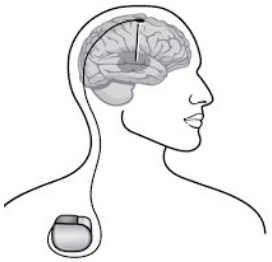
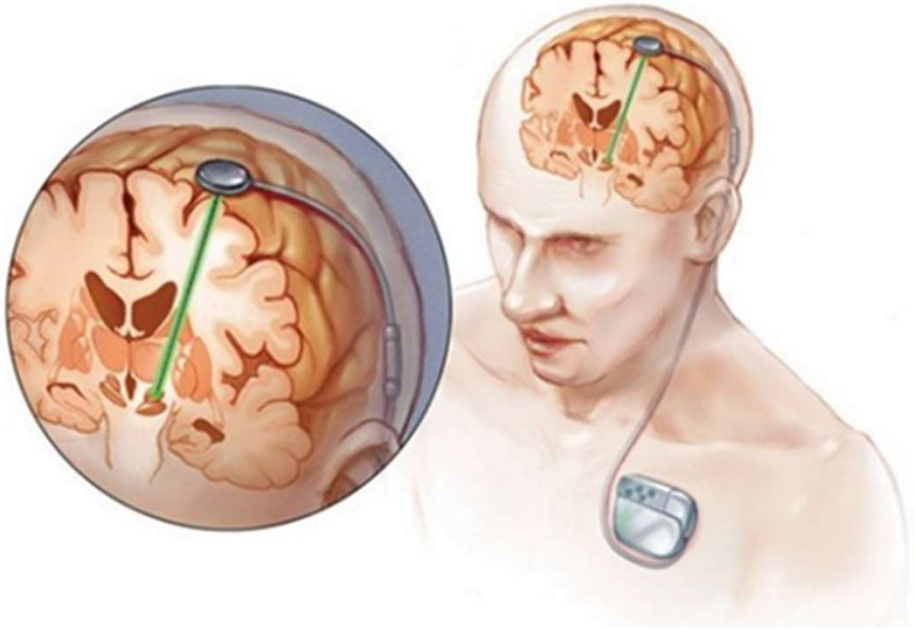
# Hluboká mozková stimulace- klinická praxe, výzkumné směry

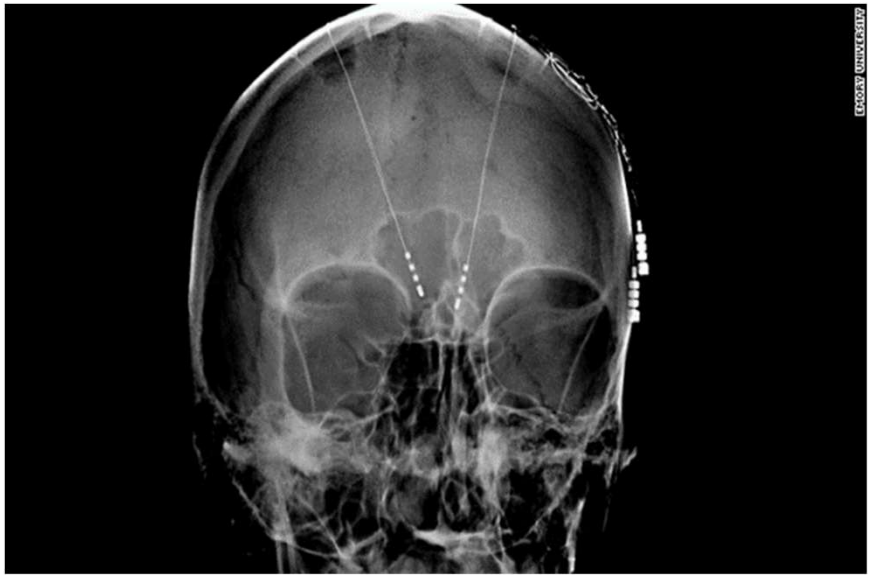
doc. MUDr. Martina Bočková, Ph.D.

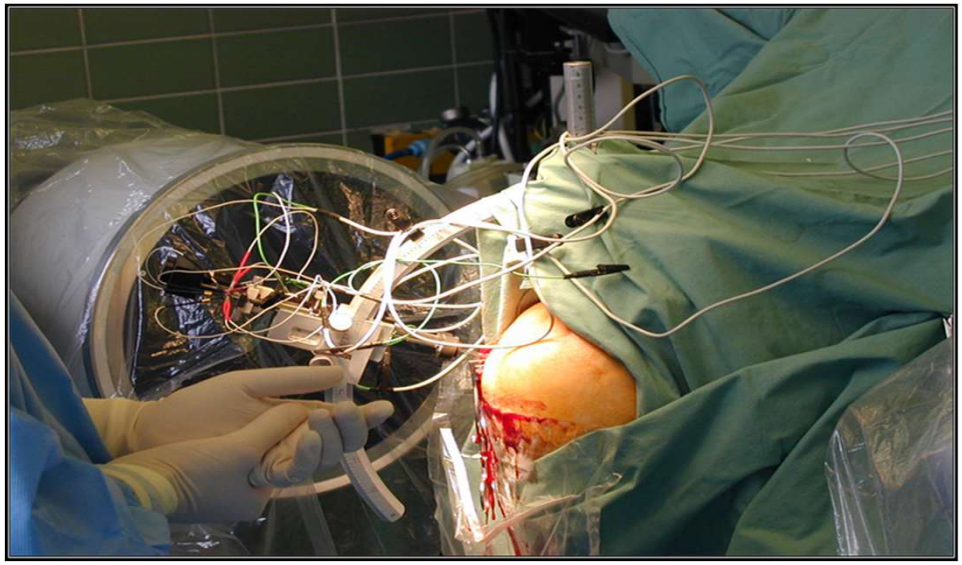
# DBS- hluboká mozková stimulace (deep brain stimulation)



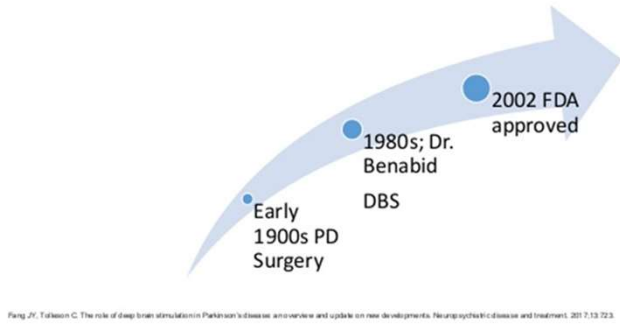
- Moderní chirurgická léčba různých příznaků neurologických a psychiatrických onemocnění
- Stimulace určitých mozkových oblastí prostřednictvím implantovaných elektrod spojených se stimulátorem, který generuje pulzy elektrického napětí
- Nejčastější indikace: *Parkinsonova nemoc* (STN, Gpi), *dystonie* (Gpi), *esenciální třes* (Vim, STN), *farmakorezistetní epilepsie, Tourettův syndrom, deprese a OCD…..*







