Impact of subthalamic deep brain stimulation on auditory information processing in patients with advanced Parkinson´s disease

Universitätsklinikum Hamburg-Eppendorf

A. Gulberti[1], C.K.E Moll[1], T.R. Schneider[1], W. Hamel[2], A. Münchau[3], C. Buhmann[3], Kai Boelmans[3], S. Zittel[3], C. Gerloff[3], M. Westphal[2], A.K. Engel[1]

[1] Department of Neurophysiology and Pathophysiology,
[2] Department of Neurosurgery, [3]Department of Neurology
University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Introduction

Some of the cardinal symptoms of Parkinson´s disease (PD) share a pathological rhythmic dysregulation as common feature. Involuntary movements like resting tremor or impaired voluntary movements like hastened gait, freezing, stuttering, progressive miniaturization of handwriting or difficulty to follow a given rhythm indicate a disturbing rhythmicity within cortical and subcortical networks involving also the basal ganglia. Parkinson patients are induced to switch to an „internal" pathological rhythm which seems to pace their motor actions.

Sensori-motor interaction is important for advanced Parkinson's disease (PD) patients to overcome motor impairments. For instance following rhythmic music can help PD patients to overcome freezings. In most cases rhythms between 1 and 2 Hz (like music or counting) particularly help patients to move more fluently. In fact some companies offer pocket-metronomes to give patients pulses to synchronize with. All this points to a sensorimotor interaction between pathological Parkinsonian motor impairments and external rhythms. We investigated the early stages of sensorimotor integration and tried to define the most salient features on a pure sensory level for the sensorimotor interaction.

- 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?

Bilateral deep brain stimulation (DBS) of the subthalamic nucleus (STN) clearly improves dopamine-dependent motor deficits in patients with Parkinson's disease (PD). While there is evidence for dopaminergic sensitivity of central sensory processing, the effects of DBS on sensory information processing are less clear.

We therefore investigated the effects of STN-DBS on auditory information processing, using auditory evoked potentials (AEP). To this end, we compared amplitude, latency and habituation of AEPs in 12 patients with advanced PD to those of age and education matched controls.

In contrast to the numerous studies of peak latencies, there have been few studies that have examined amplitude changes in Parkinson's disease.

In general, peak amplitudes provide a measure of the amount of mental effort required in a task and the amount of capacity used in evaluating the significance of the stimuli. For example, in the oddball task, N1 amplitude is considered a measure of the general state of the subject and their capacity for stimulus discrimination, and stimulus feature selection. N2 amplitude measures the attentional effort required in stimulus categorization and therefore target detection (Wright, 1995).

The N1 components, are controlled by the physical and temporal aspects of the stimulus and by the general state of the subject. The other three components are not necessarily elicited by a stimulus but depend on the conditions in which the stimulus occurs (Näätänen, 1987).

Patients and methods

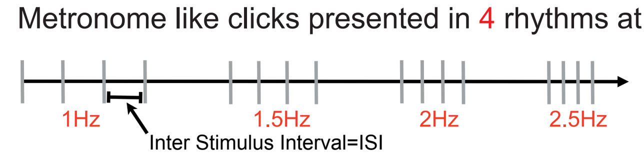
The stimulus paradigm consisted of rhythmic metronome-like clicks presented at 4 different inter-stimulus intervals (ISI): 1Hz, 1.5 Hz, 2Hz and 2.5 Hz rhythms. 64-channel high-density EEG was recorded prior to and 3-12 months following surgery for STN-DBS in the practically defined OFF-state. We studied the effects of STN-DBS at different stimulation frequencies (5, 20 and 130 Hz).

Patients and methods

	Sex	Age	Education (years)	Smell test /40	MCST Modified Wisconsin (persev. errors)	Stroop Test (seconds)	Hoehn & Yahr stage (0-5)	Disease duration (years)	DBS duration (months)	UPDRS part III (Dopa-off) pre Op /108	UPDRS part III (Dopa-off, Stim-on) post Op /108	MDRS (Mattis Dementia Rating Scale) /144	MMST (Mini-mental) /30	Gait and Falls Questionnaire (GFQ) pre Op /64	Gait and Falls Questionnaire (GFQ) post Op /64
12 Patients	7 female	61 ±6	13 ±4	20 ±9	2 ±2	39 ±13	3 ±1	14 ±3	5 ±2	31 ±13	20 ±8	143	29 ±1	21 ±17	15 ±12
P-value		0.2	0.2	<0.001		0.97				0.02				0.3	
12 Controls	8 female	65 ±8	15 ±3	32 ±4	1 ±1	39 ±8									

