Data-driven biomarkers for motor Subthalamic Nc. in PD during DBS electrode implantation

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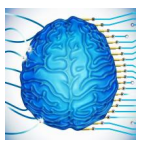

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GRADUATE TRAINING CENTRE OF NEUROSCIENCE
International Max Planck Research School

Introduction

Parkinson's Disease: Symptoms

as in 2023 ICD-10-CM Diagnosis Code G20: Parkinsonism [1]

- progressive motor disability: tremors, shaking, muscular rigidity, stiffness, slowing of movements, and lack of postural reflexes.
- Non-motor symptoms: Slurrish speach, sleeping problems, depression, anxeiety

Parkinson's Disease: Assessment

e.g. with MDS-UPDRS [2][1] consisting of 4 parts:

I. Nonmotor aspects of daily living: Cognitive impairments, mood, depression & anxiety, sleep problems, pain, ...

II. Motor aspects: Speech, eating, dressing, hygiene, handwriting ...

III. Motor examination by clinicean (Speech, facial expressions, rigidity, hand movements, ...) with/out medication with L-DOPA

IV. treatment-related motor complications: fluctuations and dyskinesia

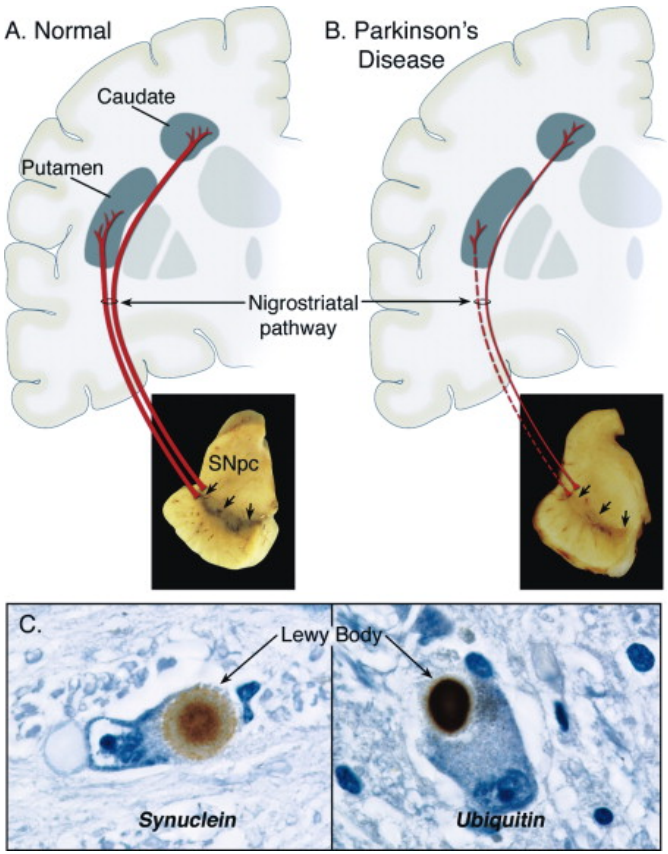
Also possible: SPECT for DA transporters[2]

[1] Movement Disorder Society Unified Parkinson's Disease Rating Scale
[2] Single Photon Emission Computed Tomography

Parkinson's Disease: Mechanisms I

- loss of dopamine-producing/melanin-containing neurons in substantia nigra pars compacta [3]
- accumulation of lewy bodies in SN and VTA [4] among others
- Reason unknown; Combination of genetic and environmental factors hypothesized [3], [5]

Parkinson's Disease: Mechanisms II



- Degradation of nigrostriatal DA pathway
- impairs regulation of Basal Ganglia circuit
- greater inhibition of voluntary movements

Parkinson's Disease: Mechanisms III

↓ dopamine deficit in SNc

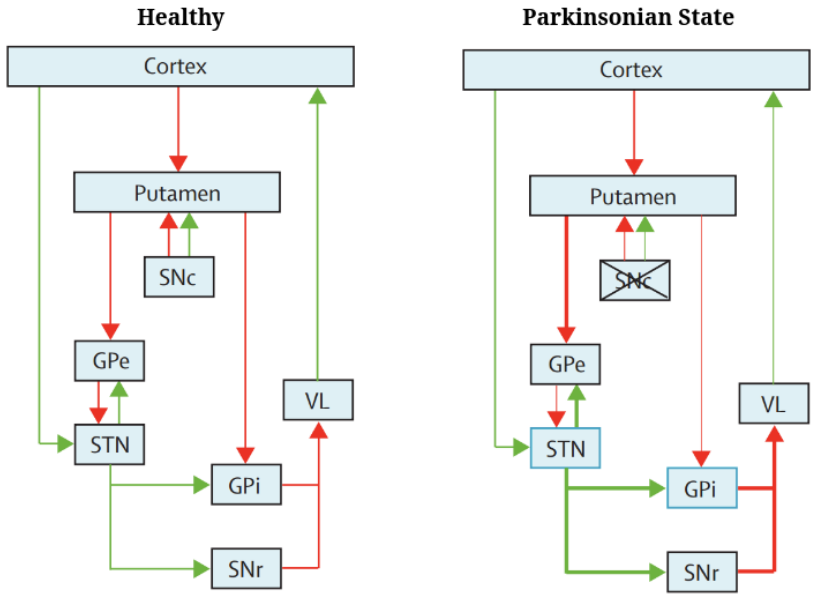
- Direct pathway
  - Putamen - GPi/SNr [2]
- Indirect pathway
  - Putamen - GPe - STN- GPi/SNr
- Hyperdirect Pathway
  - Cortex - STN