# Historie DBS



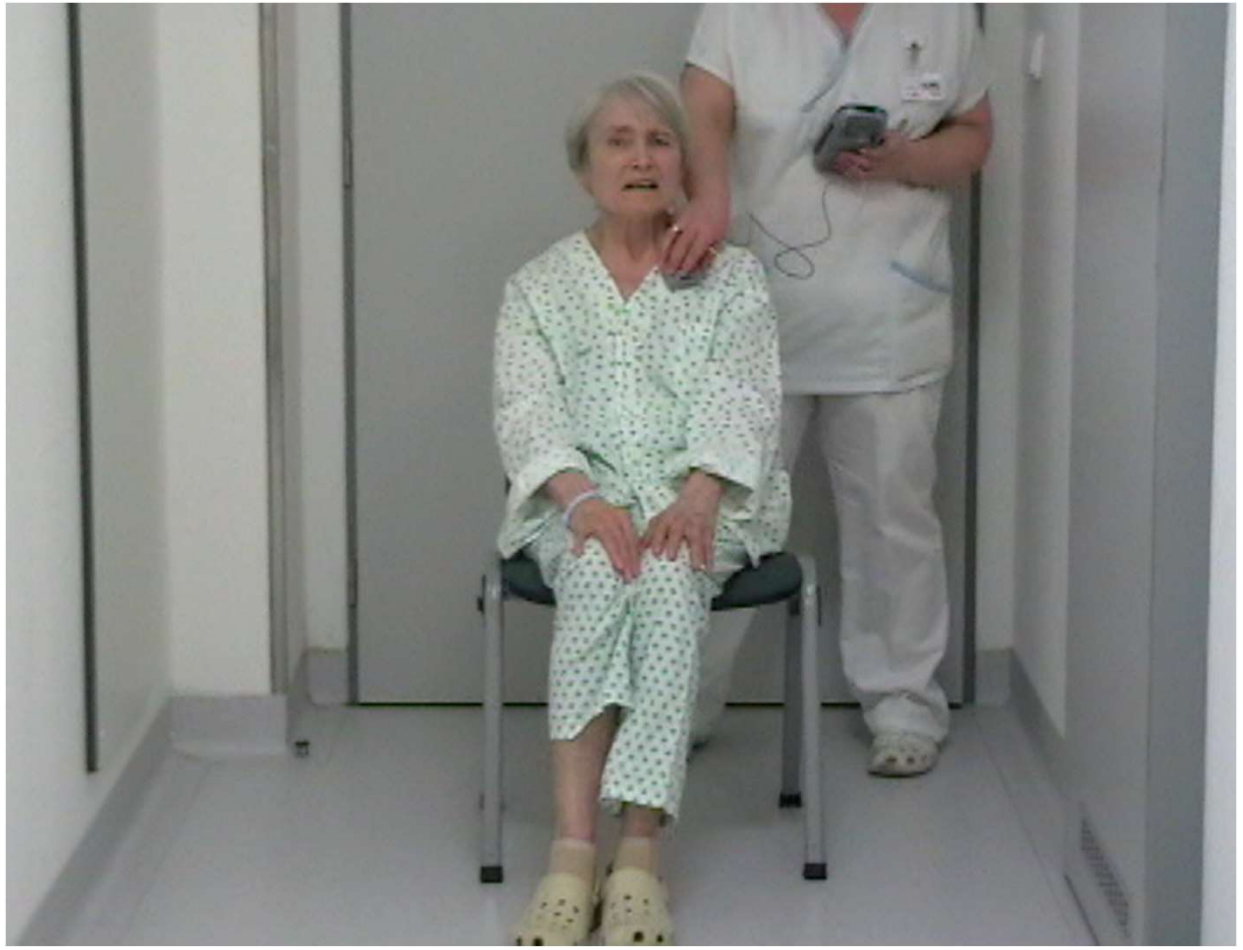

- Navazuje na stereotaktické ablativní výkony
- První moderní DBS v roce 1987 Grenoble (tremor)
- Do klinické praxe v druhé polovině 90. let
- V ČR poprvé v roce 1998 (tremor)
- Celkem více než 175000 pacientů (2020)
- v ČR kolem 1000


- Krack P, Volkmann J, Tinkhauser G, Deuschl G. Deep Brain Stimulation in Movement Disorders: From Experimental Surgery to Evidence-Based Therapy. Mov Disord. 2019 Dec;34(12):1795-1810.

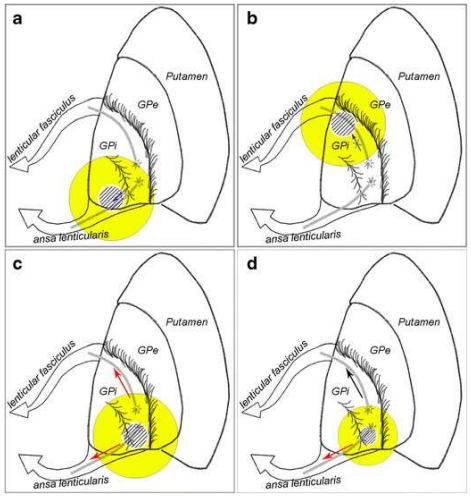
# Video 1- Parkinsonova nemoc

# Video 2- Dystonie

# Video 3- Esenciální třes



# Variabilita účinnosti




- Úspěšnost léčby je variabilní i ve zkušených centrech, což může vést k určité skepsi u ambulantních neurologů i pacientů
- Non-respondérů je cca 25%
- Důležité je správné zacílené stimulované oblasti (VTA- volume of tissue activated)
- Zásadní je správný výběr vhodných kandidátů

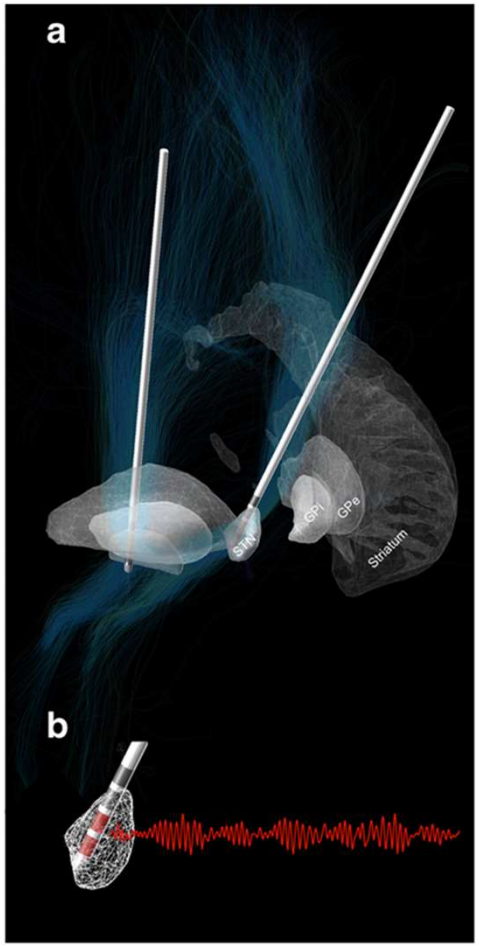

- Krack P, Volkmann J, Tinkhauser G, Deuschl G. Deep Brain Stimulation in Movement Disorders: From Experimental Surgery to Evidence-Based Therapy. Mov Disord. 2019 Dec;34(12):1795-1810.

