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Deep brain stimulation of the subthalamic nucleus normalizes Parkinson's disease related abnormalities of auditory evoked potentials and quantitative EEG

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Introduction

Some of the cardinal symptoms of Parkinson´s disease (PD) share a pathological **rhythmic dysregulation** as common feature

Involuntary movements
- Resting tremor

Voluntary movements
- Hastened gait vs. freezing
- Stuttering
- Progressive miniaturization of handwriting
- Difficulty to follow a given rhythm

Our hypothesis:

Parkinson patients are induced to switch to an „internal" pathological rhythm which seems to pace their motor actions

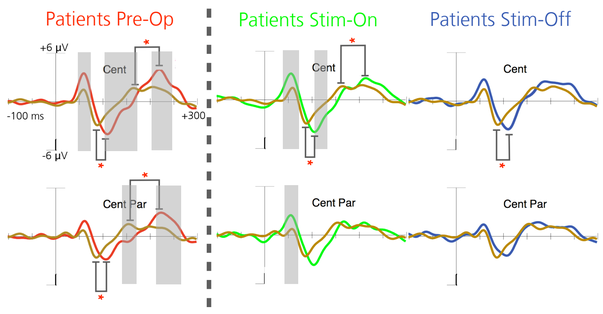
- Following a **rhythmic music helps** PD patients to overcome their motor impairments
- Frequencies between **1** and **2 Hz** (like music or counting), are particularly helpful for patients to **move more fluently**
- Some companies offer **pocket-metronoms** to give patients pulses to synchronize with
- All this points to a **sensorimotor interaction** between pathological Parkinson motoric and external rhythms

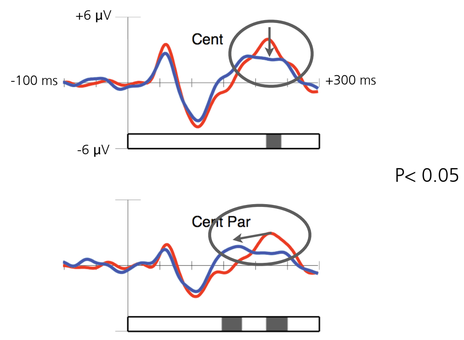
Sensorimotor interaction is important for advanced PD patients to overcome motor impairments

Experimental questions related to **sensory** processing in the auditory domain:

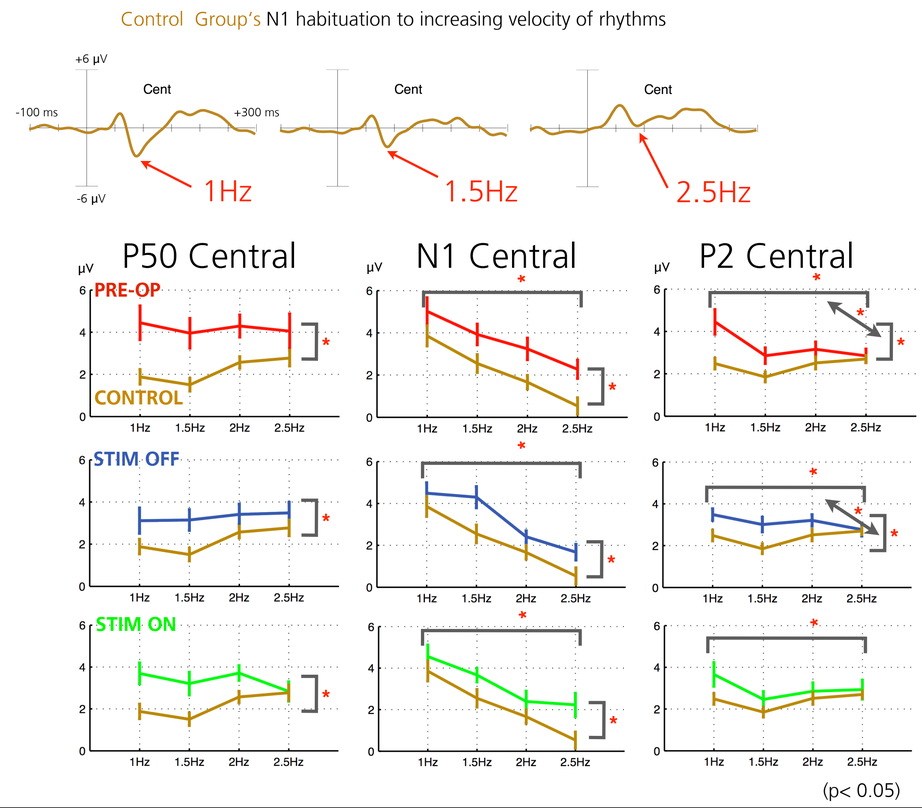
- *Is the auditory processing of rhythmic stimuli in PD patients altered?*
- *Do rhythms at different frequencies have distinct effects on auditory processing ?*
- *Does STN-DBS modulate the auditory information processing in advanced PD patients?*