Results in

- ↑ inhibition of thalamus (VL)
- ↓ activation of cortex

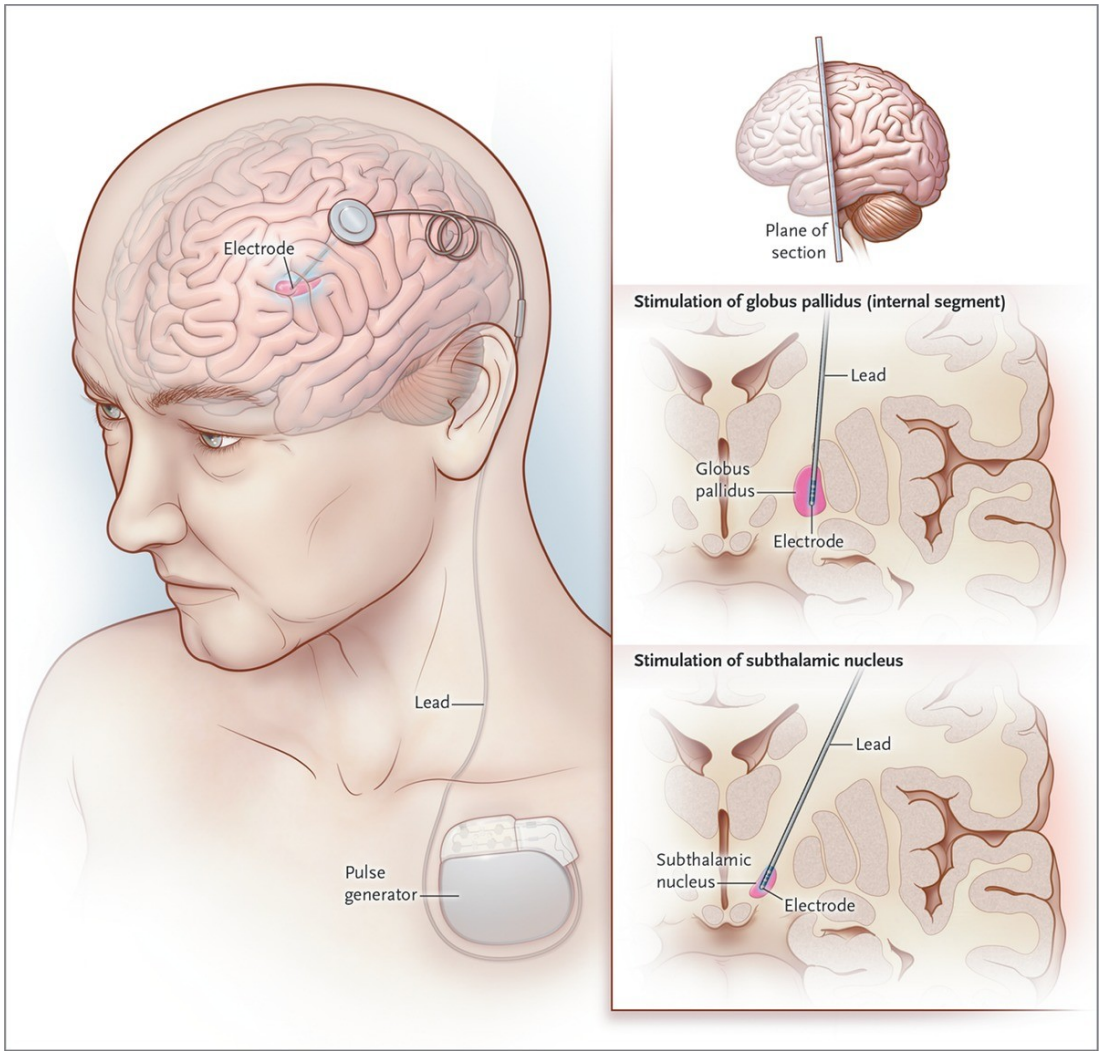
Therapy

- Dopaminergic medication
- Deep brain stimulation (DBS)

