Neurology, Christian-Albrechts-University,

Kühn et al., MDS Abstracts, 2016

Volkmann et al., Lancet Neurol, 2012

Goals of DBS programming

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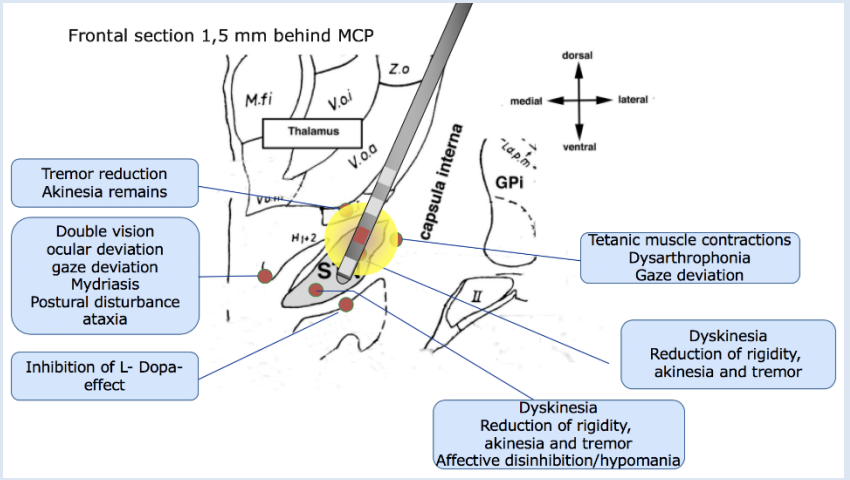
1. Optimize clinical benefit
2. Avoid adverse effects
3. Minimize current consumption



Procedure: Deliver the therapy to the brain target of interest while minimizing stimulation of surrounding structures

Programming algorithm of the German dystonia study

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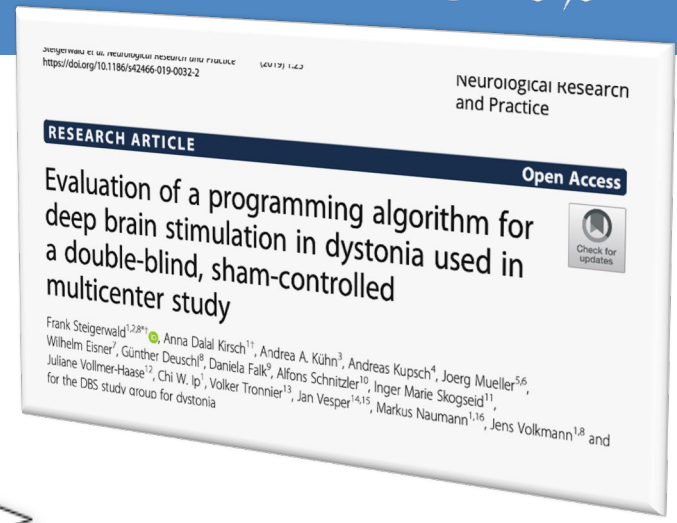
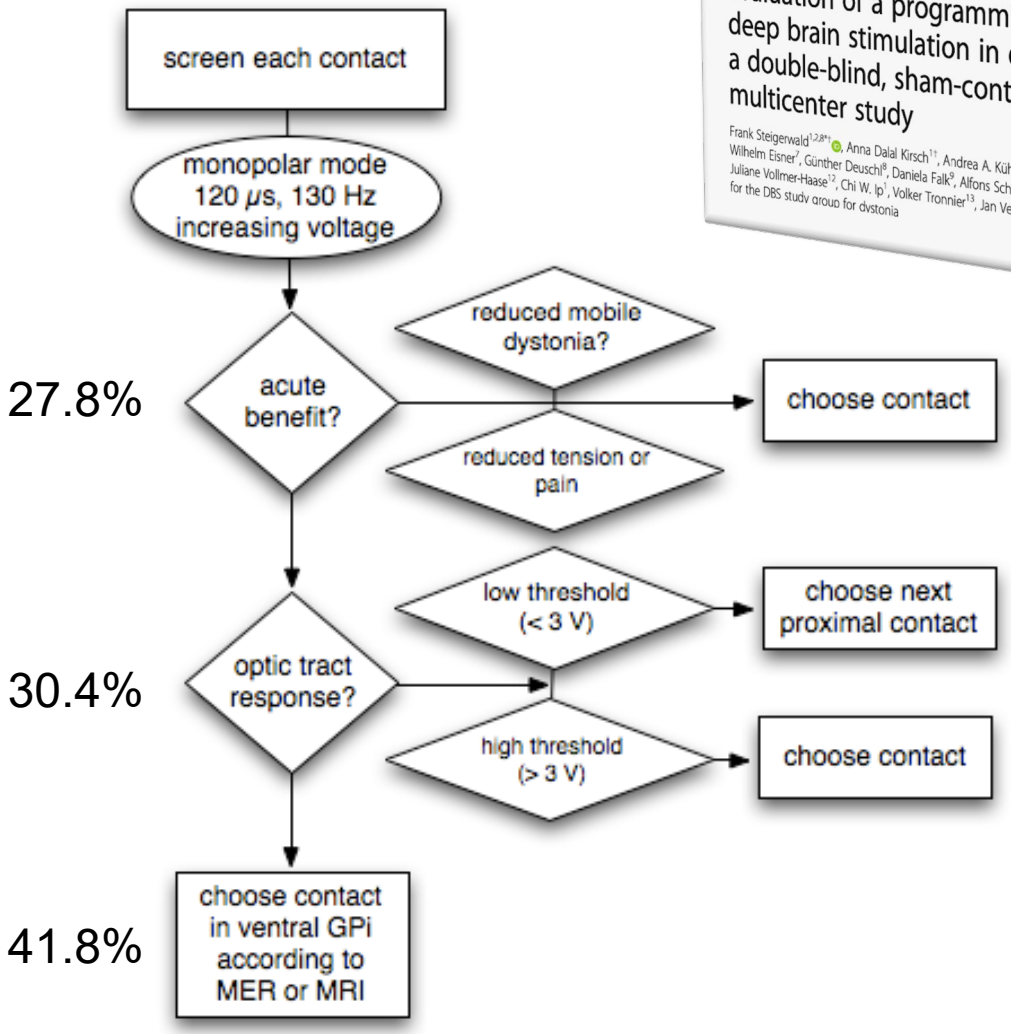
- Monopolar review of all contacts
  - 120 µs PW
  - 130 Hz frequency
  - Steps of 0.5 V, min. 30 sec stimulation
  - Upper limit 6 V
- Choose contact according to algorithm
- Set amplitude to 0.5 V below AE threshold





