Dopamine alleviates subthalamic vulnerability to cortical synchrony in Parkinson's disease

Parkinson's disease: Invasive mapping of cortico-subthalamic connectivity in humans

Thomas Samuel Binns[1,2], Richard Köhler[1], Jonathan Vanhoecke[1], Meera Chikermane[1], Franziska Pellegrini[3], Katharina Faust[4], Gerd-Helge Schneider[4], Andrea A. Kühn[1], Stefan Haufe[3], Wolf-Julian Neumann[1]

[1] Movement Disorder and Neuromodulation Unit, Department of Neurology, Charité – Universitätsmedizin Berlin, Charitéplatz 1, 10117 Berlin, Germany; [2] Einstein Center for Neurosciences Berlin, Charité – Universitätsmedizin Berlin, Charitéplatz 1, 10117 Berlin, Germany; [3] Berlin Center for Advanced Neuroimaging, Charité – Universitätsmedizin Berlin, Charitéplatz 1, 10117 Berlin, Germany; [4] Department of Neurosurgery, Charité – Universitätsmedizin Berlin, Charitéplatz 1, 10117 Berlin, Germany

INTRODUCTION

- Excessive beta activity in the subthalamic nucleus of the dopamine-depleted basal ganglia is a hallmark of Parkinson's disease.
- Cortical beta synchrony is not elevated in the hypodopaminergic state, but may drive pathological basal ganglia activity.
- Results from previous studies addressing this paradox with non-invasive cortical recordings have been inconclusive [1].
- Using a fully invasive neurophysiological approach, we provide authoritative evidence on pathological brain circuit communication in Parkinson's disease.

METHODS

- Electrocorticography and subthalamic local field potential signals were recorded in eleven Parkinson's disease patients at rest following withdrawal (OFF) and administration (ON) of dopaminergic medication.
- The periodic components of power spectra were extracted using Gaussian-based parameterisation [2].
- Connectivity was quantified with maximised imaginary coherence – a multivariate form of imaginary coherence [3] – and spatial maps of connectivity derived from this measure.
- The directionality of connectivity was quantified with multivariate net time-reversed Granger causality [4].

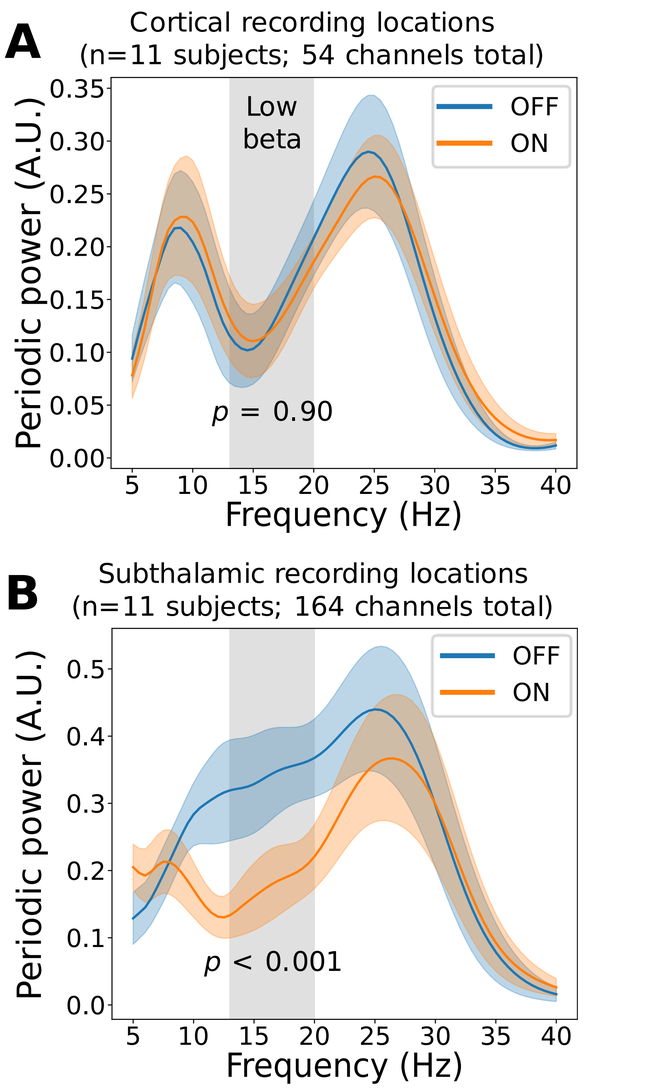

Figure 1: Periodic power in cortex (A) and subthalamic nucleus (B). Coloured areas show standard error of the mean. *P* values derived from Wilcoxon signed-rank tests on the average values of the grey areas across subjects.

