Beyond volume conduction: toward genuine functional connectivity between bilateral basal ganglia

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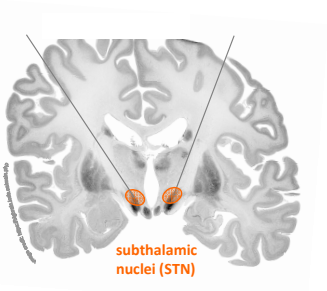


Background – Parkinson's Disease (PD)

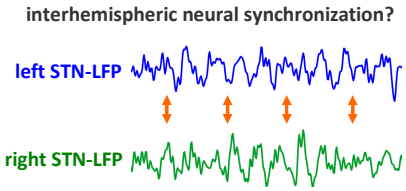
- bilateral effects of unilateral deep brain stimulation (DBS) suggested neural interactions between the left and right hemispheres[1]
- demonstration of interhemispheric coherence ("functional connectivity") in local field potentials (LFP) recorded from left and right subthalamic nuclei (STN) in beta oscillations (approx. 10–30 Hz)[2–4], modulation by levodopa medication[2]
- no direct anatomical connections between bilateral STN[2,4]
- functional distinction between low and high beta oscillations[2,5]

Challenges

- excluding severe artifacts due to volume conduction, especially for close recording sites (like both STN)
- clinical relevance regarding motor symptoms?

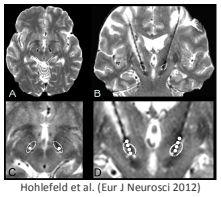
Research questions[6]

- "genuine" (ie, no volume conduction) interhemispheric coherence in LFP recorded from left and right STN (10–30 Hz)?
- relation between motor symptoms and interhemispheric STN-LFP coherence, specifically in low beta oscillations (10–20 Hz)?
- frequency-specific effects of levodopa medication (OFF vs. ON)?



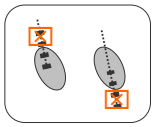
Patients and recordings[6]

- patients with idiopathic PD (n=8; 4 males), mean age 59.5 yrs; OFF and ON levodopa
- bipolar LFP, resting state (14 min)
- channel rejection if outside left or right nucleus

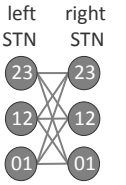


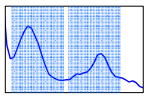
Hohlefeld et al. (Eur J Neurosci 2012)

bipolar channel rejection[7,8]...



... if both contacts were outside the STN





10–20, 21–30 Hz

mean (i)COH$_d$ within beta bands

max. n=9 bipolar connections

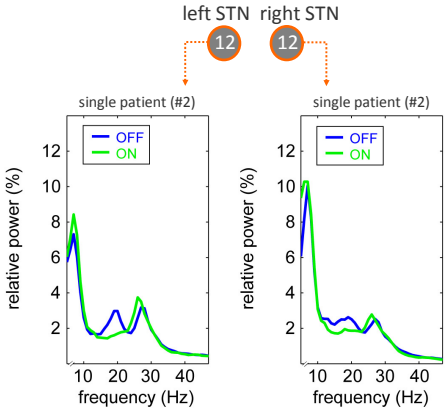
- imaginary part of coherency[9,10] (insensitive to volume conduction); time-lagged synchronization
- standard coherence

estimating (i)coherence detectability[9,10]

- jackknife normalization[9]
  iCOH$_d$ = |iCOH/STD(iCOH_jn)|
  > 2.58 indicates p< 0.01

spatial average approach

- across available connections (iCOH$_{dm}$) robustness to data heterogeneity



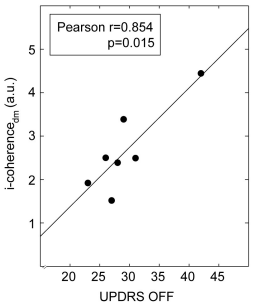
Results[6]

- mean N of significant connections with p<0.01:

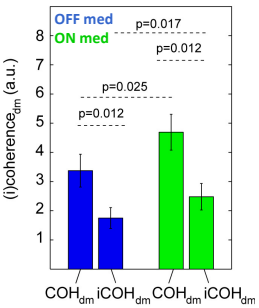
COH$_{dm}$	79 %
iCOH$_{dm}$	30 %
shuffled	0 %

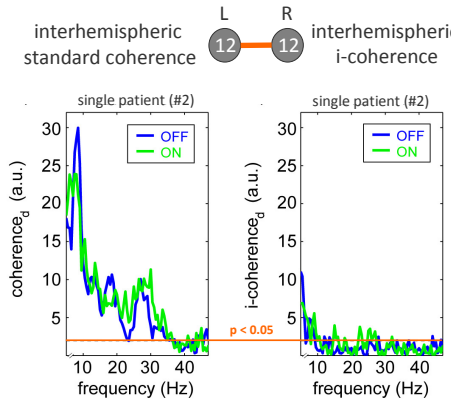
- increased severity of motor symptoms (UPDRS) OFF medication correlated with increased interhemispheric i-coherence (10–20 Hz oscillations); no correlation with standard coherence
- levodopa medication associated with increased interhemispheric connectivity (21–30 Hz oscillations)

single patients correlation
10–20 Hz, OFF medication,
interhemispheric i-coherence



grand-average (n=8)
Friedman analysis, 21–30 Hz
(post hoc Wilcoxon)



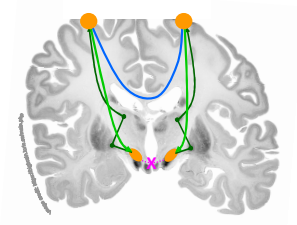


Conclusions[6]

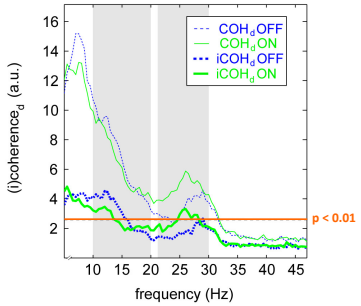
- genuine interhemispheric coherence (iCOH) in STN-LFP (no volume conduction)
- clinical relevance (correlation with motor scores): advantage using iCOH and a spatial average
- functional distinction high vs. low beta oscillations, relevance for motor symptoms (10–20 Hz)
- long-distance interhemispheric synchronization might be functional evidence for bilaterally effective unilateral DBS

Routes for interhemispheric STN-connectivity?

- cortico-subcortical route (corpus callosum) and/or
- subcortico-cortical-subcortical route (thalamus, CC)



grand-average (n=8)
interhemispheric (i)coherence



References

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[9] Nolte et al. (Clin Neurophysiol, 2004)
[10] Hohlefeld et al. (Neuroscience, 2013)

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