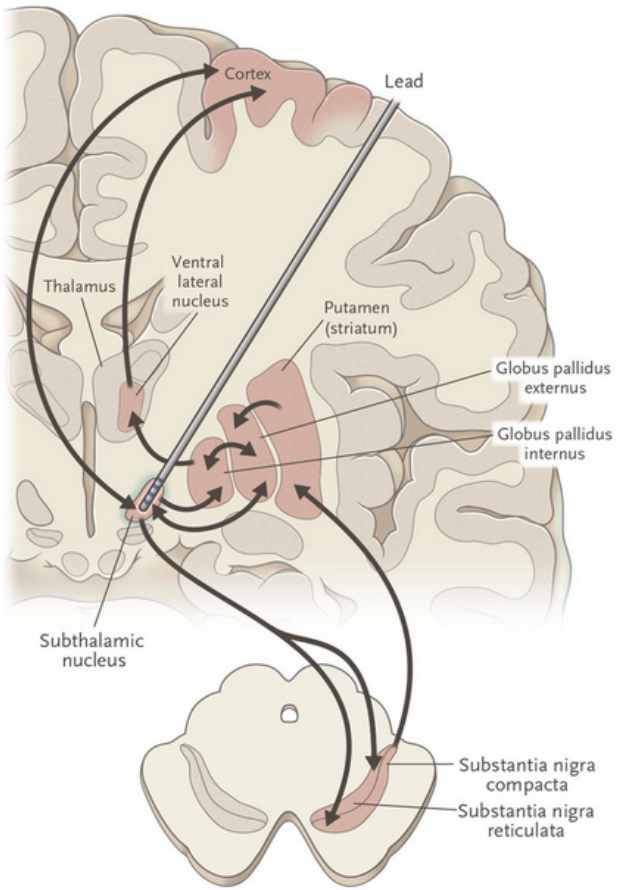


GPe=globus pallidus pars externa. GPi=globus pallidus pars interna. SNc=substantia nigra pars compacta. SNr=substantia nigra pars reticulata. STN=subthalamic nucleus. VL=ventrolateral nucleus.

Parkinson's Disease: DBS [6] I

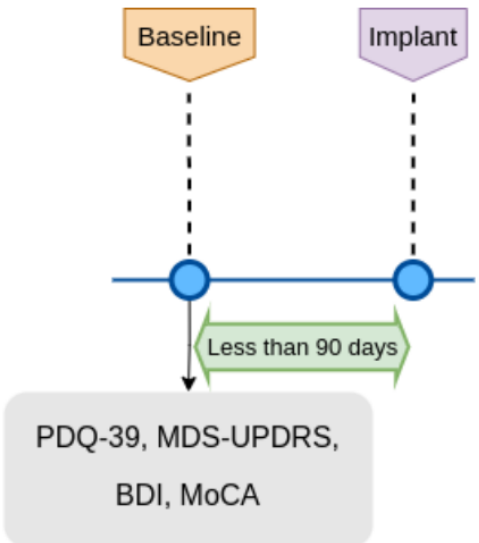


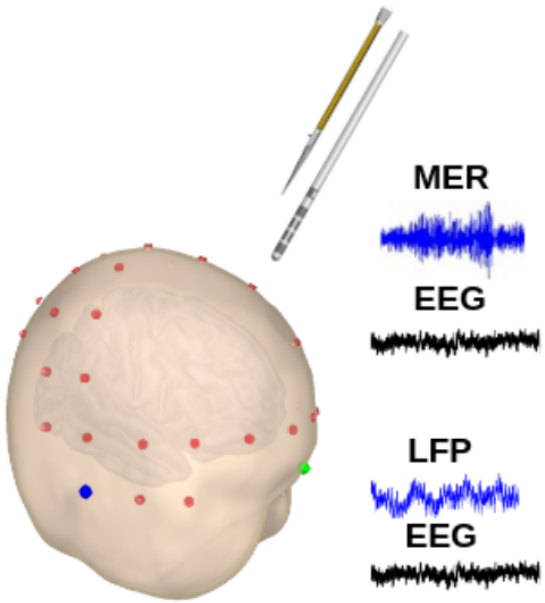
Parkinson's Disease: DBS [6] II

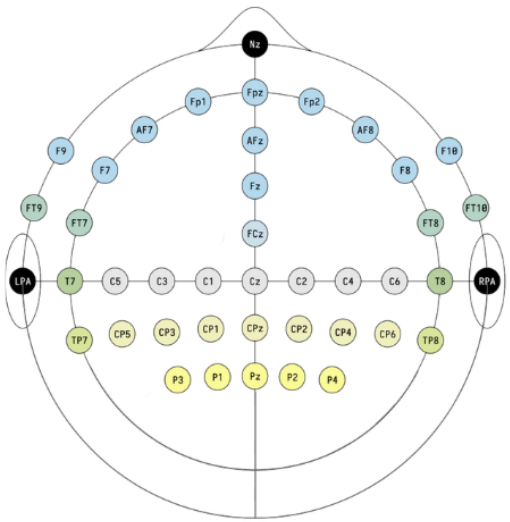


Stimulation with high frequency to inhibit target structure

Data I







39 Channel - EEG Montage

MER=Microelectrode Recording, LFP=Local Field Potential, BDI=Beck's Depression Inventory, MDS-UPDRS=MDS-Unified Parkinson's Disease Rating Scale, PDQ-39=Parkinson's Disease Questionnaire, MoCA=Montreal Cognitive Assessment