Steigerwald et al., Neurol Res Pract. 2019

Deep brain stimulation for dystonia: a programming algorithm evaluated by long-term results of the German multicentre study for generalized or segmental dystonia

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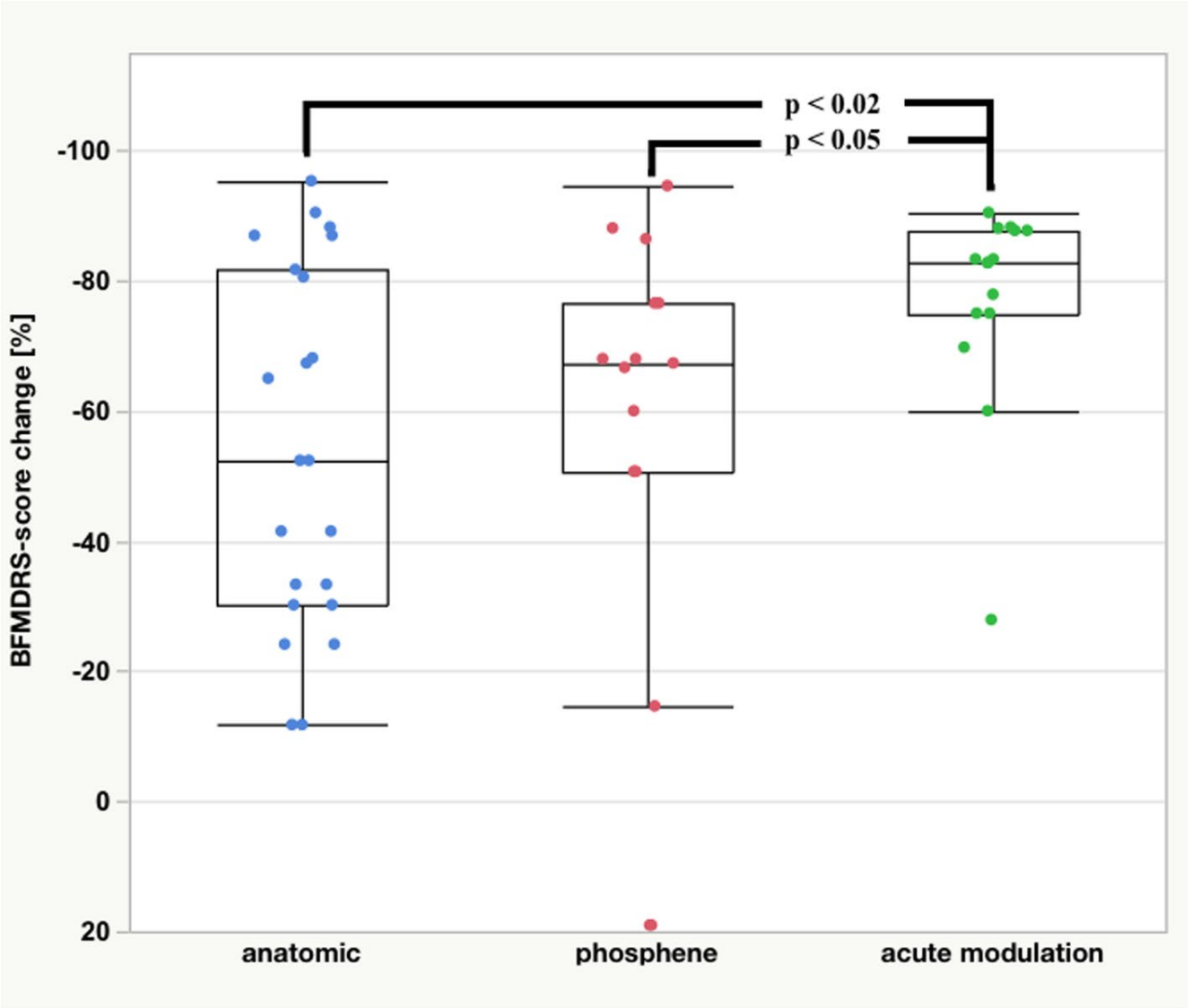
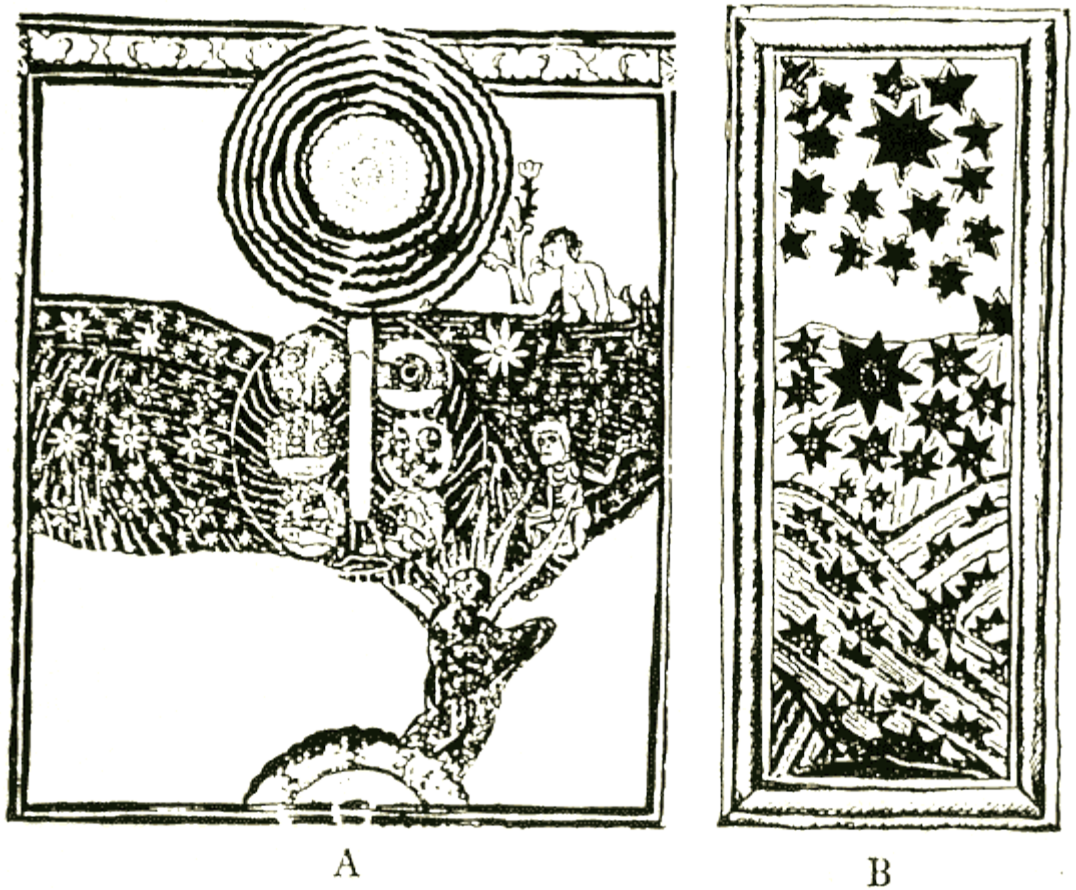
- 86% compliance with algorithm.
- More electrode choices remained in the long-term compliant with algorithm
- Average decrease of motor score was 73±24% after 3 years and 63±38% after 5 years for contacts showing acute improvement of dystonia (n=17) during the MR
- Contacts without acute benefit exhibited a change of 58±30% after 3years (n=63) and 53%±31% after 5 years (n=59).