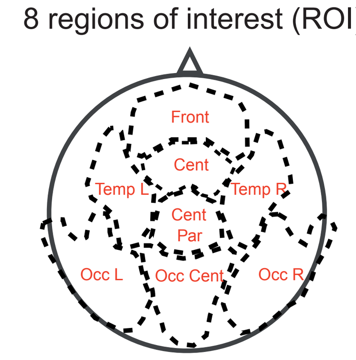
EXPERIMENTAL DESIGN

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

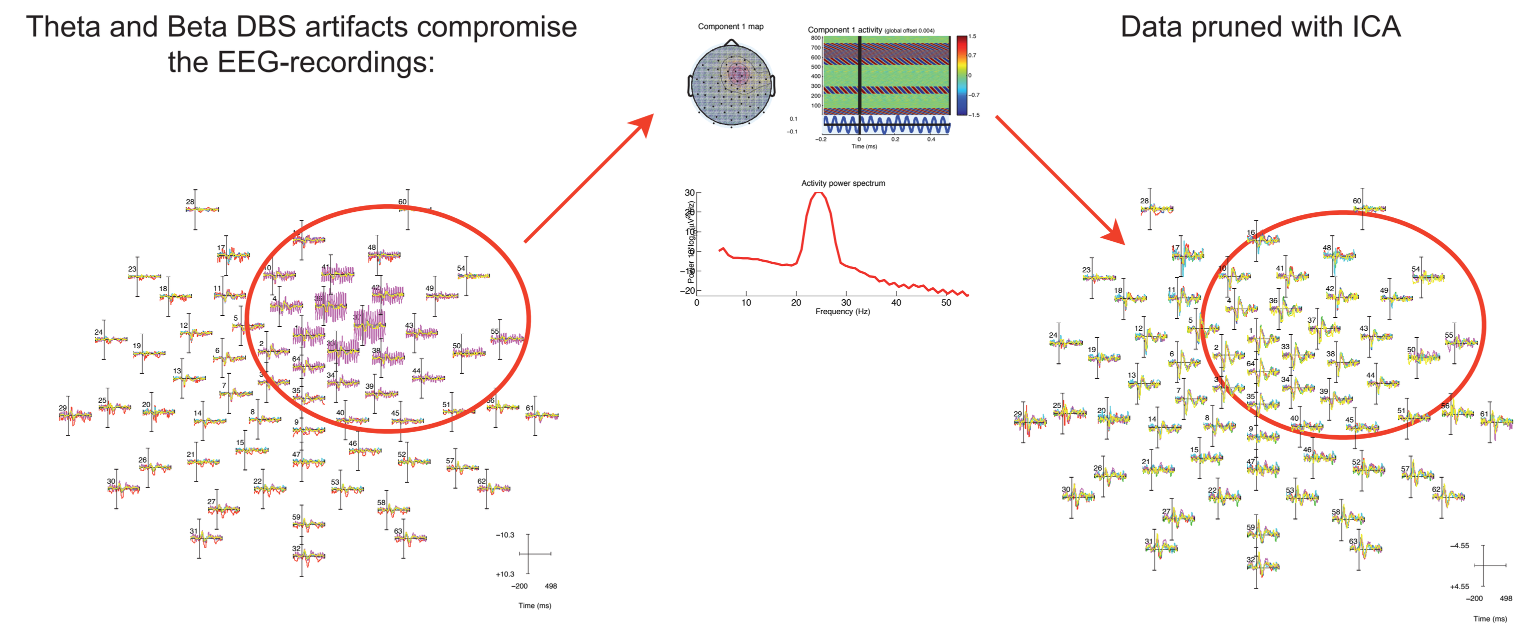


Two recording sessions:
- 1 week **before** stereotactic intervention and
- 5 months **after** chronic STN DBS-stimulation, with high-frequency DBS ON & OFF