# Nežádoucí účinky

- Přibývání na váze
- Dysarthrie
- Neuropsychiatrické komplikace (kognitivní poruchy, psychiatrické obtíže)


- Saint-Cyr JA, Trépanier LL, Kumar R, Lozano AM, Lang AE (2000) Neuropsychological consequences of chronic bilateral stimulation of the subthalamic nucleus in Parkinson's disease. Brain 123:2091-2108.
- Temel Y, Kessels A, Tan S, Topdag A, Boon P, Visser-Vandewalle V (2006) Behavioural changes after bilateral subthalamic stimulation in advanced Parkinson disease: a systematic review. Parkinsonism and Related Disorders 12:265-272.
- Witt K, Daniels C, Reiff J, Krack P, Volkmann J, Pinsker MO, et al. (2008) Neuropsychological and psychiatric changes after deep brain stimulation for Parkinson's disease: a randomised, multicentre study. Lancet Neurology 7:605-614.
- Balestrino R, Baroncini D, Fichera M, Donofrio CA, Franzin A, Mortini P, Comi G, Volontè MA. Weight gain after subthalamic nucleus deep brain stimulation in Parkinson's disease is influenced by dyskinesias' reduction and electrodes' position. Neurol Sci. 2017 Dec;38(12):2123-2129.

# Význam elektrofyziologie a pokrok v DBS

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https://doi.org/10.1007/s13311-018-00705-0

REVIEW

# Toward Electrophysiology-Based Intelligent Adaptive Deep Brain Stimulation for Movement Disorders

Wolf-Julian Neumann[1] · Robert S. Turner[2] · Benjamin Blankertz[3] · Tom Mitchell[4] · Andrea A. Kühn[1,5,6] · R. Mark Richardson[7]

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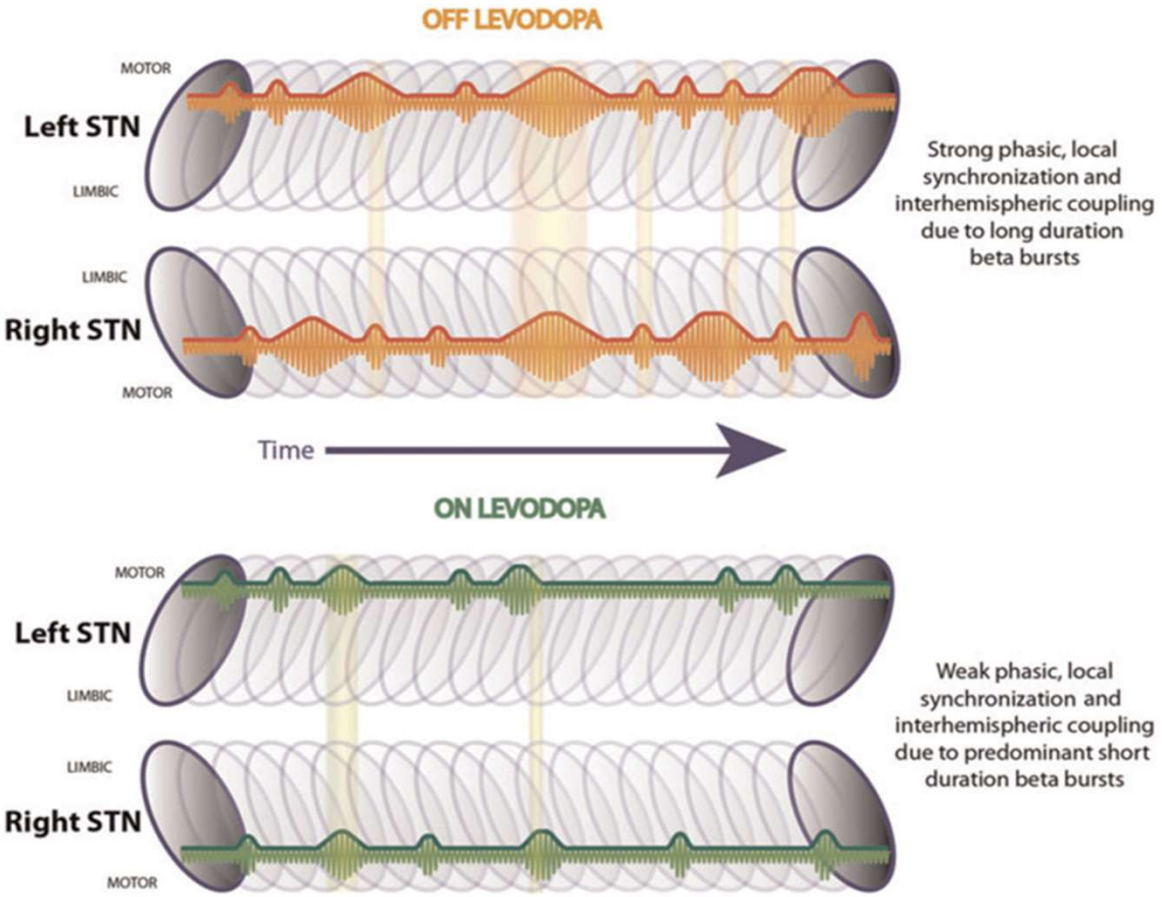
## Abstract