Steigerwald et al., Neurol Res Pract. 2019

Phosphenes and Gpi programming

Hl. Hildegard v. Bingen



Gpi and optic tract

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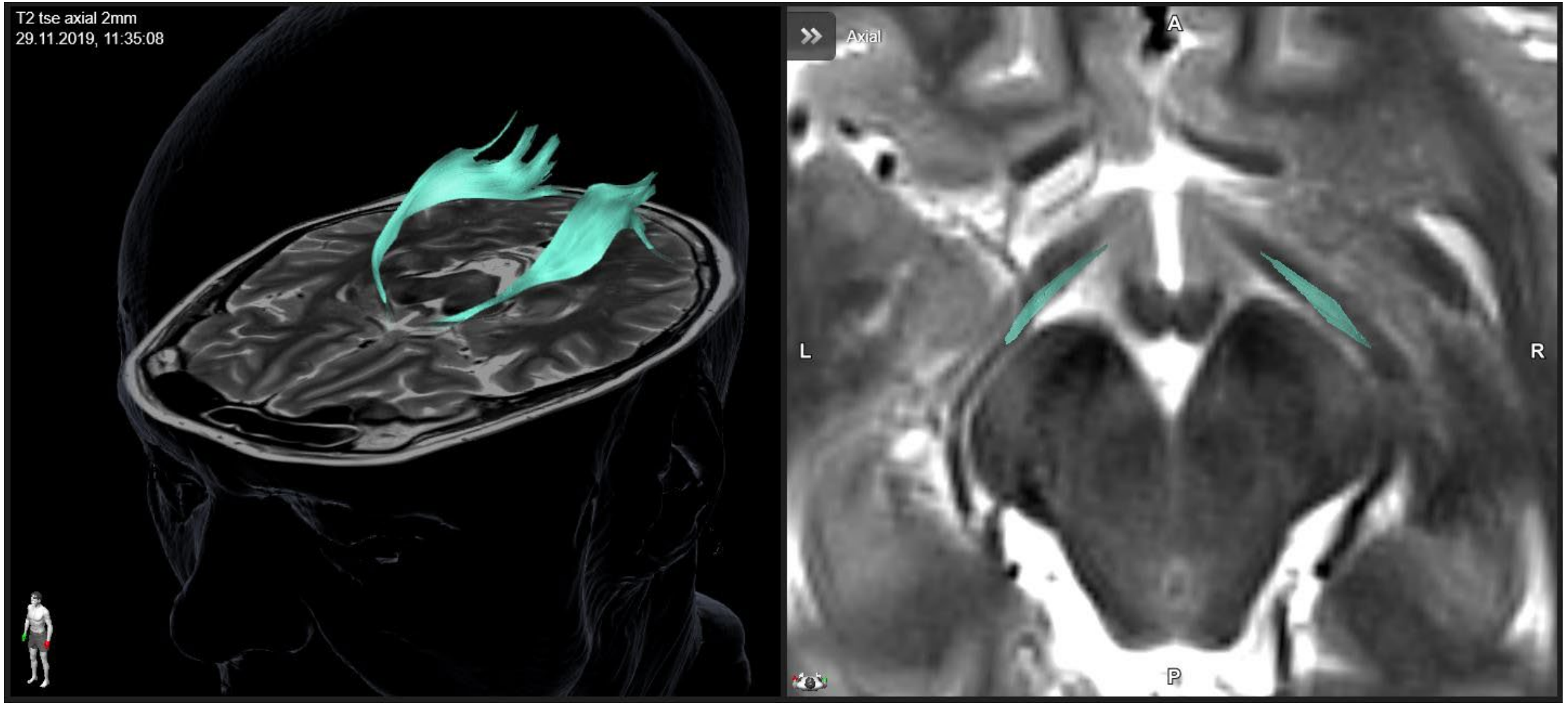