Results I: 1 Hz auditory stimulatiotion



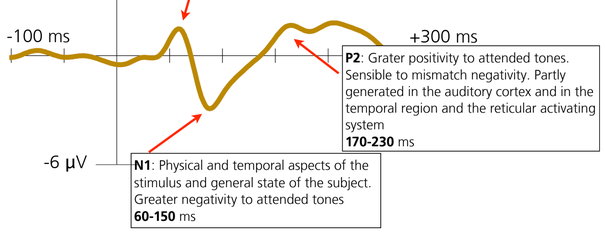


Results II: From I to 2,5 Hz auditory stimulation: habituation effects of the ISIs on the AEPs



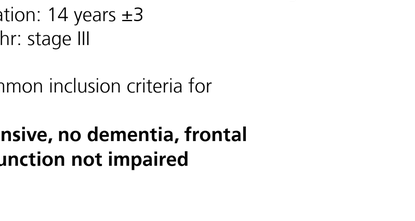
Methods

Metronome-like clicks presented in 4 rhythms at 70 dB(SPL)



2 EEG recordings sessions:

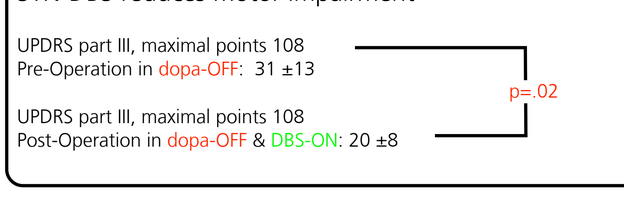
- 1 week **before** stereotactic intervention and
- 5 months **after** chronic STN DBS-stimulation, with high-frequency DBS **ON** & **OFF**



Which kind of signals did we record and analyzed?

- Event related potentials (**ERPs**) are very small electrical voltage potentials originating from the brain recorded from the scalp in response to a stimulus
- For auditory evoked potentials (**AEPs**), the "event" is a sound (**metronome like clicks**)

Central auditory ERPs in the Control Group:1Hz stimulus



Participants

12 advanced **Parkinson's disease patients** in Dopa-Off state

Age: 61±6
Disease duration: 14 years ±3
Hoehn & Yahr: stage III

Fulfilling common inclusion criteria for STN-DBS:
Dopa responsive, no dementia, frontal executive function not impaired