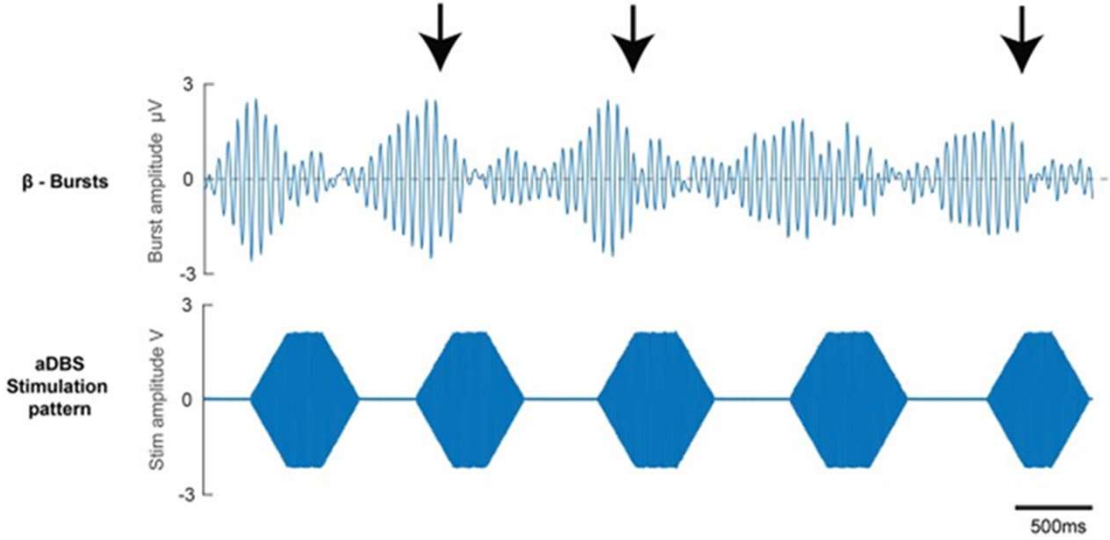
Deep brain stimulation (DBS) represents one of the major clinical breakthroughs in the age of translational neuroscience. In 1987, Benabid and colleagues demonstrated that high-frequency stimulation can mimic the effects of ablative neurosurgery in Parkinson's disease (PD), while offering two key advantages to previous procedures: adjustability and reversibility. Deep brain stimulation is now an established therapeutic approach that robustly alleviates symptoms in patients with movement disorders, such as Parkinson's disease, essential tremor, and dystonia, who present with inadequate or adverse responses to medication. Currently, stimulation electrodes are implanted in specific target regions of the basal ganglia–thalamic circuit and stimulation pulses are delivered chronically. To achieve optimal therapeutic effect, stimulation frequency, amplitude, and pulse width must be adjusted on a patient-specific basis by a movement disorders specialist. The finding that pathological neural activity can be sampled directly from the target region using the DBS electrode has inspired a novel DBS paradigm: closed-loop adaptive DBS (aDBS). The goal of this strategy is to identify pathological and physiologically normal patterns of neuronal activity that can be used to adapt stimulation parameters to the concurrent therapeutic demand. This review will give detailed insight into potential biomarkers and discuss next-generation strategies, implementing advances in artificial intelligence, to further elevate the therapeutic potential of DBS by capitalizing on its modifiable nature. Development of intelligent aDBS, with an ability to deliver highly personalized treatment regimens and to create symptom-specific therapeutic strategies in real-time, could allow for significant further improvements in the quality of life for movement disorders patients with DBS that ultimately could outperform traditional drug treatment.

# Patologická beta 13-35 Hz




- Gerd Tinkhauser, Alek Pogosyan, Huiling Tan, Damian M Herz, Andrea A Kühn, Peter Brown. Beta Burst Dynamics in Parkinson's Disease OFF and ON Dopaminergic Medication. Brain 2017 Nov 1;140(11):2968-2981.

# Adaptivní DBS

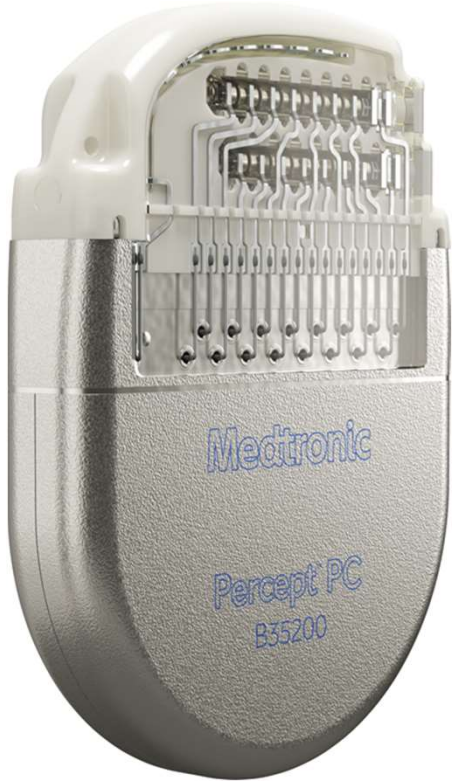



- Optimalizace stimulace, intermitentní na základě aktuálních klinických potřeb pacienta
- Ušetření energie stimulátoru, snížení výskytu nežádoucích účinků

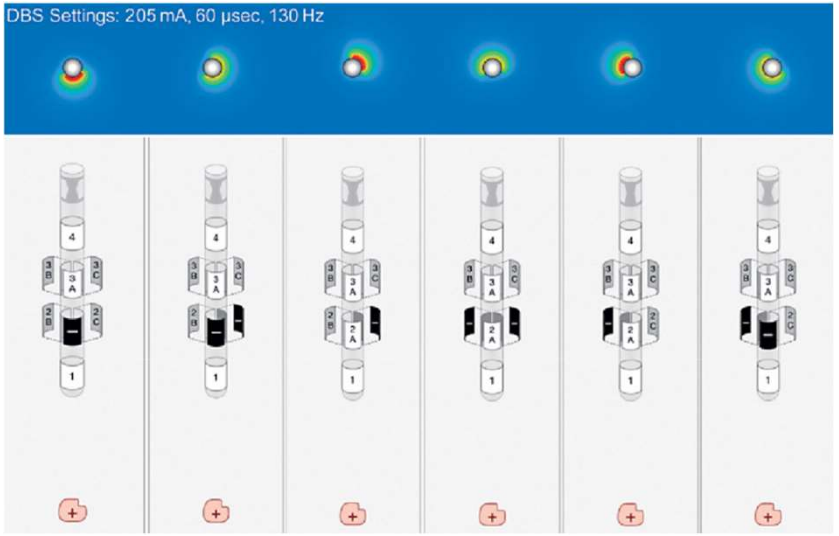

- Gerd Tinkhauser, Alek Pogosyan, Simon Little, Martijn Beudel, Damian M Herz, Huiling Tan, Peter Brown. The Modulatory Effect of Adaptive Deep Brain Stimulation on Beta Bursts in Parkinson's Disease. Brain 2017 Apr 1;140(4):1053-1067.

# Percept

- BrainSense technology
- Kontinuální registrace LFP´s
- MRI kompatibilní i v on stavu, i 3T
- Delší životnost, nový tvar
- Pacientský programátor v mobilním telefonu