Gpi topology and neurostimulation

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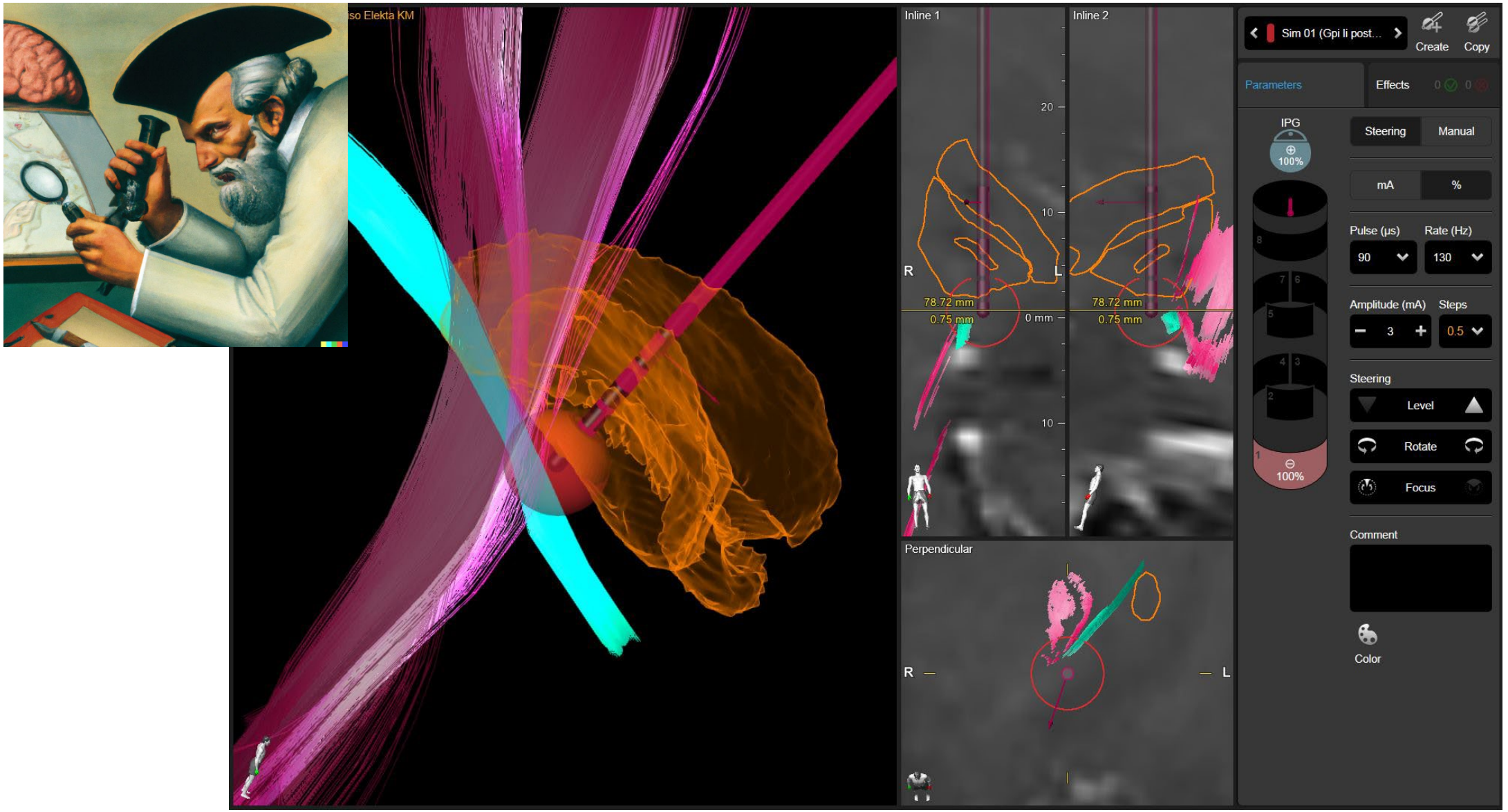

Outcome related to contact location

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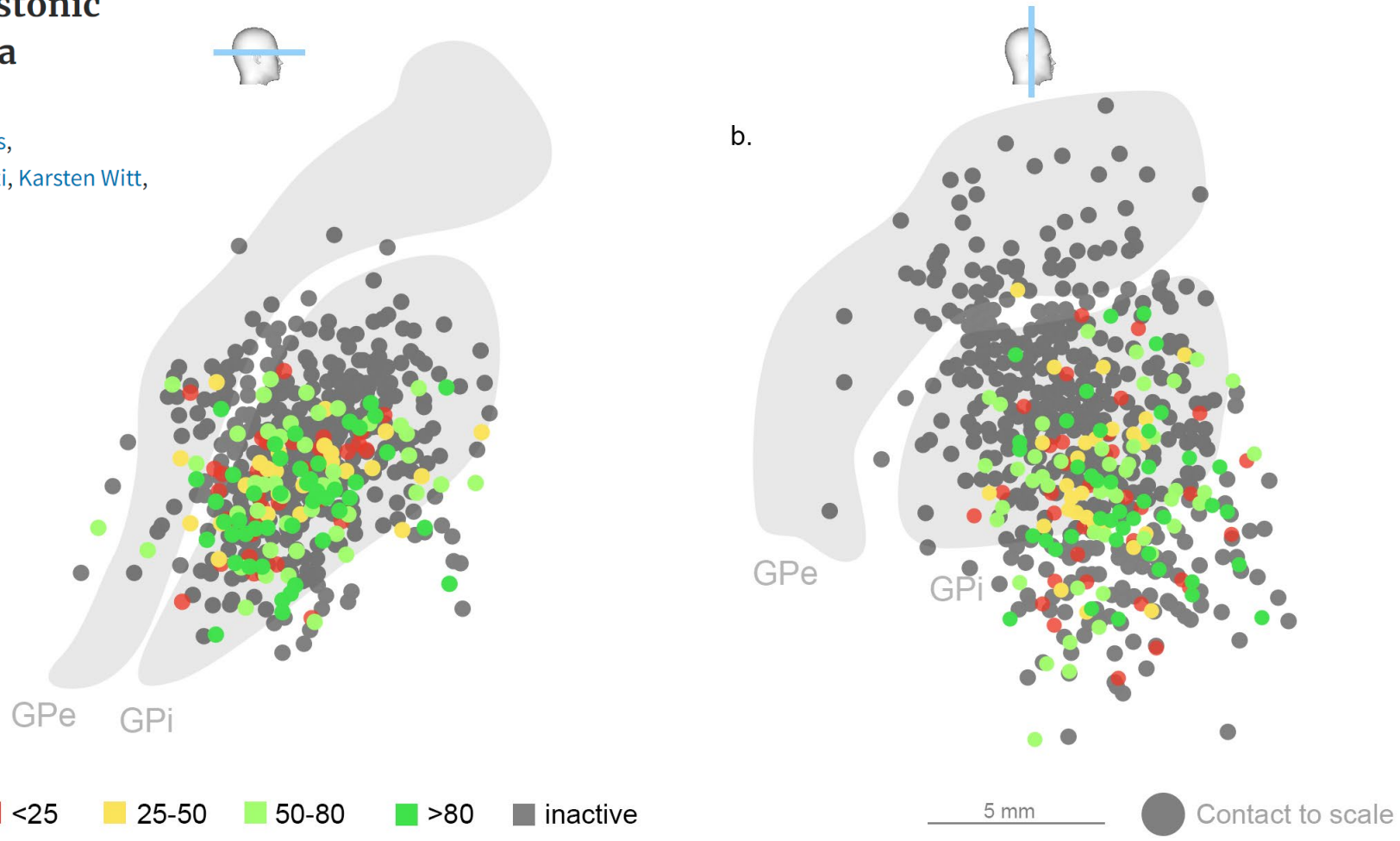
Probabilistic mapping of the antidystonic effect of pallidal neurostimulation: a multicentre imaging study FREE