Data II

- Pre-Operative:
  - Imaging: CT, MRT (incl. DTI)
  - Questionaires: MDS-UPDRS, PDQ39, BDI, MoCA
- Intra-Operative:
  - (Bio-)Signals: EEG, Micro-electrode recordings, DBS electrode recordings
  - Imaging: CT/Angiography
- Post-Operative:
  - Imaging: CT, MRT
  - Questionaires: as above
  - (Future Work: Wearables, Sleep EEG)

Surgery I

1. Plan implantation stereotactically using CT and MRT.

...

2. Fixate stereotactic frame & EEG on patient.

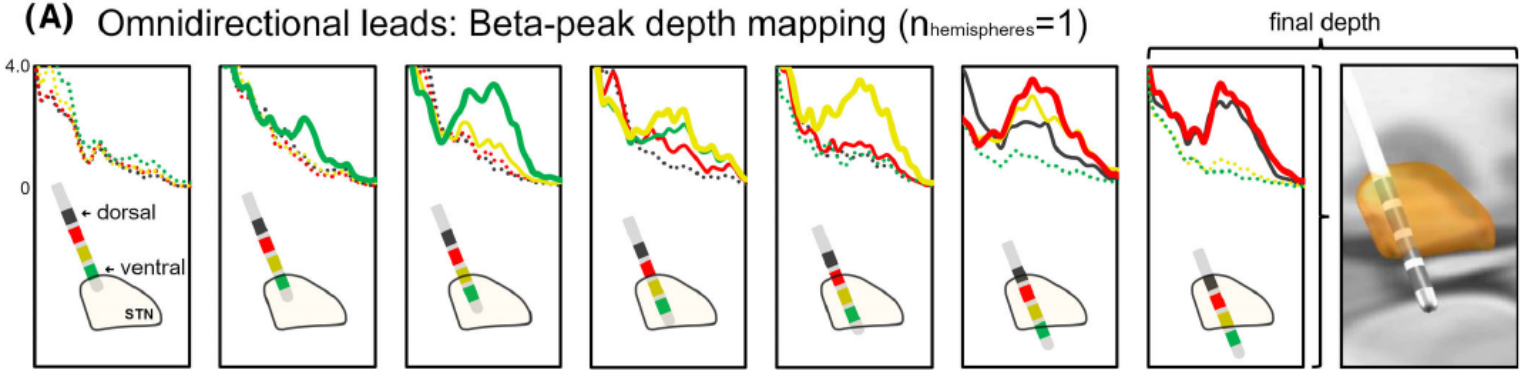
...

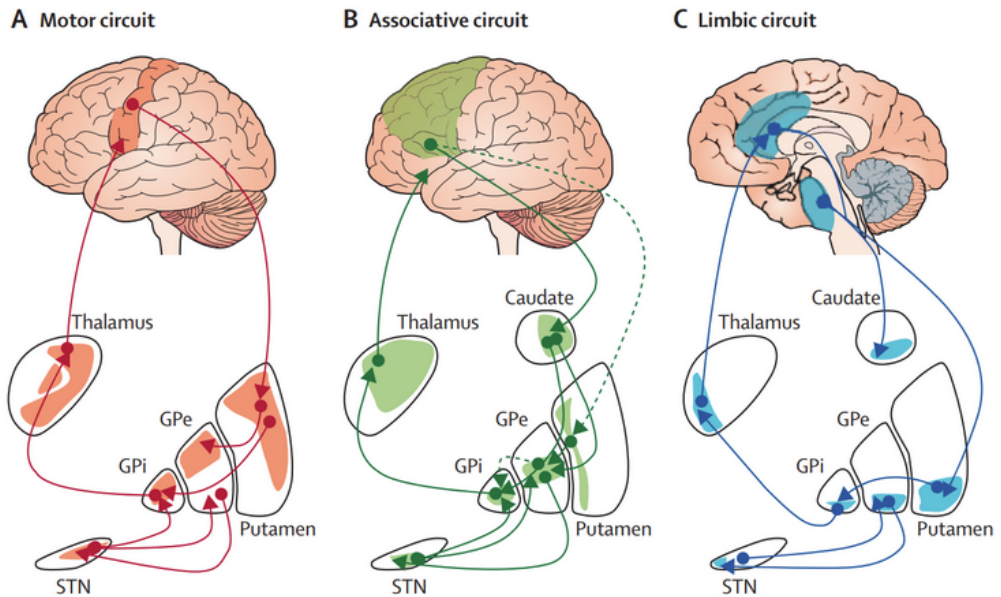
3. First trajectroy with micro-electrode to quantify activity (spiking).
4. Then with Deep Brain Stimulation electrode (e.g. Abott St. Jude 6172) milimeterwise, measuring at each position for 30s & calculate PSD. Implant according to patient profile.

