Dopamine and stimulation distinctly modulate cortico-subthalamic communication in Parkinson's disease

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

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INTRODUCTION

- Excessive beta band (13-35 Hz) activity in the subthalamic nucleus (STN) 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 [1].
- Results from previous studies addressing this paradox with non-invasive cortical recordings have been inconclusive [2].
- Using a fully invasive approach, we provide authoritative evidence on pathological brain circuit communication in Parkinson's disease.

METHODS

- Electrocorticography (Fig. 1A) and subthalamic local field potential (Fig. 1B) signals were recorded in 13 Parkinson's disease patients at rest following withdrawal and administration of dopaminergic medication.
- Further recordings were taken from a subset of 6 patients with deep brain stimulation, without medication.
- Periodic components of power spectra were extracted using Gaussian-based parameterisation [3].
- Connectivity was quantified with a multivariate form of the imaginary part of coherency [4], and spatial maps of connectivity were derived from this.
- Directionality of connectivity was quantified with multivariate time-reversed Granger causality based on state-space models [5, 6].

Figure 1: Cortex and STN recording locations

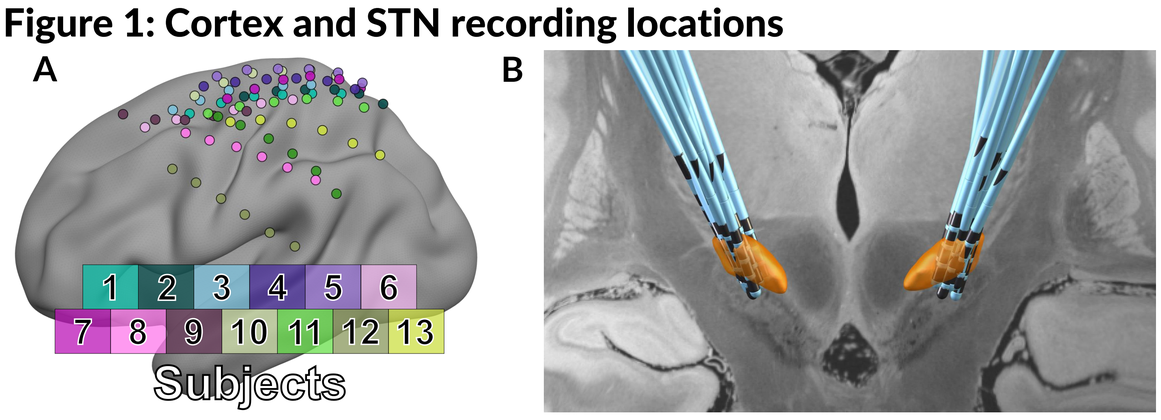


Figure 2: Cortex and STN periodic power

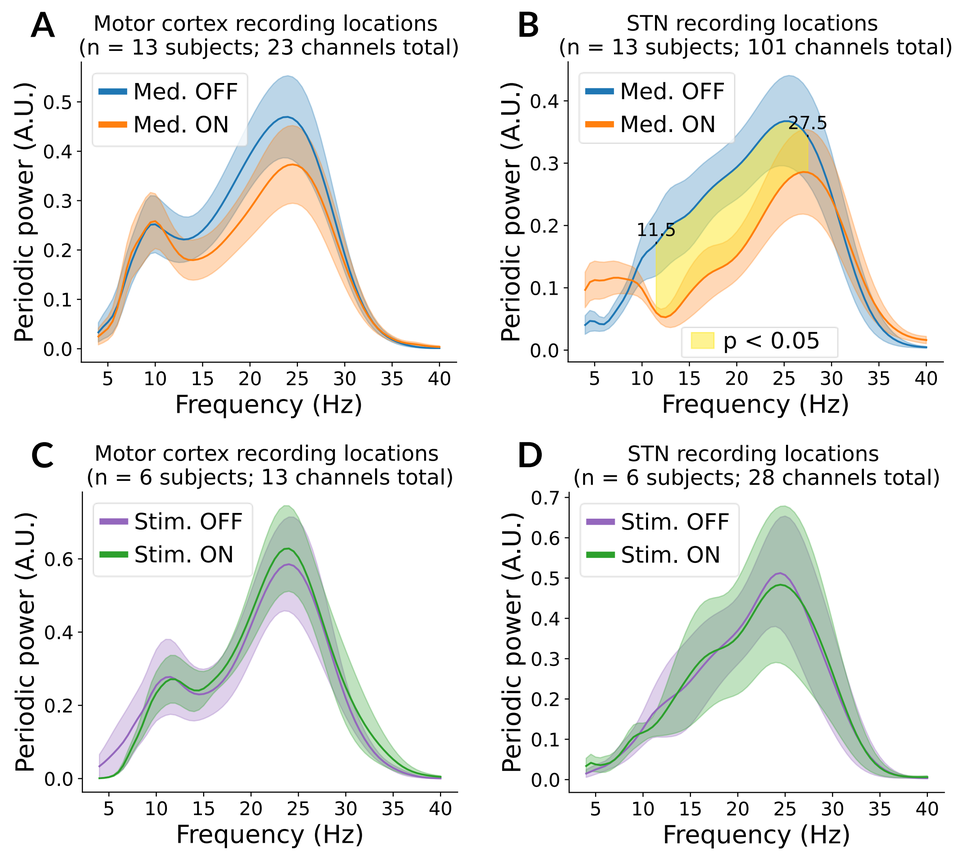


Figure 3: Cortico-subthalamic connectivity maps

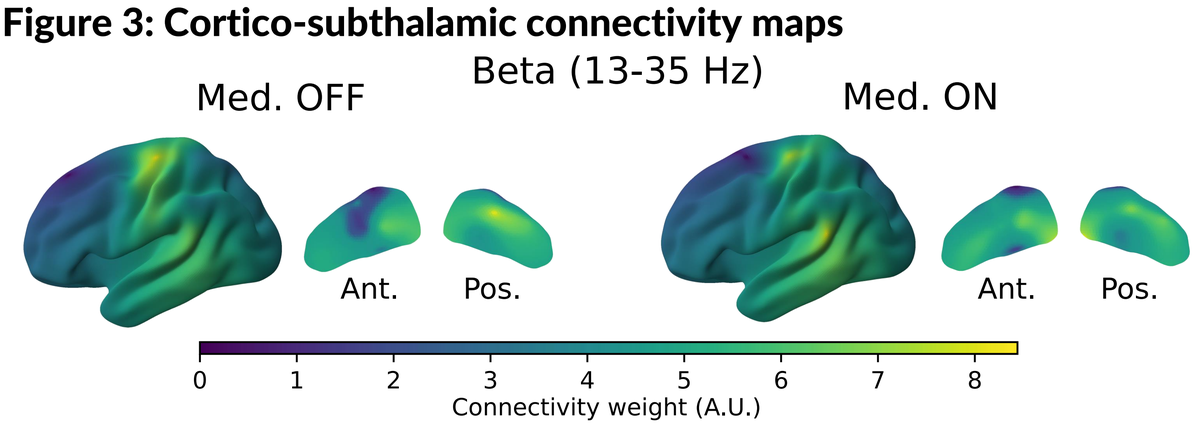
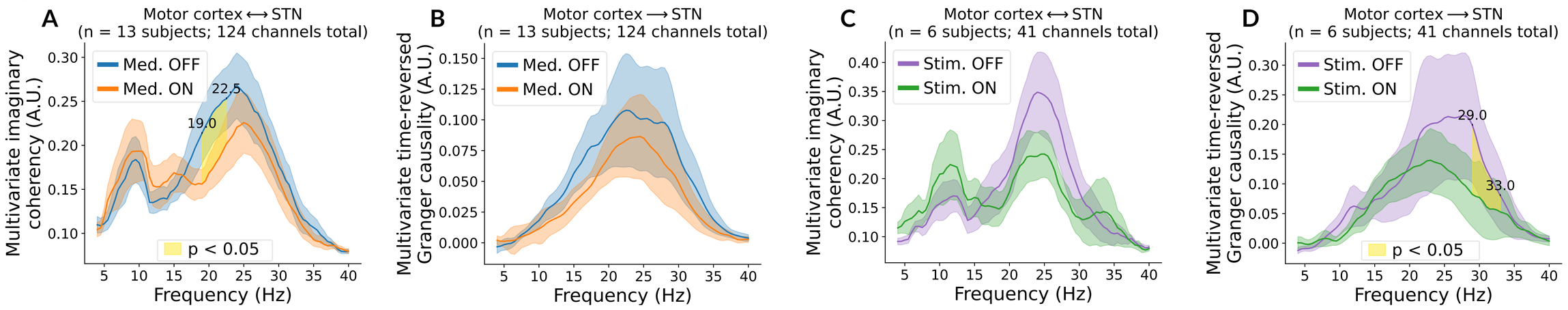


Figure 4: Cortico-subthalamic spectral connectivity



RESULTS

- Dopamine suppresses beta power in the STN but not in the cortex (Fig. 2A-B). Stimulation does not significantly affect power in the cortex or STN (Fig. 2C-D).
