Invasive mapping of cortico-subthalamic coherence in Parkinson's disease

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INTRODUCTION

- Synchronisation of activity between the cortex and subthalamic nucleus (STN) is of interest in Parkinson's disease (PD) pathophysiology.
- Work investigating cortico-subthalamic coupling and the influence of dopaminergic medication has relied on non-invasive cortical recordings [1].
- We used invasive electrocorticography (ECoG) and STN local field potential (LFP) recordings to study spatial and spectral cortico-subthalamic coupling, and the accompanying influence of dopamine on this connectivity.

METHODS

- Seven PD patients at rest (six off- and on-dopaminergic medication, one off-medication).
- Rest recordings of ECoG signals – common average re-referenced – and STN LFP signals – bipolar re-referenced using the upper- and lower-most contacts.
- Time-frequency analysis was performed using wavelets, with power normalised to % total power.
- Cortico-subthalamic synchronisation was quantified using wavelet analysis of the imaginary part of coherence – a measure of correlation in the frequency domain immune to false connectivity arising from volume conduction [2] – and normalised with z-scoring.
- Average coherence within frequency bands was also determined for: theta (4-8 Hz); alpha (8-12 Hz); low-beta (13-20 Hz); high-beta (20-35 Hz); and gamma (60-90 Hz) bands.

RESULTS

- Similar power spectra in the cortex and STN across medication conditions (Figure 1).
- Peaks in cortico-subthalamic coherence in the alpha, low-beta, and high-beta bands in both medication conditions, with coherence being lower across frequency bands in the on- vs. off-medication condition (Figure 2).
- Coherence with STN in alpha, low-beta, and high-beta bands greatest over sensorimotor and frontal cortex, with theta and gamma coherence more widespread (Figure 3).

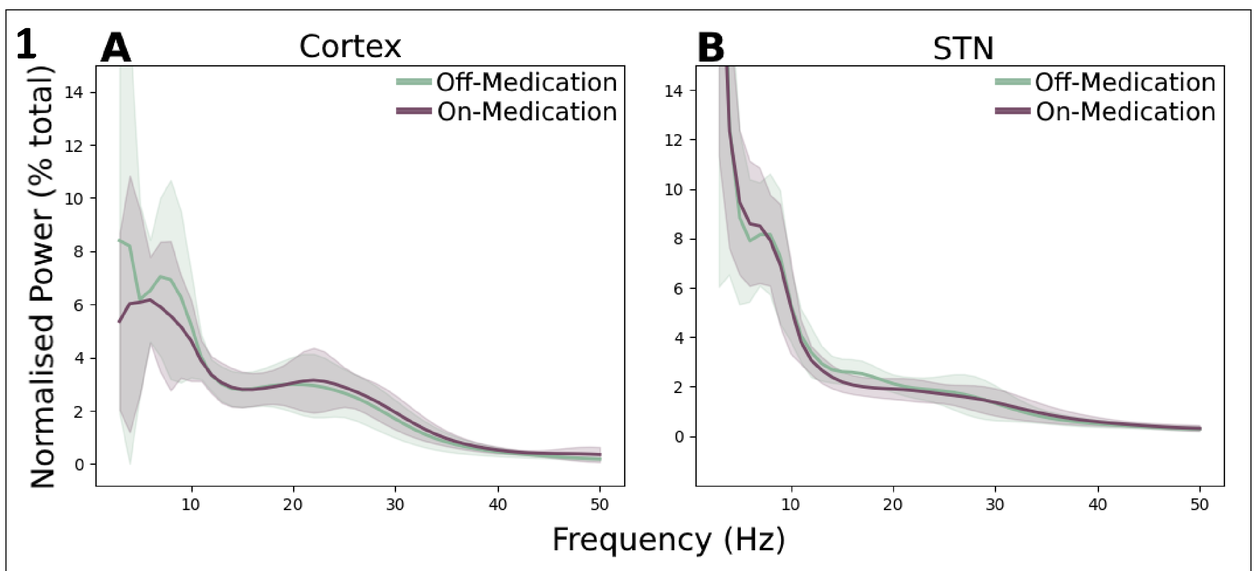

Figure 1: Power spectra. *Spectra of* ***(A)*** *ECoG and* ***(B)*** *STN LFP recordings off- and on-medication. Shaded areas show S.E.M.*