...

5. continue with other side.
6. End surgery for DBS lead implantation, continue with generator and cable.

Surgery II


(A) Omnidirectional leads: Beta-peak depth mapping (n hemispheres=1)
final depth
4.0
0
dorsal
ventral
STN


A Motor circuit
B Associative circuit
C Limbic circuit
Thalamus
Caudate
GPe
GPi
Putamen
STN

Task & Approach

Task

Given: A set of potiential biomarkers/features.

Desired: Framework for quantifying the quality of (combinations of) biomarkers/features.

Ansatz: Apply classification to predict and Shapley values [7] to assess feature importance.

Shapley Values

Roots in game theory [8]

- Coalition of players obtaining overall gain from cooperation
- Shapley values answer the questions: How important is each player to the coalition overall? What payoff can they expect?

Transfer [9]

- Coalition = set of features. Player = single feature.
- How important was one feature to the prediction (using the set of features) overall?

Application

Given: Signals recorded during surgery

Desired: What are electrophysiological biomarkers of motor part of STN?

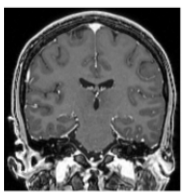
Ansatz: Use Classification to predict if DBS electrode is inside/outside of motor STN and Shapley values [7] to assess feature importance

Setup I

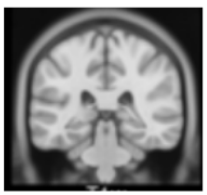
- Use normalized[3] PSD binned by 5 Hz
- Use simple classifier: DecisionTree from sklearn
- Electrode position gathered from reconstruction

patients	samples	depth range	recording time	in motor STN
42	5122	$[10, 20]$ mm	$42.68\overline{3}$ hours	1052

Setup II



Pre-op T1

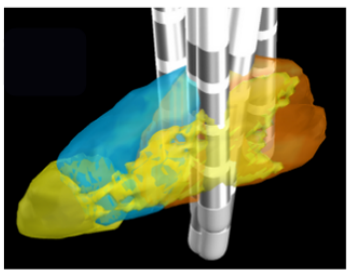


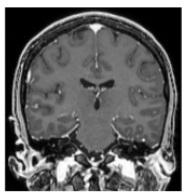
MNI T1

Normalization

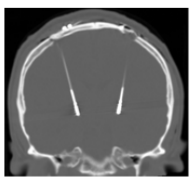
Forward and Inverse transformation to MNI