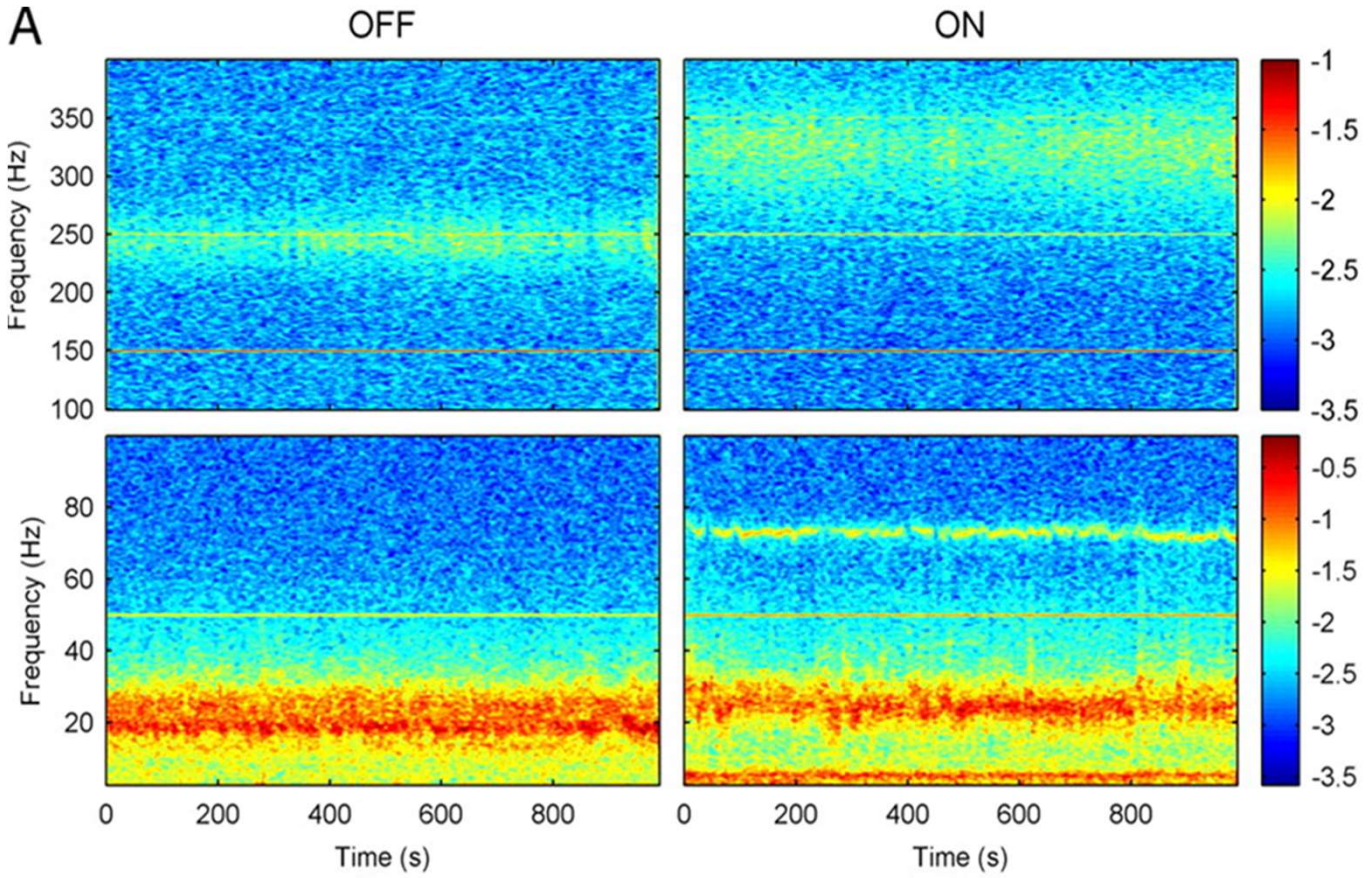
# Stimulační kontakty




- Hodnocení beta výkonu v LFP může pomoci identifikovat nejlepší stimulační kontakty pro klinickou praxi


- Deffains M, Iskhakova L, Katabi S, Israel Z, Bergman H (2018) Longer β oscillatory episodes reliably identify pathological subthalamic activity in Parkinsonism. Mov Disord 33(10):1609-18.
- Tinkhauser G, Pogosyan A, Debove I, Nowacki A, Shah SA, Seidel K, et al. (2018) Directional local field potentials: A tool to optimize deep brain stimulation. Mov Disord 33(1):159-164.