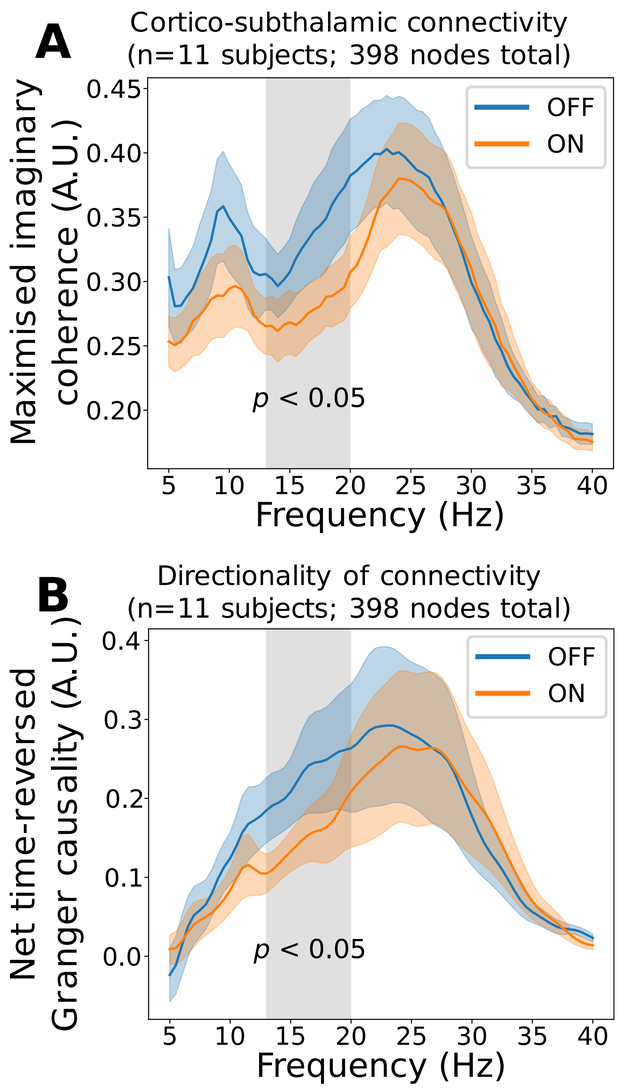

Figure 2: Cortico-subthalamic connectivity (A; absolute values) and its directionality (B). Coloured areas show standard error of the mean. *P* values derived from Wilcoxon signed-rank tests on the average values of the grey areas across subjects.