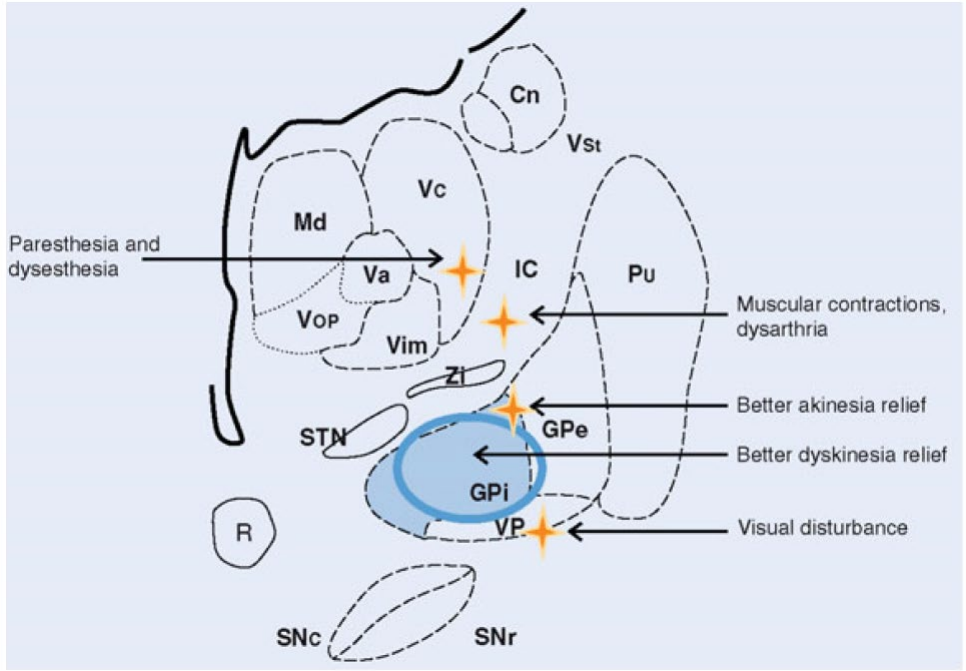
Martin M Reich, Andreas Horn, Florian Lange, Jonas Roothans, Steffen Paschen, Joachim Runge, Fritz Wodarg, Nicolo G Pozzi, Karsten Witt, Robert C Nickl ... Show more