12 healthy **control persons** matched for age, gender and education

Age: 65±8

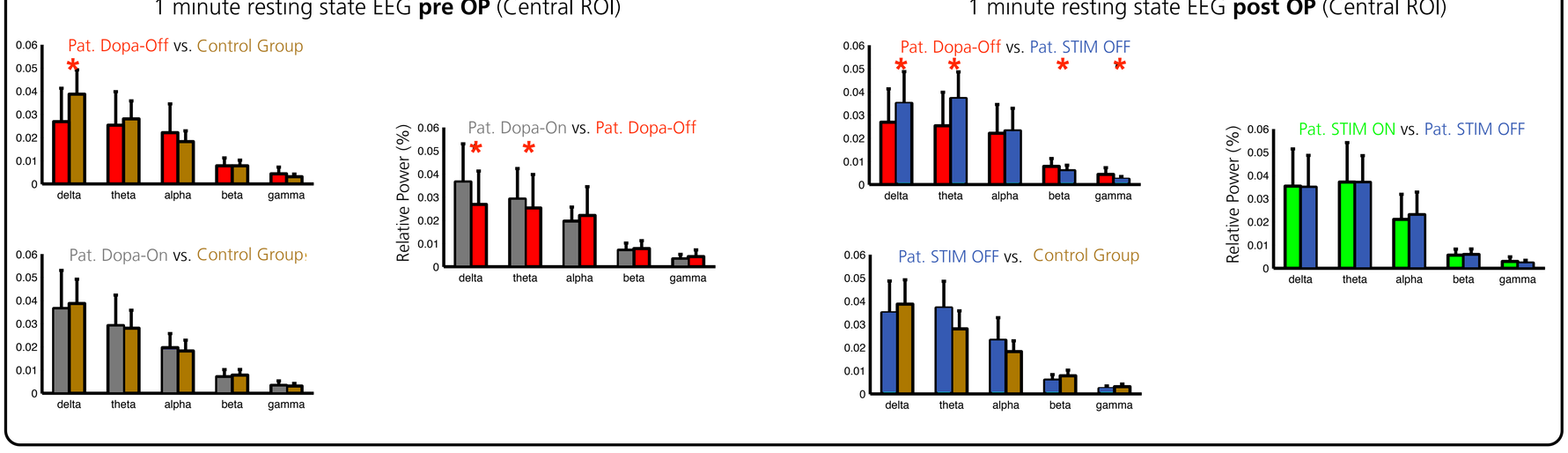
STN-DBS reduces motor impairment

UPDRS part III, maximal points 108
Pre-Operation in dopa-OFF: 31 ±13

UPDRS part III, maximal points 108
Post-Operation in dopa-OFF & DBS-ON: 20 ±8

p=.02

Results III: Effects of treatment on 1minute resting state EEG



Results I: 1 Hz auditory stimulation

- In PD patients the amplitudes of the auditory P50, N1 and P2 components are larger compared to control group amplitudes
- PD patients show an unusually large P50 amplitude in the frontal and central areas
- In PD patients the latencies for N1 and P2 are significantly longer than the control group latencies
- After operations, patients' P2 amplitudes are no longer significantly different from controls' P2 amplitudes

Results II: Different rhythm conditions

- In PD patients the amplitudes of the ERPs show a linear habituation to increasing velocity of rhythms (decreasing ISIs) like the control group, but the amplitudes are always significantly larger
- Particularly before the operation, the amplitude of the PD patients' P2 is strongly modulated by the frequency of the rhythms

Summary of the results: patients vs. control group

pre OP	Latency	Amplitude	Habituation
P50	n.s.	↑	n.s.
N1	↑	↑	n.s.
P2	↑	↑	↓

post OP	Latency	Amplitude	Habituation
P50	n.s.	↑	n.s.
N1	↑	↑	n.s.
P2	n.s	n.s	n.s

pre OP	Delta
EEG	↓

post OP	Delta
EEG	n.s

Results III: Effects of treatment on 1minute resting state EEG

- Levodopa shows a normalizing effect on the low-frequency activity (increase of delta and theta power)
- Long lasting STN-DBS shows a similar normalizing effect on resting state EEG like levodopa therapy (increase of delta and theta power)
- We could not find any significant difference between the two post-operative conditions: Stimulation ON vs. Stimulation OFF

Discussion

Prior to surgery, PD patients showed significantly larger AEP amplitudes (P50, N1 and P2) in central and frontal areas compared to controls. Moreover, compared to controls N1 and P2- latencies were significantly increased and AEP habituation reduced in PD patients. In the resting state EEG recordings we observed a significant reduction of delta and theta power in the dopa-off state. Levodopa therapy, electrode implantation per se as well as STN-DBS had a normalizing effect on low-frequency EEG-activity and AEPs. In particular, high-frequency STN-DBS led to a normalization of P2, but not P50 and N1 amplitudes. We could not find any significant difference between the two post-operative conditions: Stimulation ON vs. Stimulation OFF. One Possible explanation could be the long lasting effects of chronic High-frequency DBS. Due to long lasting plastic neuronal changing, switching off the stimulator for 20 minutes is probably not enough to re-stabilize the pre-operative resting-EEG and auditory processing state.

Conclusions

- **Reduced AEPs habituation** supports and expands previous reports of **dysregulated auditory-** and **attentional-processing in PD**
- **STN-DBS** differentially **affects resting state EEG** as well as the **auditory evoked responses** and may thus also **influence sensorimotor processing at higher order sensory levels**

References

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