- Connectivity is focal between the motor cortex and the sensorimotor STN across medication states (Fig. 3).
- Connectivity in the beta band is reduced with dopamine (Fig. 4A) but not stimulation (Fig. 4C).
- Cortex drives connectivity with the STN across medication and stimulation states. This drive is not significantly affected by medication (Fig. 4B) but is reduced with stimulation in the beta band (Fig. 4D).

DISCUSSION

- Cortex drives information flow in cortico-subthalamic connectivity.
- Dopamine suppresses cortico-subthalamic connectivity as well as subthalamic, but not cortical beta power. Stimulation suppresses cortico-subthalamic information flow.
- Accordingly, medication and stimulation may elicit their therapeutic effects via distinct modulations of cortico-subthalamic communication.
- This further highlights a role for excessive cortico-subthalamic communication in the origin of pathological beta synchrony in Parkinson's disease.

References: [1] Oswal *et al.* (2021) Neural signatures of hyperdirect pathway activity in Parkinson's disease. *Nature Communications*; [2] Litvak *et al.* (2011). Resting oscillatory cortico-subthalamic connectivity in patients with Parkinson's disease. *Brain*; [3] Donoghue *et al.* (2020). Parameterizing neural power spectra into periodic and aperiodic components. *Nature Neuroscience*; [4] Ewald *et al.* (2012). Estimating true brain connectivity from EEG/MEG data invariant to linear and static transformations in sensor space. *NeuroImage*; [5] Seth & Barnett (2015). Granger causality for state-space models. *Physical Review E*; [6] Winkler *et al.* (2016). Validity of time reversal for testing Granger causality. *IEEE Transactions on Signal Processing*.

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