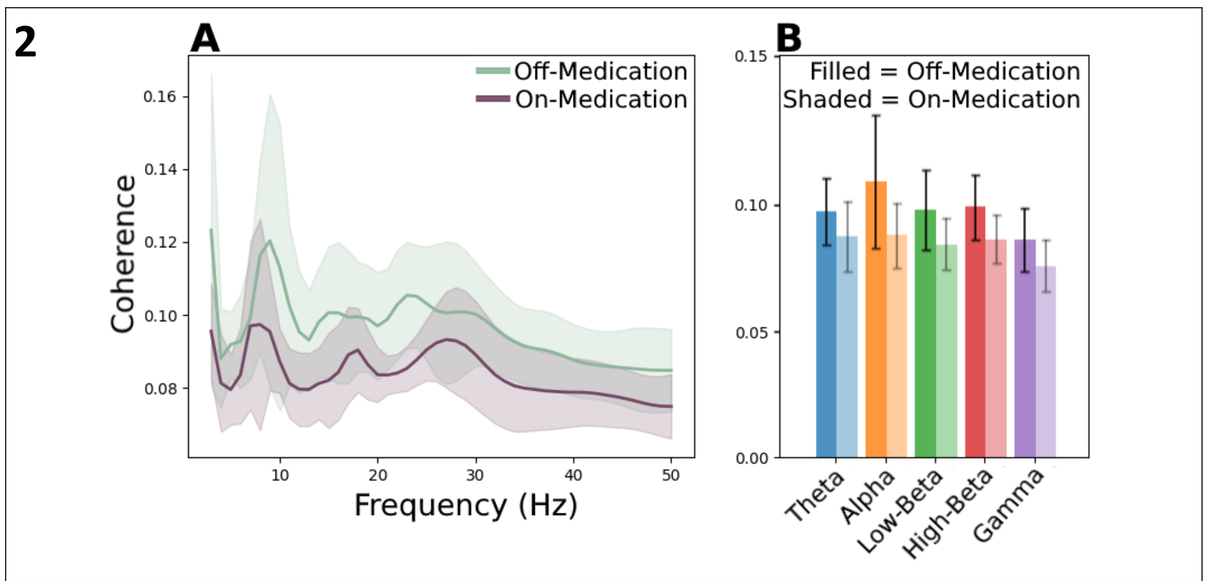

Figure 2: Averaged coherence. *Cortico-subthalamic coherence averaged across subjects and ECoG channels* ***(A)*** *at individual frequencies and* ***(B)*** *further averaged within frequency bands off- and on-medication. Shaded areas and error bars show S.E.M.*

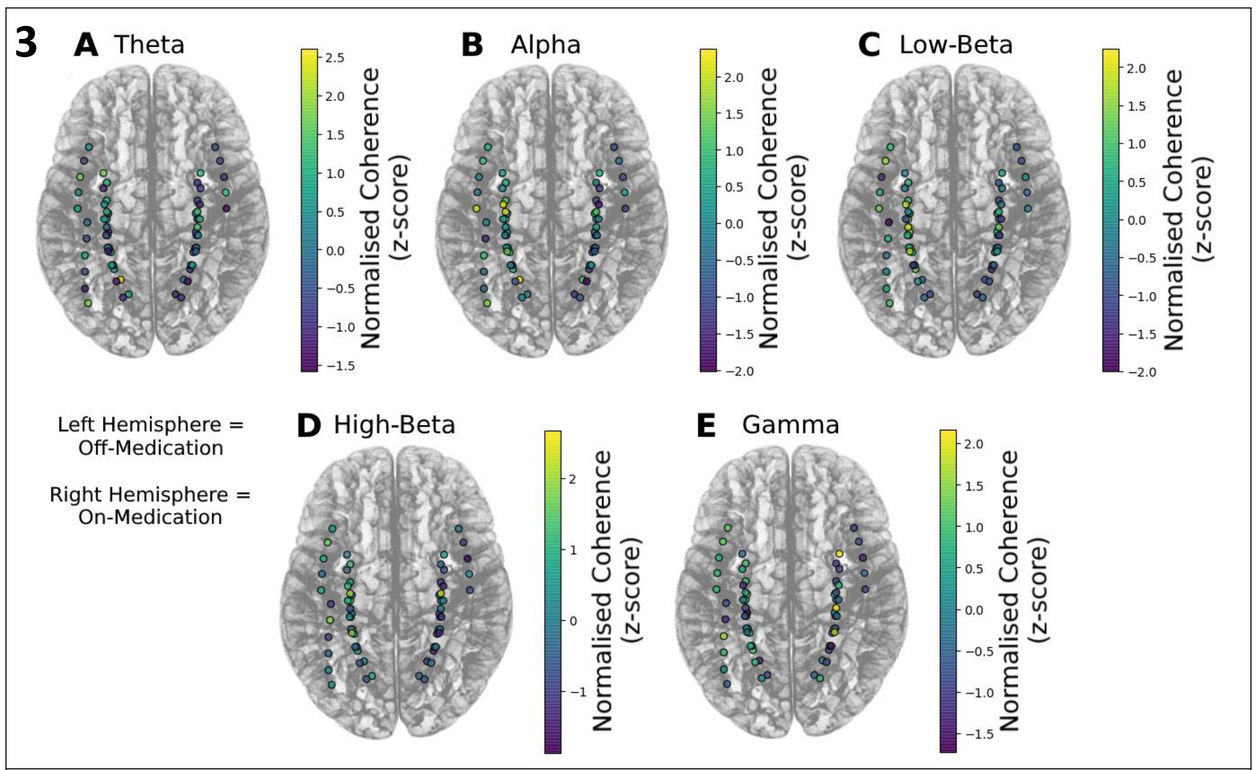

Figure 3: Spatial plots of coherence*. Coherence with STN at the various cortical recording locations averaged within* ***(A)*** *theta,* ***(B)*** *alpha,* ***(C)*** *low-beta,* ***(D)*** *high-beta, and* ***(E)*** *gamma frequency bands off-and on-medication.*

DISCUSSION

- This is the first work using invasive neurophysiology to investigate cortico-subthalamic connectivity and the effects of dopaminergic medication in PD.
- Coherence with STN in alpha and beta bands is dominant over sensorimotor and frontal cortex, and is reduced with medication – in contrast to results from non-invasive cortical recordings [1].
- Further subjects will enable the development of an atlas of cortico-subthalamic coupling in PD, allowing for characterisation of the spatial and spectral specificity of pathological frequency band networks.
- This atlas could be reproduced with MRI-based whole-brain connectomics to identify network hubs of pathological activity beyond the coverage of invasive recordings.

CONCLUSION

- Preliminary analyses indicate a spatial and spectral pattern of cortico-subthalamic coupling modulated by dopaminergic medication in PD.
- This relationship will become clearer in the near future with the addition of data from further patients, with relevance for our understanding of PD mechanisms.

REFERENCES

[1] Litvak *et al.* (2011). Resting oscillatory cortico-subthalamic connectivity in patients with Parkinson's disease. Brain.

[2] Nolte *et al.* (2004). Identifying true brain interaction from EEG data using the imaginary part of coherency. Clin. Neurophysiol.