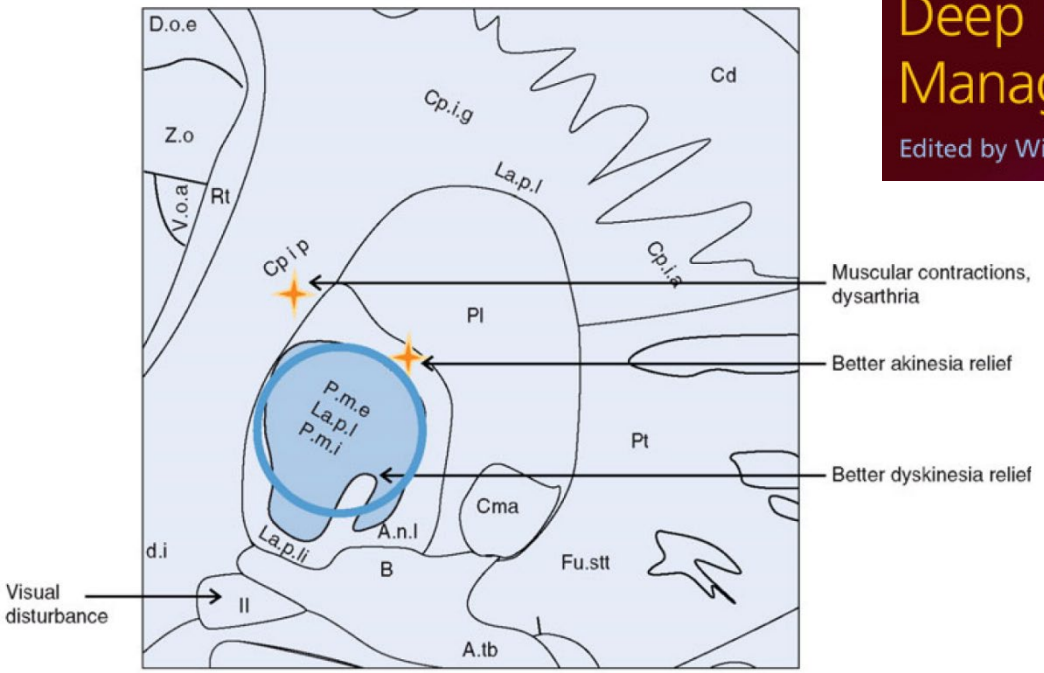
Author Notes

Brain, Volume 142, Issue 5, May 2019, Pages 1386–1398,



DBS programming



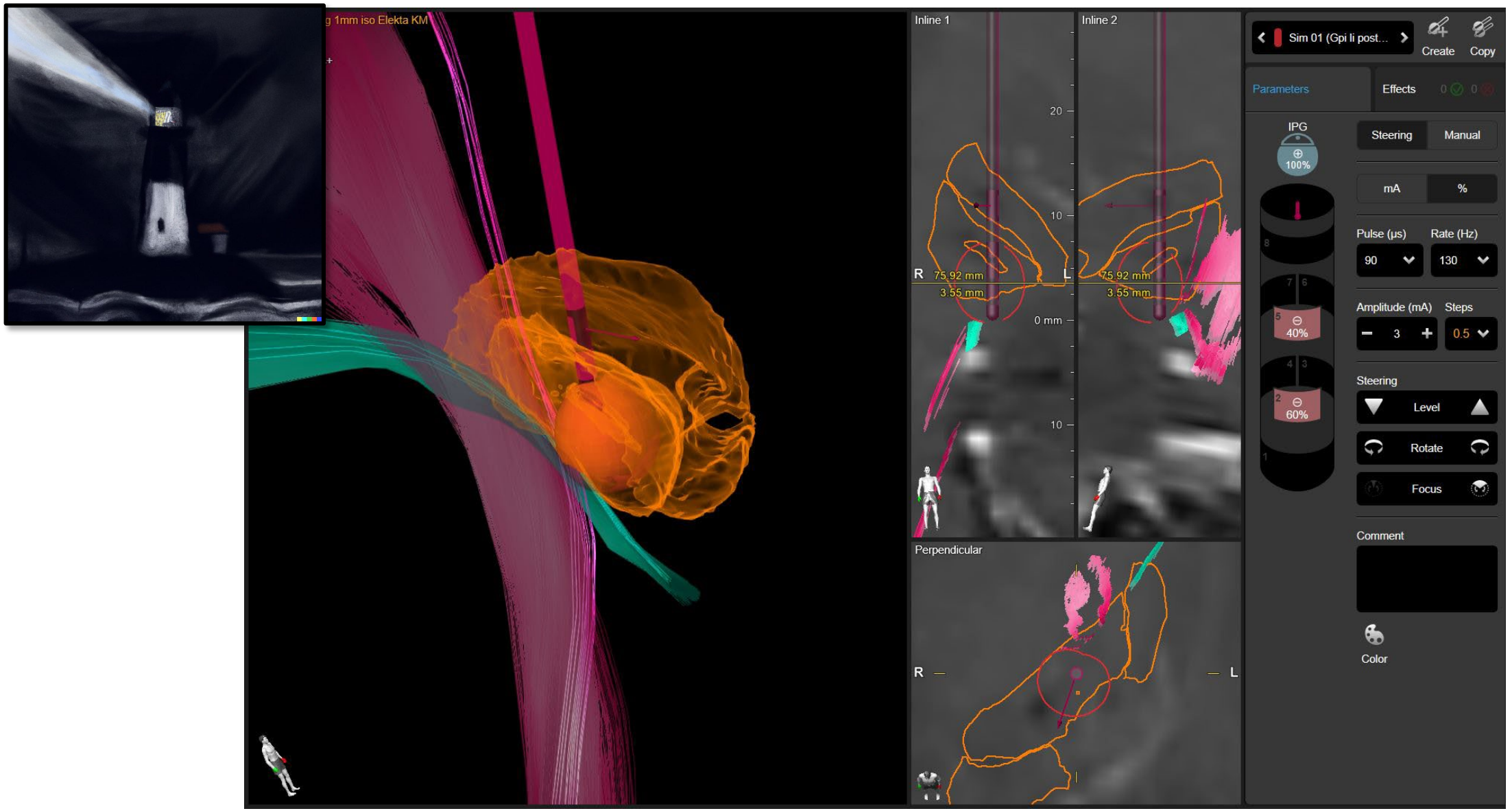


Deep Brain Stimulation Management

Edited by William J. Marks, Jr.

CLINICAL EFFECT	ELECTRODE LOCATION
Dysarthria at low amplitude of stimulation	Potentially too posteromedial
Tonic muscle contraction at low amplitude of stimulation	Potentially too posteromedial
Visual phenomena at low amplitude of stimulation	Close to optic pathways
No adverse or beneficial effects at high amplitude of stimulation	Potentially too superior, anterior, or lateral

Directional steering



Stimulation induced parkinsonism: a delayed onset adverse effect

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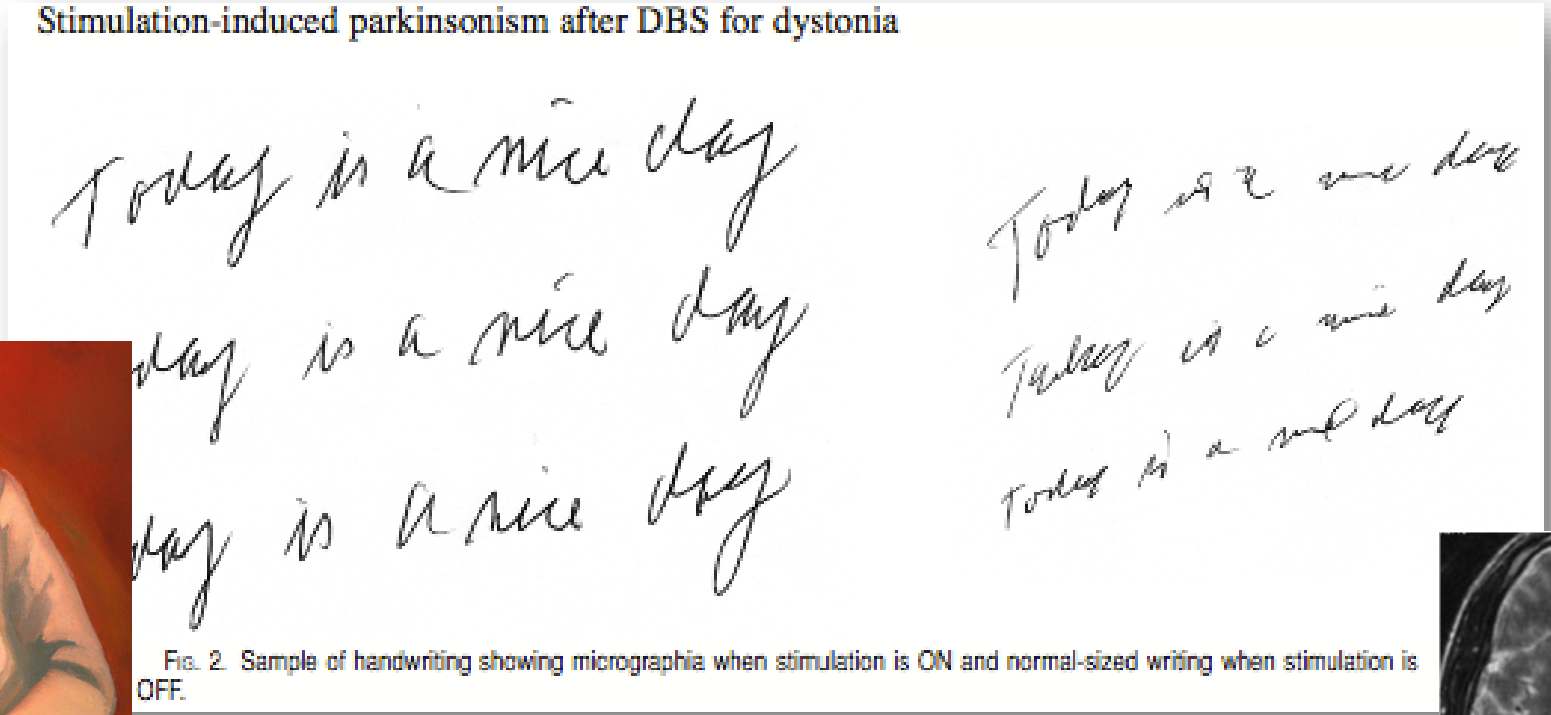

Stimulation-induced parkinsonism after DBS for dystonia

Today is a nice day

Today is a nice day

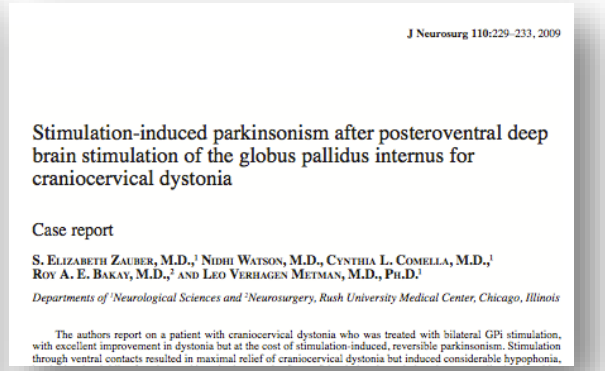
Today is a nice day

Today is a nice day

Today is a nice day

Today is a nice day

FIG. 2. Sample of handwriting showing micrographia when stimulation is ON and normal-sized writing when stimulation is OFF.