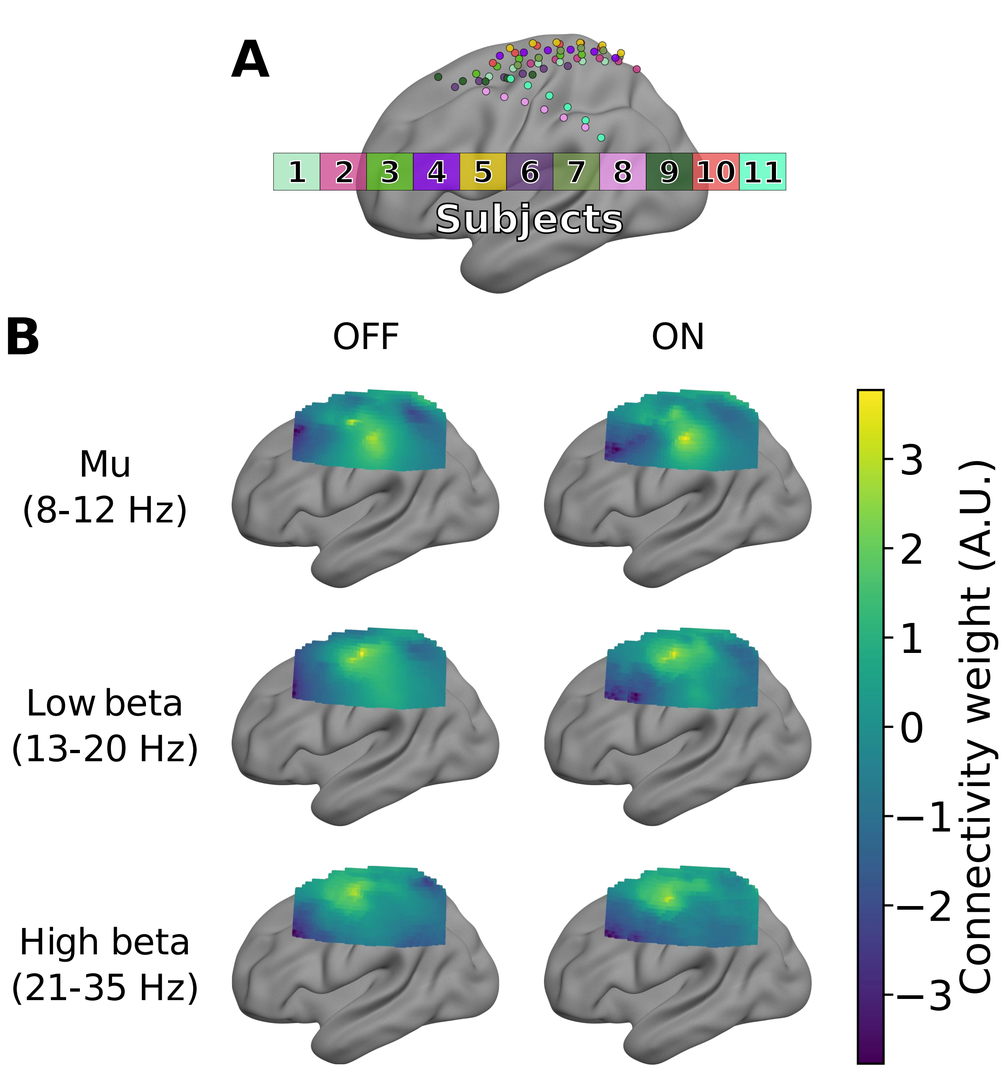

Figure 3: Electrocorticography coverage of cortex (A) and extrapolated, Gaussianised spatial maps of cortico-subthalamic connectivity derived from maximised imaginary coherence (B; n=11 subjects; 54 channels total).

RESULTS

- Dopamine suppresses low beta (13-20 Hz) power in subthalamic nucleus ($p < 0.001$; Fig. 1A), but not in cortex ($p = 0.90$; Fig. 1B).
- Dopamine suppresses cortico-subthalamic connectivity in the low beta band ($p < 0.05$; Fig. 2A).
- Cortex drives the connectivity, but this is suppressed with dopamine in the low beta band ($p < 0.05$; Fig. 2B).
- Connectivity is focal over sensorimotor cortex, and its cortical topography differs little with dopamine (Fig. 3).

DISCUSSION

- Cortex drives information flow in cortico-subthalamic beta band connectivity.
- Dopamine suppresses cortico-subthalamic connectivity as well as subthalamic, but not cortical beta power.
- Accordingly, dopamine may suppress subthalamic vulnerability to physiological cortical input.
- This highlights a role for cortico-subthalamic connectivity in the origin of pathological beta synchrony in Parkinson's disease.

References: [1] Litvak *et al.* (2011). Resting oscillatory cortico-subthalamic connectivity in patients with Parkinson's disease. *Brain*. [2] Donoghue *et al.* (2020). Parameterizing neural power spectra into periodic and aperiodic components. *Nature Neuroscience*. [3] Ewald *et al.* (2012). Estimating true brain connectivity from EEG/MEG data invariant to linear and static transformations in sensor space. *NeuroImage*. [4] Winkler *et al.* (2016). Validity of time reversal for testing Granger causality. *IEEE Transactions on Signal Processing*.

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ICN Interventional & Cognitive Neuromodulation

CONTACT
thomas-samuel.binns@charite.de
julian.neumann@charite.de

@tsbinns

Thomas Samuel Binns