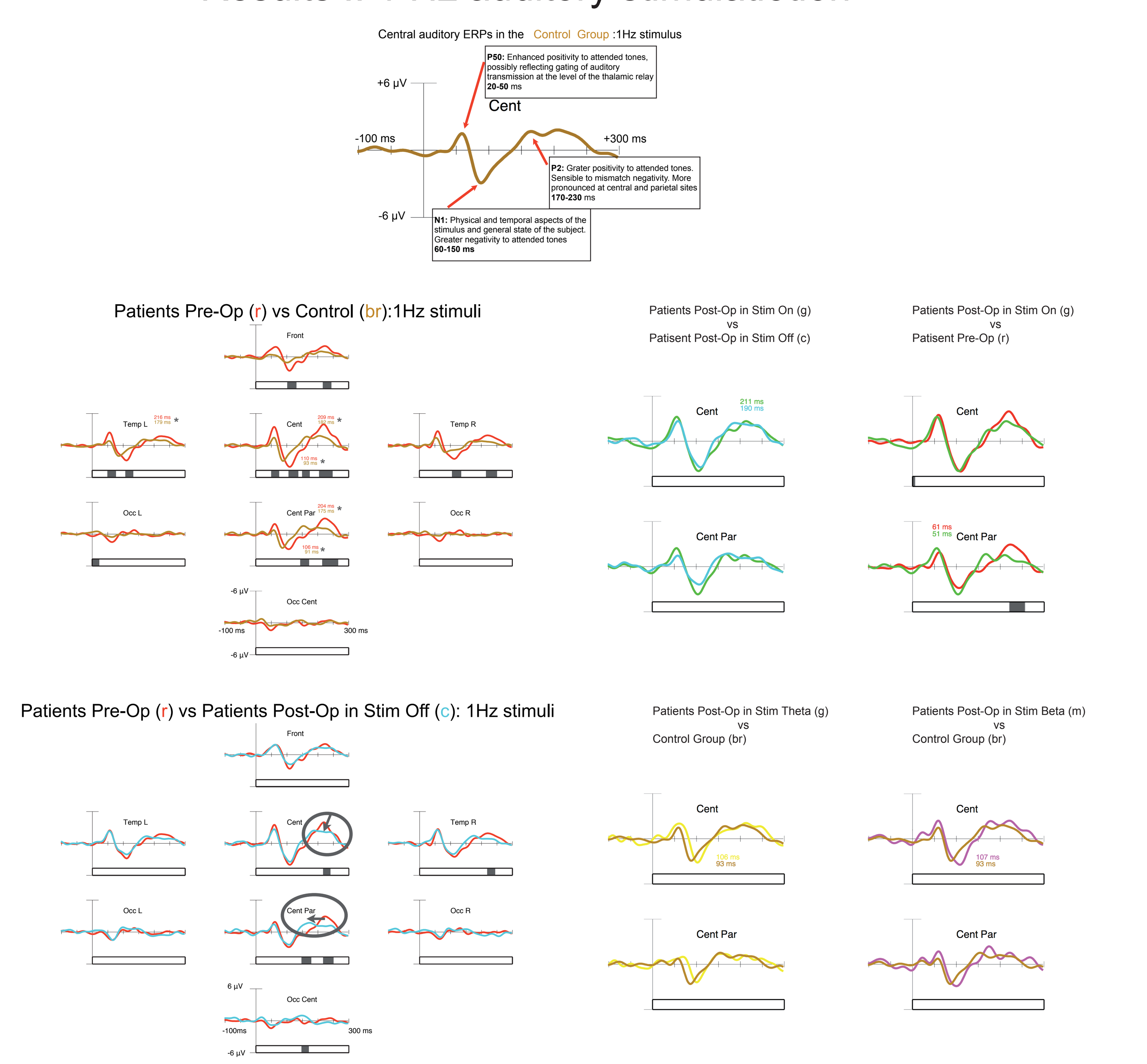
64 EEG channels combined into 8 regions of interest (ROI)