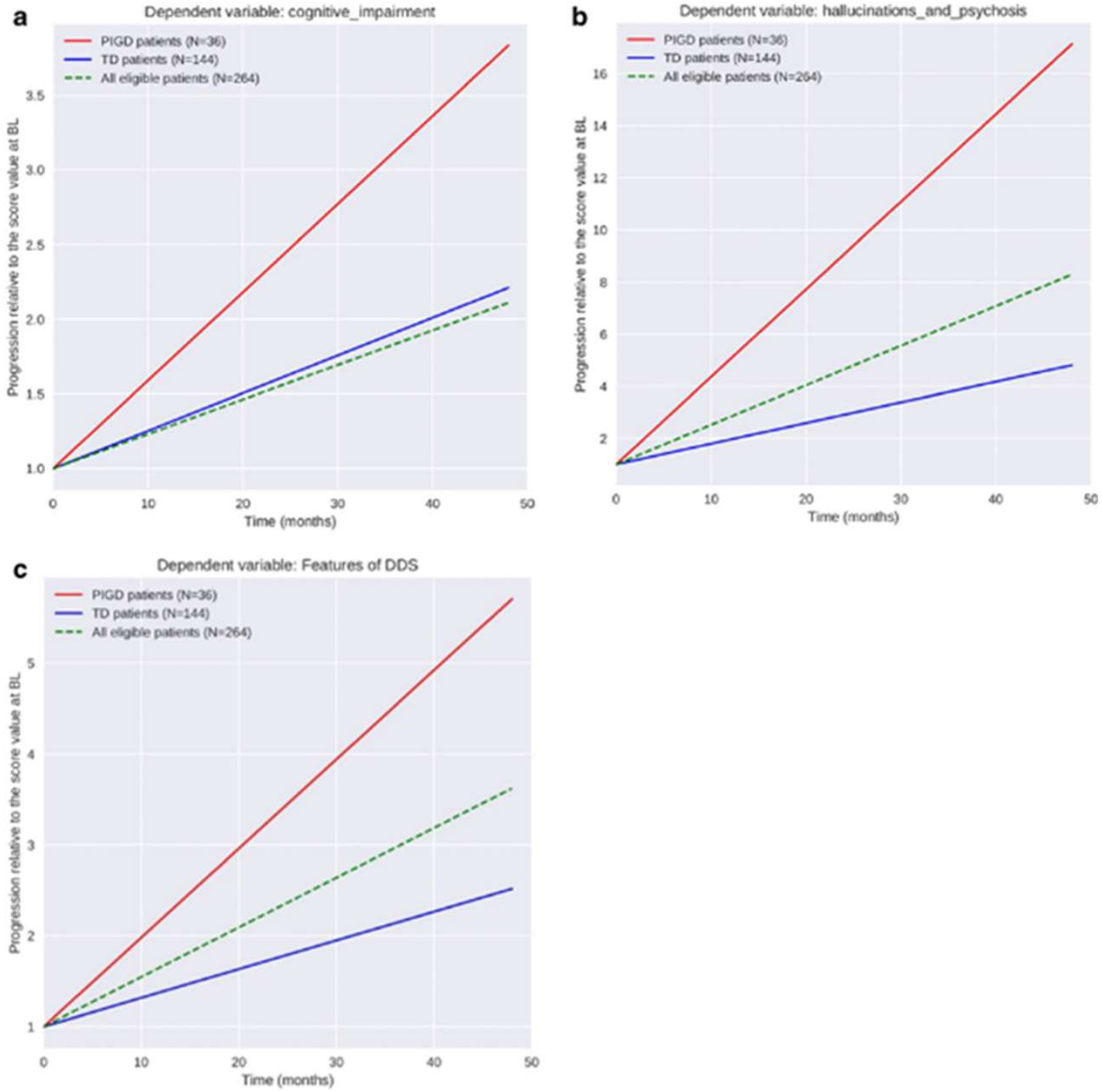
# Další markery a vstupní signály



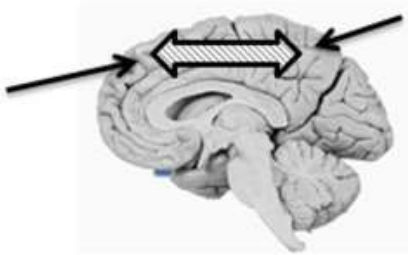

López-Azcárate J, Tainta M, Rodríguez-Oroz MC, Valencia M, González R, Guridi J, Iriarte J, Obeso JA, Artieda J, Alegre M. Coupling between beta and high-frequency activity in the human subthalamic nucleus may be a pathophysiological mechanism in Parkinson's disease. J Neurosci. 2010 May 12;30(19):6667-77.

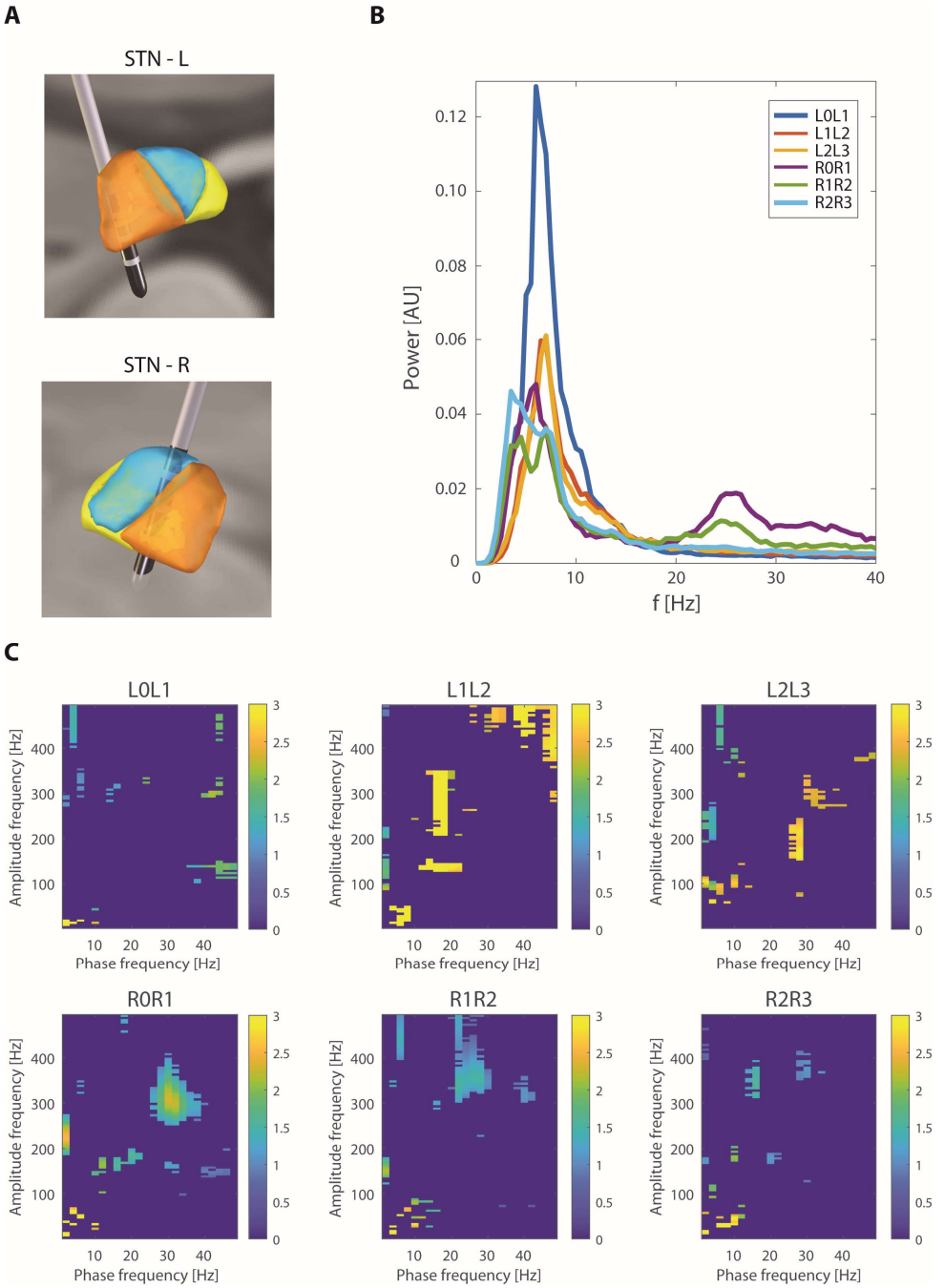
# Fenotypy PN

- Tremor- dominantní
- PIGD dominantní

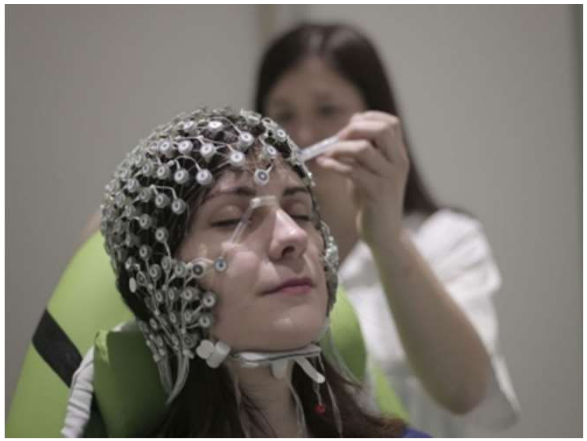


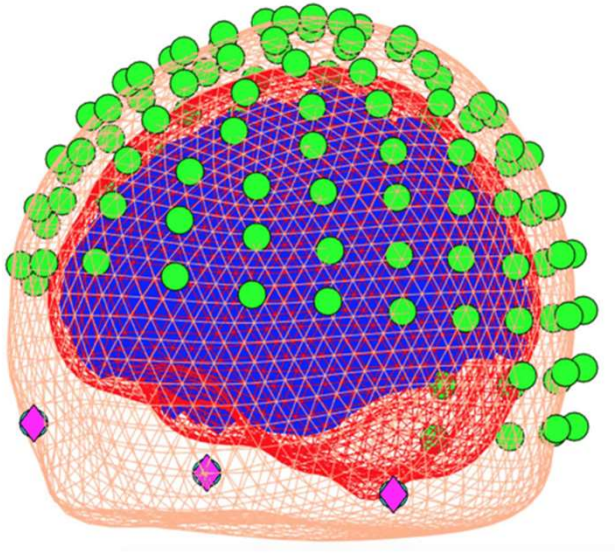

Darko Aleksovski, Dragana Miljkovic, Daniele Bravi, Angelo Antonini. Disease Progression in Parkinson Subtypes: The PPMI Dataset. Neurol Sci 2018, 39 (11), 1971-1976.