J Neurosurg 110:229–233, 2009

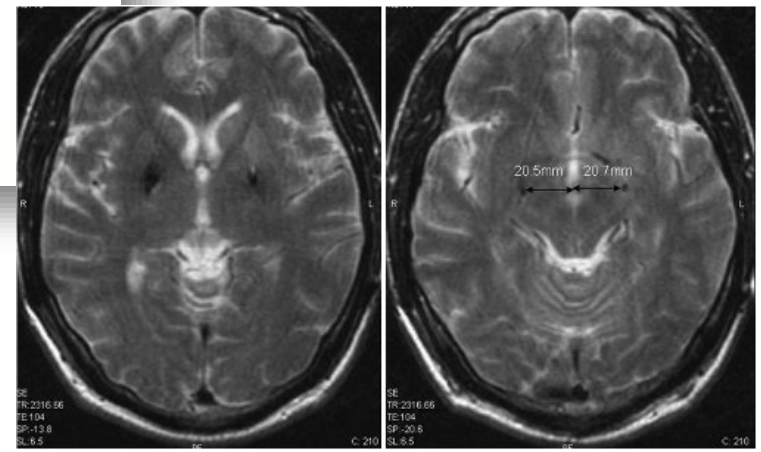
Stimulation-induced parkinsonism after posteroventral deep brain stimulation of the globus pallidus internus for craniocervical dystonia

Case report

S. Elizabeth Zauber, M.D.,[1] Nidhi Watson, M.D., Cynthia L. Comella, M.D.,[1] Roy A. E. Bakay, M.D.,[2] and Leo Verhagen Metman, M.D., Ph.D.[1]

Departments of [1]Neurological Sciences and [2]Neurosurgery, Rush University Medical Center, Chicago, Illinois

The authors report on a patient with craniocervical dystonia who was treated with bilateral GPi stimulation, with excellent improvement in dystonia but at the cost of stimulation-induced, reversible parkinsonism. Stimulation through ventral contacts resulted in maximal relief of craniocervical dystonia but induced considerable hypophonia,



Possible management:

- Goal: Keeping the beneficial clinical effect
- Reducing side effect
- Shorten pulsewidth (30 – 40 µs)
- Steering usually unsuccessful
- Stimulation “holiday” during daytime

New targets = old targets – the STN

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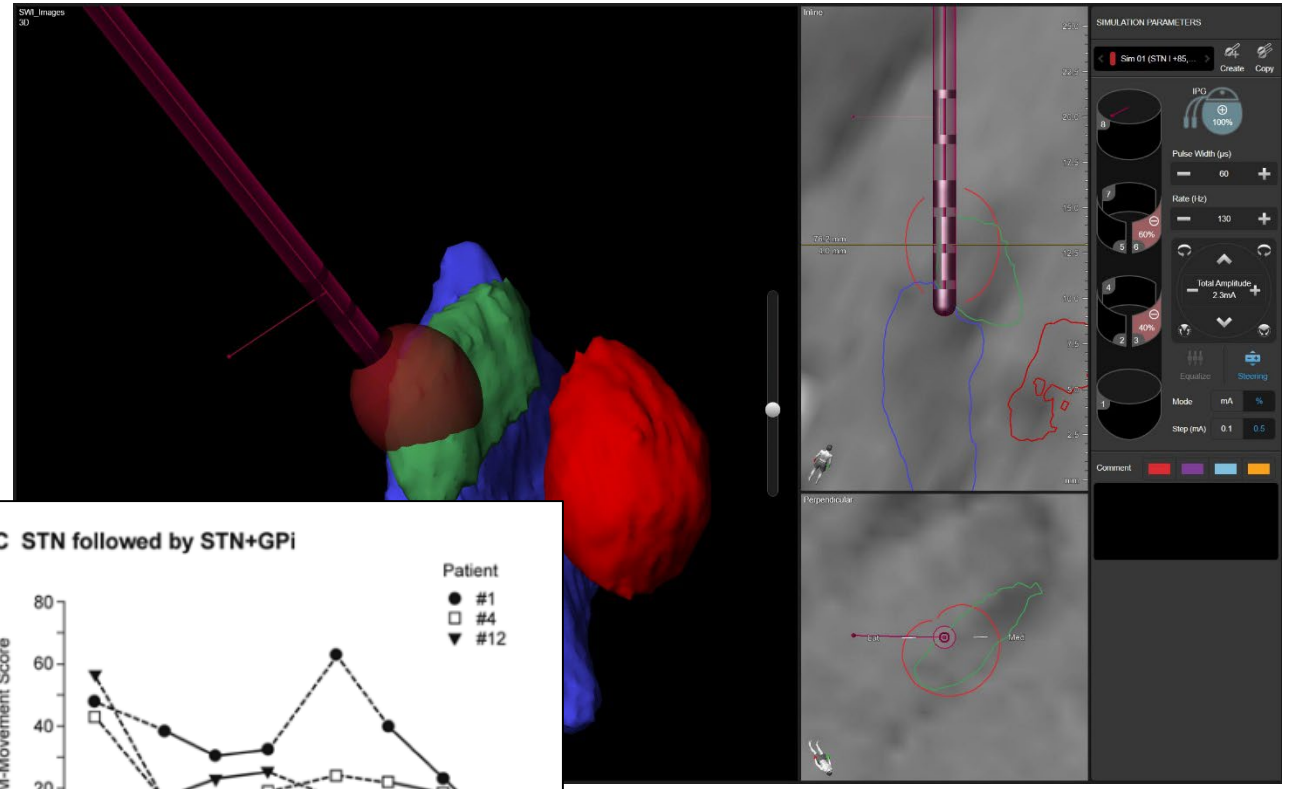
A randomized double-blind crossover trial comparing subthalamic and pallidal deep brain stimulation for dystonia