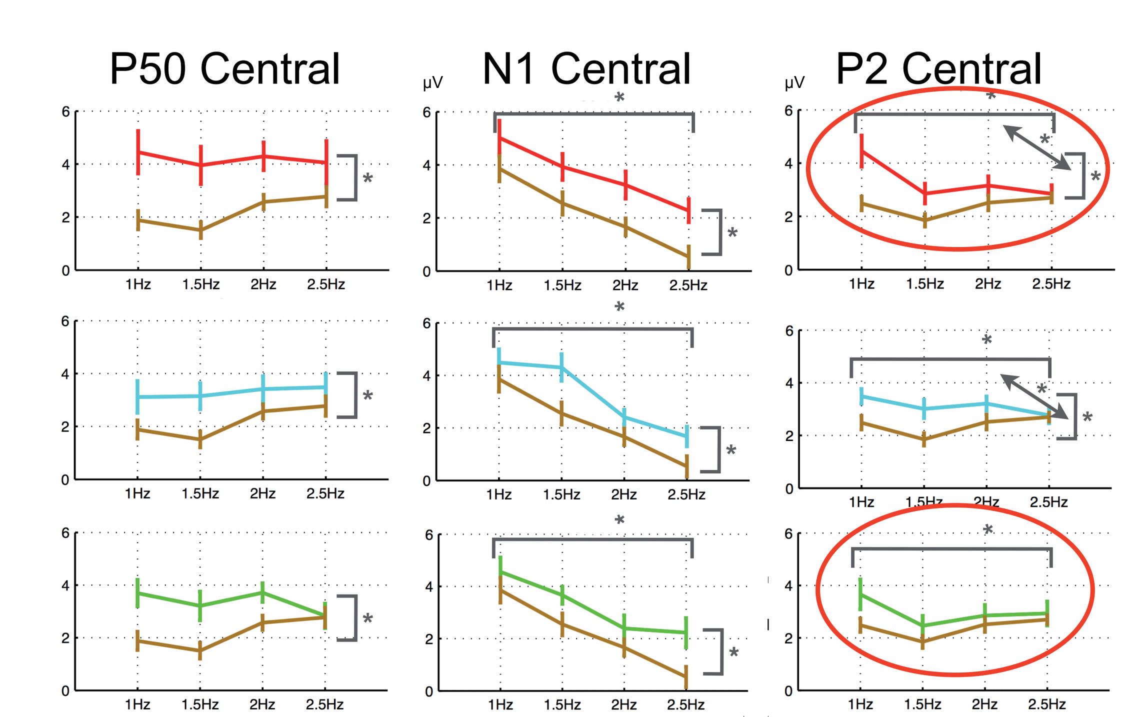
PRUNING THE EEG-SIGNAL BY MEANS OF ICA



Results I: 1 Hz auditory stimulatiotion



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



Summary of the results: patients vs. control group

Pre Op	Latency	Amplitude	Habituation	Post Op	Latency	Amplitude	Habituation
P50	n.s.	↑	n.s.	P50	n.s.	↑	n.s.
N1	↑	↑	n.s.	N1	↑	↑	n.s.
P2	↑	↑	↓	P2	n.s.	n.s.	n.s.

Results I: 1 Hz auditory stimulation

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

Results II: Different rhythm conditions

1. 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
2. Particularly before the operation, the amplitude of the PD patients' P2 is strongly modulated by the frequency of the rhythms

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. Electrode implantation per se as well as STN-DBS had a normalizing effect on AEPs. High-frequency STN-DBS led to a normalization of P2, but not P50 and N1 amplitudes. Under both theta-and beta-frequency STN-DBS, however, amplitude and latency of all three AEP components were affected. This reduction of the amplitudes under theta and beta frequencies stimulation could also be the result of the artifact rejection with ICA. Taking out components affected by the stimulation artifacts also reduces the general power of the AEPs.

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 auditory processing state. Another reason could be the changed and reduced post-operative medication. 12 hours of no medicine intake are probably not enough to guarantee a real Dopa-Off state. This is particularly true for the patients taking very large amounts of agonists and MAO-B inhibitors.

Our findings support and expand previous reports of dysregulated central auditory processing in PD as expressed by AEPs. The present results suggest that STN-DBS differentially affects the auditory evoked responses and may thus also influence sensorimotor processing at higher order sensory levels.

References

Teo C, Rasco L, al-Mefty K, Skinner RD, Boop FA, Garcia-Rill E.: Decreased habituation of midlatency auditory evoked responses in Parkinson's disease. Mov Disord. 1997 Sep;12(5):655-64.

Woldorff MG, Hillyard SA.: Modulation of early auditory processing during selective listening to rapidly presented tones. Electroencephalogr Clin Neurophysiol. 1991 Sep;79(3):170-91.

Wright MJ, Geffen GM, Geffen LB.: ERP measures of stimulus processing during an auditory oddball task in Parkinson's disease: Evidence for an early information processing deficit. Parkinsonism Relat Disord. 1996 Jan;2(1):13-21.

Raudino F, Garavaglia P, Beretta S, Pellegrini G.: Auditory event-related potentials in Parkinson's disease. Electromyogr Clin Neurophysiol. 1997 Oct;37(7):409-13.

Laffont F, Bruneau N, Roux S, Agar N, Minz M, Cathala HP.: Effect of age on auditory evoked responses (AER) and augmenting-reducing. Neurophysiol Clin. 1989 Mar;19(1):15-23.