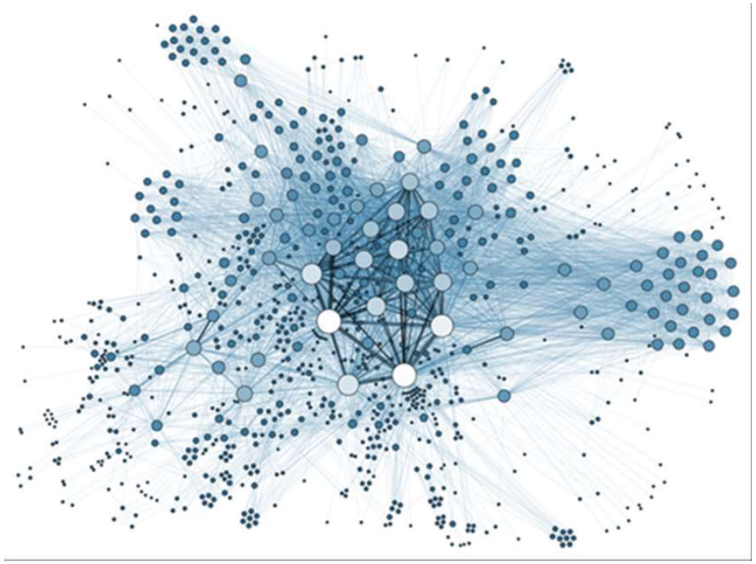
| Brainstem route[3] | Consequent phenotype | NMS dominant profile (subtype) |
|---|---|---|
|  | Brainstem dominant (often with late onset hyposmia) | Sleep dysfunction (RBD/EDS)<br>Dysautonomia (Adrenergic) |
| Olfactory to limbic[2] | | |
|  | Limbic dominant (often with anosmia) | Depression/Anxiety<br>Fatigue (Sertonergic?)<br>Central Pain (Opioidergic?)<br>Weight loss |
| Cognitive (Neocortical subtype) [13,14] | | |
|  | Cognitive dominant (late onset PD) | Amnestic MCI (Cholinergic)<br>Apathy<br>Anxiety<br>Falls with cognitive impairment |


A
STN - L
STN - R
B
Power [AU]
f [Hz]
L0L1
L1L2
L2L3
R0R1
R1R2
R2R3
C
L0L1
L1L2
L2L3
R0R1
R1R2
R2R3
Amplitude frequency [Hz]
Phase frequency [Hz]

# Skalpové EEG







- Nové akviziční systémy- HD EEG s 256 kanály
- Pokročilé analytické metody- např. objemová rekonstrukce, síťová analýza, konektivita, mikrostavy…


- Bočková M, Rektor I. Impairment of brain functions in Parkinson's disease reflected by alterations in neural connectivity in EEG studies: A viewpoint. Clin Neurophysiol. 2018;130(2):239-247.

HUMAN BRAIN MAPPING
Open Access

RESEARCH ARTICLE | Open Access

# Cortical network organization reflects clinical response to subthalamic nucleus deep brain stimulation in Parkinson's disease

Martina Bočková, Eva Výtvarová, Martin Lamoš, Petr Klimeš, Pavel Jurák, Josef Halámek, Sabina Goldemundová, Marek Baláž, Ivan Rektor

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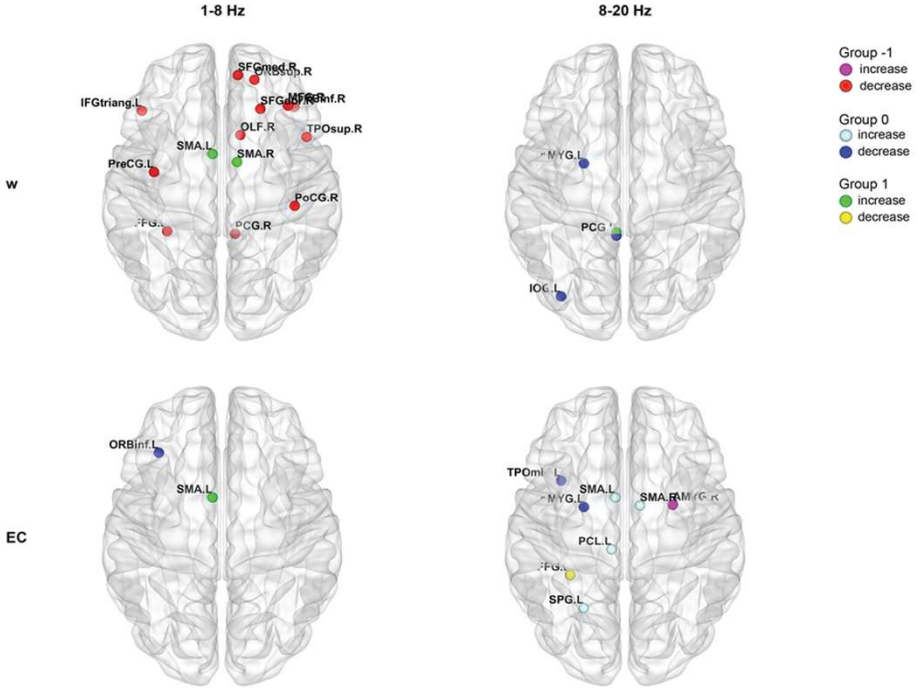

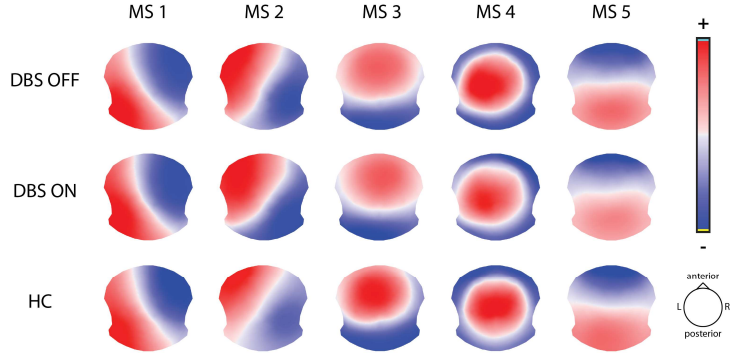


npj | parkinson's disease

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ARTICLE OPEN

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# The effect of deep brain stimulation in Parkinson's disease reflected in EEG microstates

Martin Lamoš[1], Martina Bočková[1,2], Sabina Goldemundová[1], Marek Baláž[1,2], Jan Chrastina[1,3] and Ivan Rektor[1,2]✉