Electrodes localization in MNI space



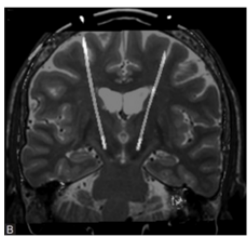


Pre-op T1



Post-op CT

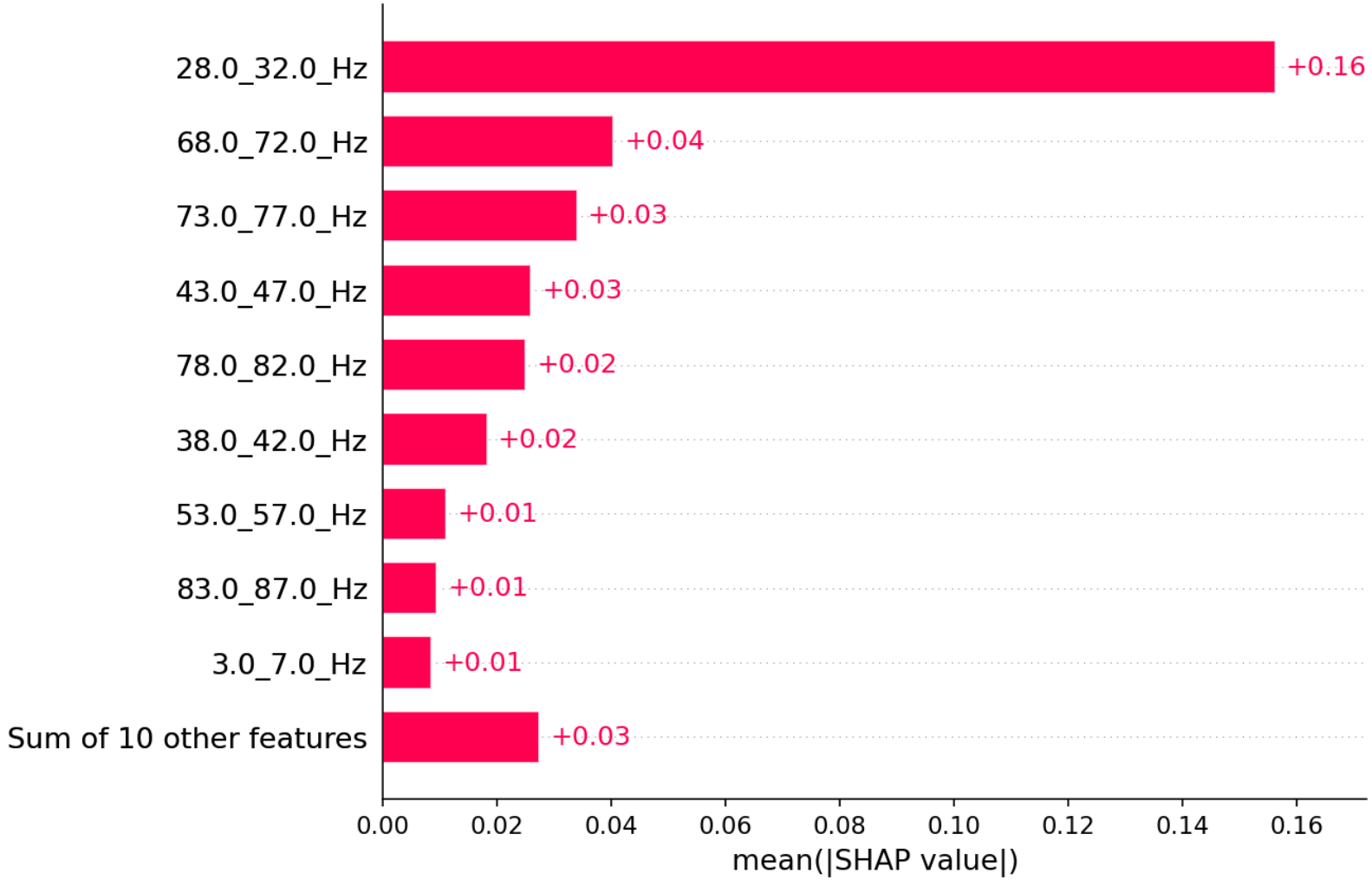
Coregistration



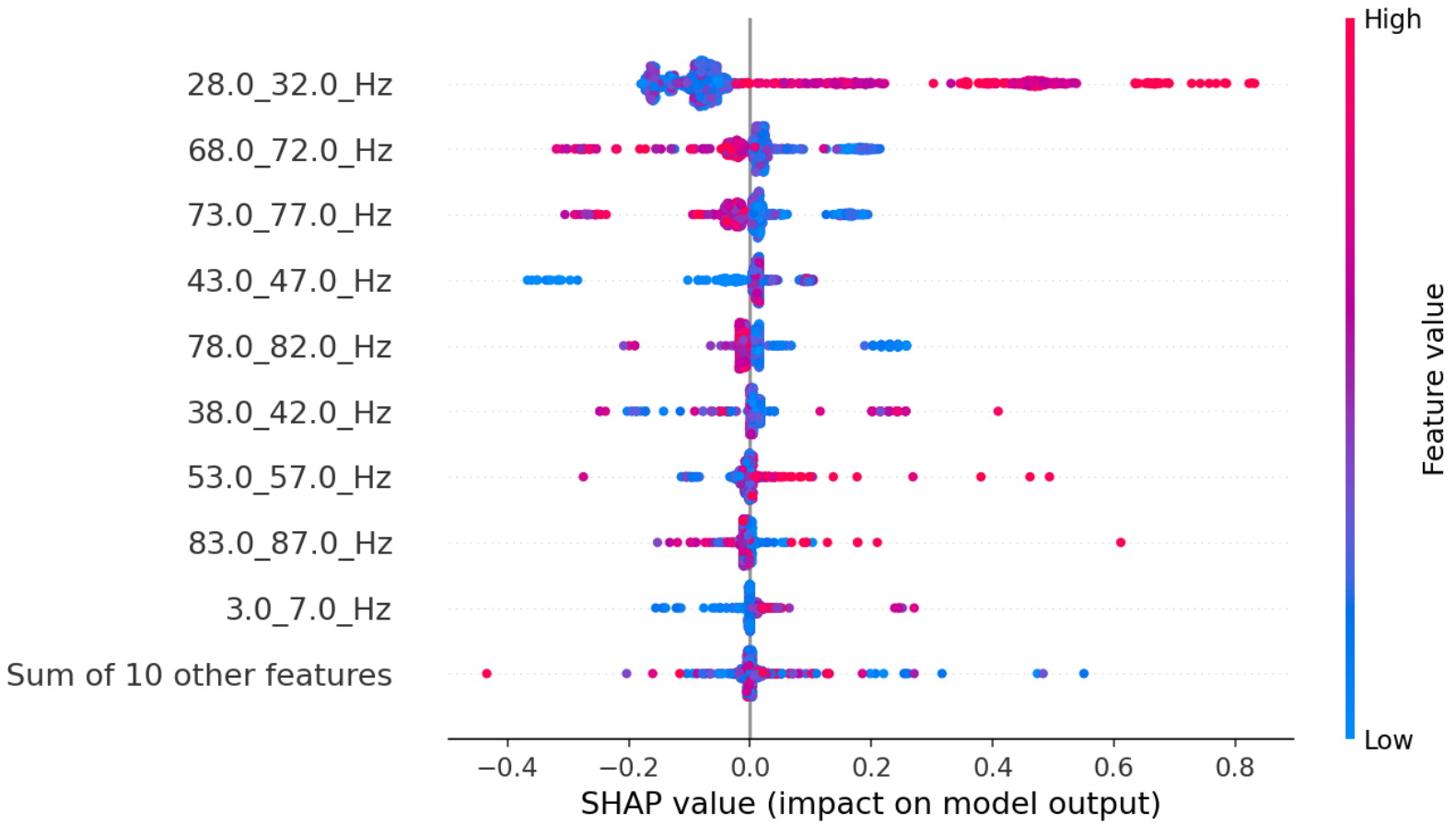
Coregistered acquisitions

[3] Fit the spectrum with FOOOF and subtract the aperiodic part

Results I


28.0_32.0_Hz
+0.16
68.0_72.0_Hz
+0.04
73.0_77.0_Hz
+0.03
43.0_47.0_Hz
+0.03
78.0_82.0_Hz
+0.02
38.0_42.0_Hz
+0.02
53.0_57.0_Hz
+0.01
83.0_87.0_Hz
+0.01
3.0_7.0_Hz
+0.01
Sum of 10 other features
+0.03
0.00
0.02
0.04
0.06
0.08
0.10
0.12
0.14
0.16
mean(|SHAP value|)

Results II

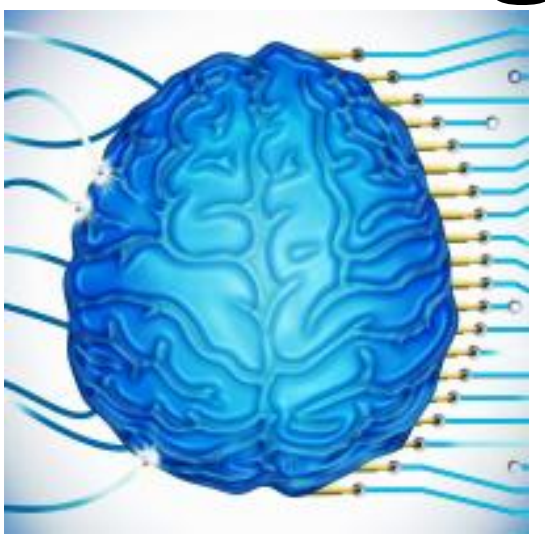

28.0_32.0_Hz
68.0_72.0_Hz
73.0_77.0_Hz
43.0_47.0_Hz
78.0_82.0_Hz
38.0_42.0_Hz
53.0_57.0_Hz
83.0_87.0_Hz
3.0_7.0_Hz
Sum of 10 other features
−0.4
−0.2
0.0
0.2
0.4
0.6
0.8
SHAP value (impact on model output)
High
Feature value
Low

Outlook

Outlook

- Extend PSD frequency range
- additional types of features (e.g. median absolute deivation)
- other means than mean absolute shap value!
- within STN classification (motor, associative, limbic), STN vs SN, ...
- Use features with highest shap value to cluster/reclassify
- more complex classifier (e.g. those applying transformations)
- multi-label classification

Institute for Neuromodulation & -technology



Overview

- Stimulating & Recording:
  - Non-invasive: tACS, tDCS, tMS, VNS + EEG
  - Invasive: MER, DBS, (VNS) **in-vivo intracranial subcortical data!**
- Diseases:
  - Parkinson's disease
  - Stroke
  - Motor deficits
  - Some brain tumors, some epilepsy
- Other topics: sleep, plasticity, surgical methods