Clinical article

Lisbeth Schjerling, M.D.,[1,2] Lena E. Hjermind, M.D., Ph.D.,[3,4] Bo Jespersen, M.D.,[1] Flemming F. Madsen, M.D., D.Sc.,[1] Jannick Brennum, M.D., D.Sc.,[1] Steen R. Jensen, R.N.,[5] Annemette Løkkegaard, M.D., Ph.D.,[5] and Merete Karlsborg, M.D.[5]

[1]*Department of Neurosurgery, Rigshospitalet, Copenhagen University Hospital;* [2]*Department of Emergency, Hilleroed Hospital, Copenhagen University Hospital;* [3]*Section of Neurogenetics, Memory Disorders Research Group, Department of Neurology, Rigshospitalet, Copenhagen University Hospital;* [5]*Department of Neurology, Bispebjerg, Copenhagen University Hospital, Copenhagen, Denmark; and* [4]*Department of Cellular and Molecular Medicine, Section of Neurogenetics, Faculty of Health Sciences, University of Copenhagen, Copenhagen, Denmark*



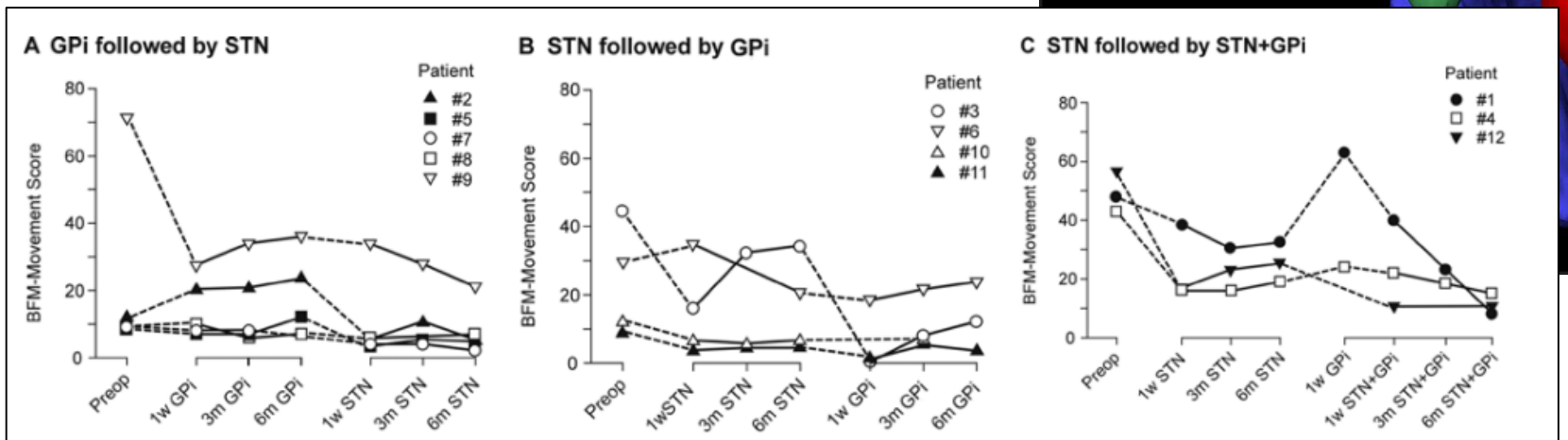


Fig. 3. Ratings in BFMDRS (BFM) movement score. **A:** The 5 patients who initially received GPi stimulation followed by STN stimulation. **B:** The 4 patients who initially received STN stimulation followed by GPi stimulation. **C:** The 3 patients who initially received STN stimulation but did not accept stimulation of the GPi and instead received 6 months of simultaneous STN and GPi stimulation. 1w = 1 week; 3m = 3 months; 6m = 6 months.

Prof. J. Volkmann
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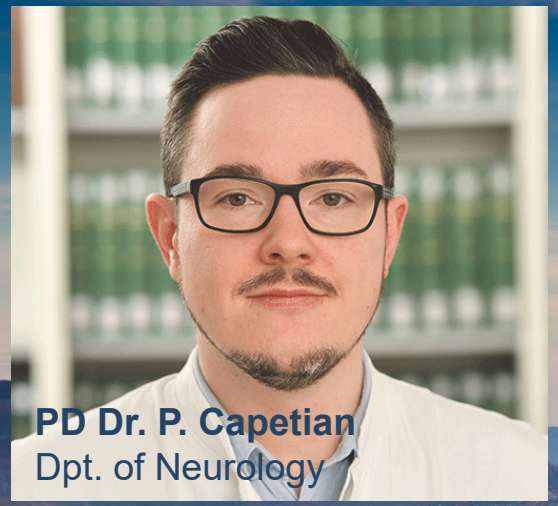
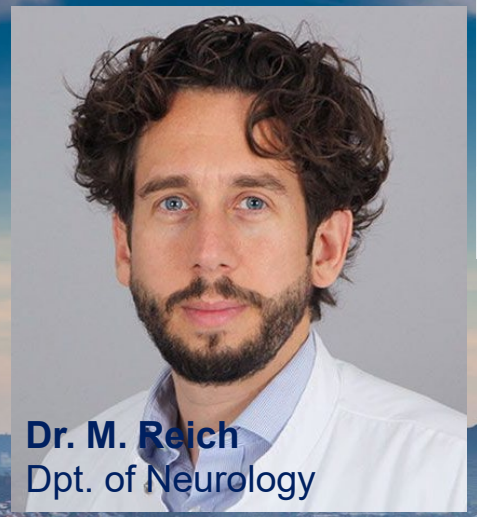


PD Dr. P. Capetian
Dpt. of Neurology



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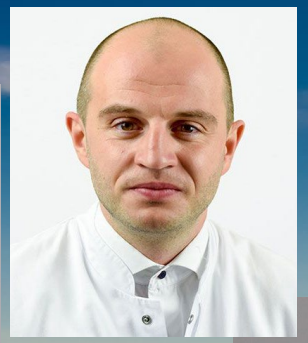

Dr. F. Lange
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The Würzburg clinical DBS team

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Dr. P. Fricke & M. Sollner
DBS-Team Dpt. of Neurosurgery

Dr. F. Gross
Dpt. of Neurology

Thank you very much for your attention!