# PAPER OF THE MONTH 07/2026

TRR 295 ReTune

## Varying patterns of association between cortical large-scale networks and subthalamic nucleus activity in PD.

**Kohl O, Gohil C, Sure M, Schnitzler A, Florin E.**
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Parkinson's disease (PD) is characterised by abnormal activity within the basal ganglia and altered interactions between subcortical and distributed cortical networks. Although subthalamic nucleus (STN) activity is known to couple with the cortex, it remains unclear how this coupling varies with the dynamic organisation of large-scale cortical networks. We addressed this question using simultaneous magnetoencephalography (MEG) and STN local field potential recordings from 27 individuals with PD, assessed both on and off dopaminergic medication. We applied a time-delay embedded Hidden Markov Model to the cortical MEG data to identify transient large-scale brain states and examined how STN activity and STN–cortical synchrony varied across these states. This enabled us to move beyond time-averaged measures of connectivity by testing whether STN–cortical synchrony varies across transient cortical network states and identifying the network configurations in which this coupling is most pronounced.

We identified distinct cortical network states that coincided with different patterns of STN activity and STN–cortical coupling. In particular, STN–supplementary motor area (SMA) synchrony was selectively increased during activations of the sensorimotor network and the posterior default mode network, demonstrating that enhanced STN–SMA synchrony emerges preferentially during specific large-scale cortical network states. These two network states were also associated with distinct frequency-specific signatures of STN activity. Sensorimotor network activation coincided with increased STN power between 9.5 and 23 Hz and enhanced beta bursting, whereas posterior default mode network activation was associated with increased STN power between 5 and 16.5 Hz. Thus, both network states coincided with periods of increased STN oscillatory activity, but with distinct spectral profiles. This finding suggests that transient cortical network states may provide temporal windows into variations in STN activity and function.

Together, our findings demonstrate that STN activity and its coupling with the cortex are dynamically organised rather than temporally stationary. The cortical network in which an individual is engaged may provide important spatiotemporal context for subcortical activity and define specific windows in which distinct STN–cortical interactions emerge. Importantly, the cortical network-specific signatures identified here are detectable using non-invasive recordings and could ultimately help identify physiologically informed temporal windows and network-specific targets for adaptive, closed-loop neuromodulation.

**Oliver Kohl, PhD**
Oliver Kohl is a postdoctoral researcher in Esther Florin's Lab at the Heinrich-Heine-Universität Düsseldorf. His research focuses on how interactions between distributed brain regions give rise to behaviour, and how disruptions in these interactions contribute to neurological disease.

**Prof. Esther Florin**
Florin is a Lichtenberg Professor at the Heinrich-Heine-Universität Düsseldorf, and project leader with ReTune. In her research, she analyzes neural connectivity to understand cognition and behaviour in healthy subjects and neurological patients.

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