Neuro

References I

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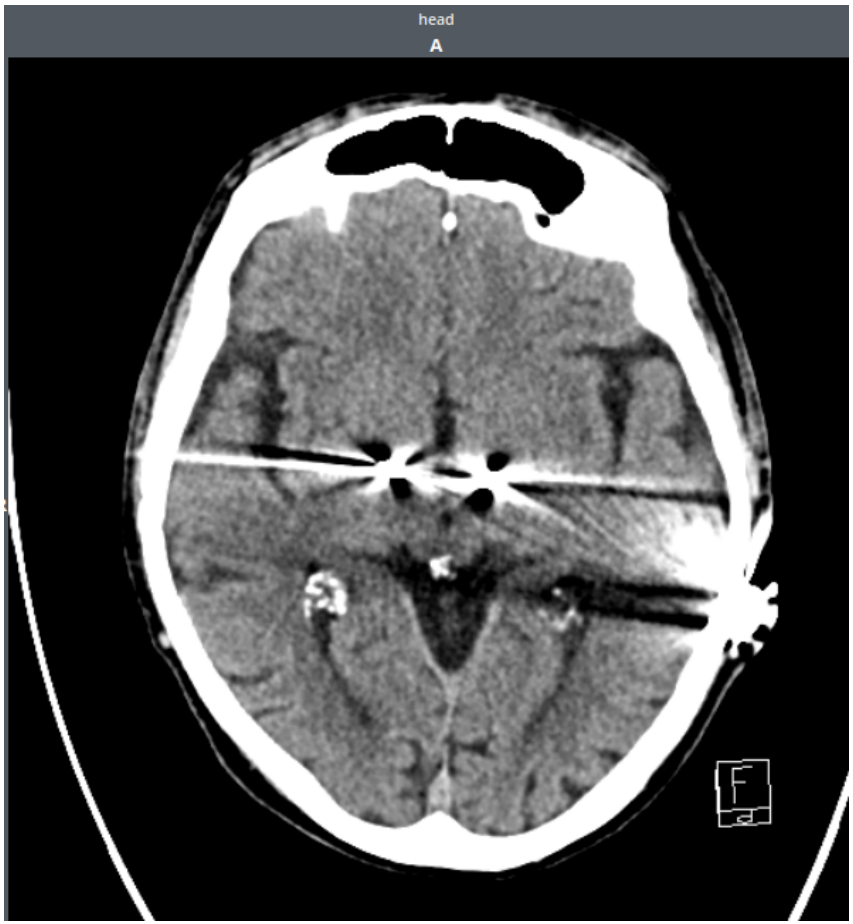
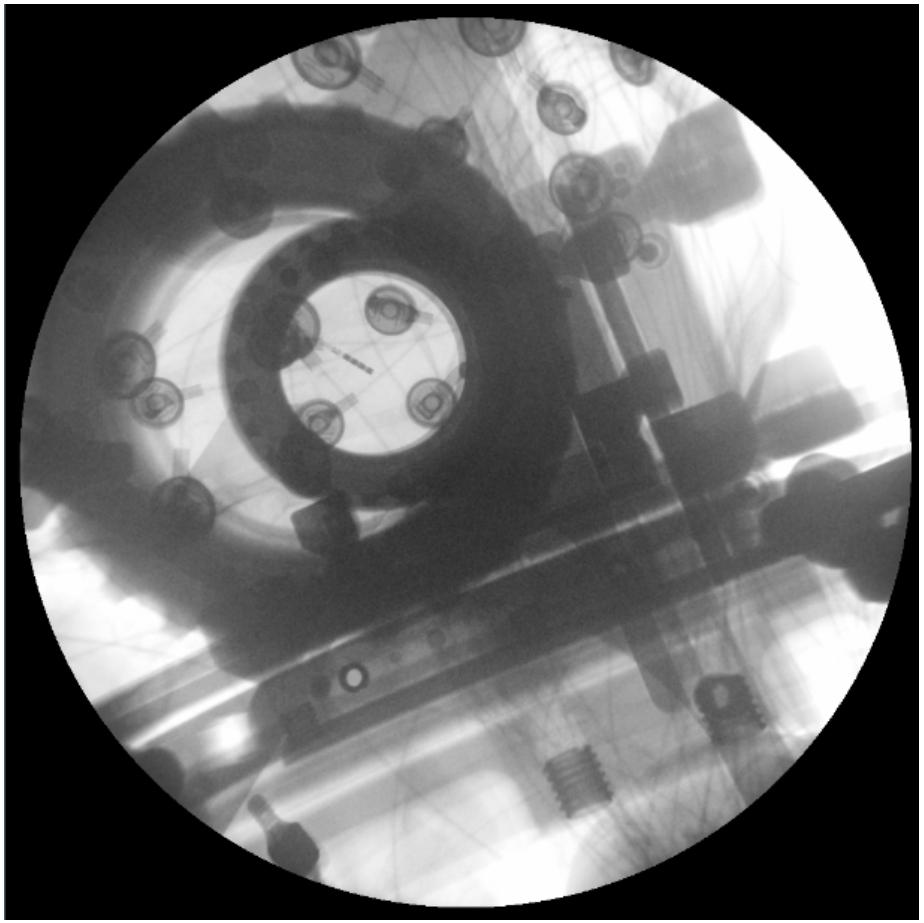
Pre-, Intra- and Post-OP CT I

Pre-, Intra- and Post-OP CT II

Pre-, Intra- and Post-OP CT III



Pre-, Intra- and Post-OP CT IV



Pre-, Intra- and Post-OP CT V