Mechanisms of deep brain stimulation (DBS) on cortical networks were explored mainly by fMRI. Advanced analysis of high-density EEG is a source of additional information and may provide clinically useful biomarkers. The presented study evaluates EEG microstates in Parkinson's disease and the effect of DBS of the subthalamic nucleus (STN). The association between revealed spatiotemporal dynamics of brain networks and changes in oscillatory activity and clinical examination were assessed. Thirty-seven patients with Parkinson's disease treated by STN-DBS underwent two sessions (OFF and ON stimulation conditions) of resting-state EEG. EEG microstates were analyzed in patient recordings and in a matched healthy control dataset. Microstate parameters were then compared across groups and were correlated with clinical and neuropsychological scores. Of the five revealed microstates, two differed between Parkinson's disease patients and healthy controls. Another microstate differed between ON and OFF stimulation conditions in the patient group and restored parameters in the ON stimulation state toward to healthy values. The mean beta power of that microstate was the highest in patients during the OFF stimulation condition and the lowest in healthy controls; sources were localized mainly in the supplementary motor area. Changes in microstate parameters correlated with UPDRS and neuropsychological scores. Disease specific alterations in the spatiotemporal dynamics of large-scale brain networks can be described by EEG microstates. The approach can reveal changes reflecting the effect of DBS on PD motor symptoms as well as changes probably related to non-motor symptoms not influenced by DBS.

*npj Parkinson's Disease* (2023)9:63 ; https://doi.org/10.1038/s41531-023-00508-x

# Současný výzkum

- **GAČR 21-25953S**

Subcortical nuclei and cortical functions – insights from deep brain stimulation perspective

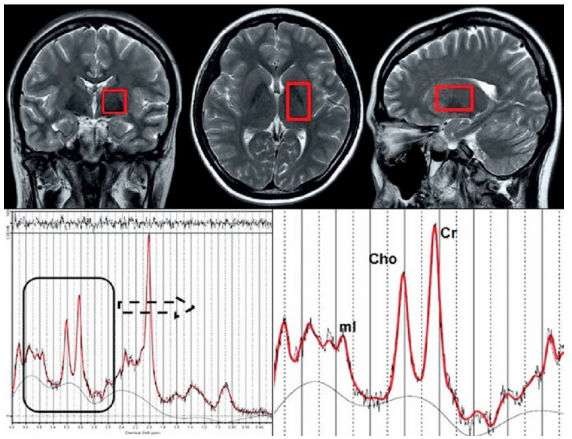
- **AZV NU21-04-00445**

STN-DBS outcomes in Parkinson´s disease: the influence of vascular, cardiovascular, metabolic, and inflammatory co-morbidities

- **NPO**

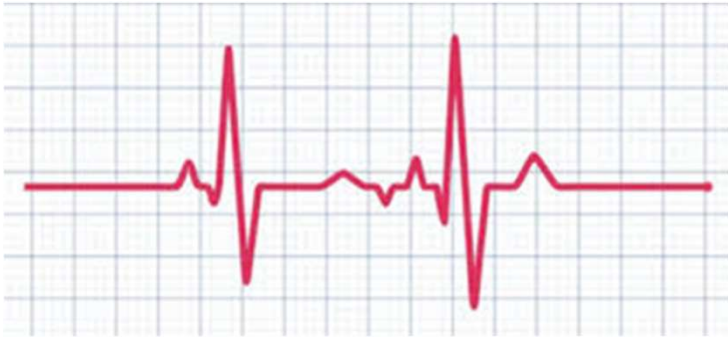
Individual brain sensing: a key step in adaptive deep brain stimulation

# Klinické parametry




- MRI (změny bílé hmoty, MR spektroskopie (SMA, BG), fMRI)
- Metabolické faktory- (metabolický screening, kys. močová, B12, foláty, lipidy..)
- Zánětlivé parametry- (CRP, C3 a C4 složky komplementu, TNF alfa a IL6
- Neuropsychologické vyšetření, klinické škály

# Kardiovaskulární symptomy a komorbidity



- Ortostatická hypotenze
- Porucha kardiální sympatické inervace (MIBG SPECT)
- Chronotropní insuficience při zátěžových testech


- Palma JA, Carmona-Abellan MM, Barriobero N, Trevino-Peinado C, Garcia-Lopez M, Fernandez-Jarne E, et al. Is cardiac function impaired in premotor Parkinson's disease? A retrospective cohort study. Mov Disord. 2013; 28:591–6.

Movement Disorders
CLINICAL PRACTICE

REVIEW

# Cardiac Involvement in Movement Disorders

*Malco Rossi, MD, PhD,*[1,2,*] *Nestor Wainsztein, MD, FCCP, FCCM, FAHA,*[3] *and Marcelo Merello, MD, PhD*[1,2,4]

**ABSTRACT:** Background: Several conditions represented mainly by movement disorders are associated with cardiac disease, which can be overlooked in clinical practice in the context of a prominent primary neurological disorder.

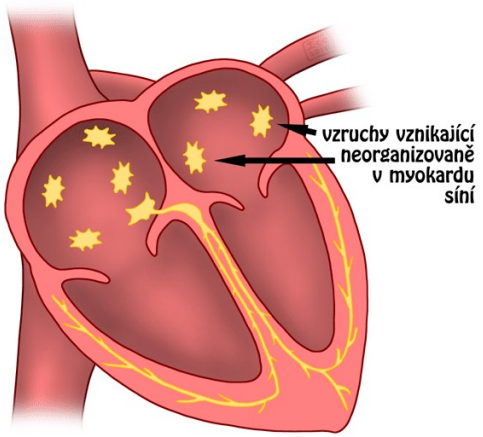
Objectives: To review neurological conditions that combine movement disorders and primary cardiac involvement.

Methods: A comprehensive and structured literature search following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses criteria was conducted to identify disorders combining movement disorders and cardiac disease.

Results: Some movement disorders are commonly or prominently associated with cardiac disease. Neurological and cardiac symptoms may share underlying physiopathological mechanisms in diseases, such as Friedreich's ataxia and Wilson's disease, and in certain metabolic disorders, including Refsum disease, Gaucher disease, a congenital disorder of glycosylation, or cerebrotendinous xanthomatosis. In certain conditions, such as Sydenham's chorea or dilated cardiomyopathy with ataxia syndrome (ATX-*DNAJC19*), heart involvement can present early in the course of disease, whereas in others such as Friedreich's ataxia or Refsum disease, cardiac symptoms tend to present in later stages. In another 68 acquired or inherited conditions, cardiac involvement or movement disorders are seldom reported.

Conclusions: As cardiac disease is part of the phenotypic spectrum of several movement disorders, heart involvement should be carefully investigated and increased awareness of this association encouraged as it may represent a leading cause of morbidity and mortality.

# Předběžné výsledky




- Dle EKG Holterů vyšší výskyt SV arytmií- extrasystolie, fibrilace síní
- Paroxysmální fibrilace síní (36%), normální prevalence je 5% (u populace nad 65 let)
- Dle MRI rozšíření levé komory i levé síně oproti zdravým kontrolám

- doc. MUDr. Vladimír Kincl, Ph.D. a doc. MUDr. Roman Panovský, Ph.D.- submitováno

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