Phase-amplitude coupling

Phase-amplitude coupling (PAC) is the most-studied type of cross-frequency coupling and is thought to be responsible for integration across populations of neurons.

Fujita et al. obtained resting-state MEG and magnetic resonance imaging in 90 patients with epilepsy during their preoperative evaluation and in 90 healthy participants. They used the cortical currents estimated from MEG and magnetic resonance imaging to calculate Power in the δ (1-3 Hz), θ (4-7 Hz), α (8-13 Hz), β (13-30 Hz), low γ (35-55 Hz), and high γ (65-90 Hz) bands and functional connectivity in the θ band. Phase-amplitude coupling (PAC) was evaluated using the synchronization index (SI) for eight frequency band pairs: the phases of δ, θ, α, and β and the amplitudes of low and high γ. First, they compared the mean SI values for the patients with epilepsy and the healthy participants. Then, using features such as PAC, Power, functional connectivity, and features extracted by deep learning individually or combined, yhey tested whether PAC improves discrimination accuracy for the two groups.

The mean SI values were significantly different for the patients with epilepsy and the healthy participants. The SI value difference was highest for θ/low γ in the temporal lobe. Discrimination accuracy was the highest, at 90%, using the combination of PAC and deep learning.

Abnormal PAC characterized the patients with epilepsy in the interictal state compared with the healthy participants, potentially improving the discrimination of epilepsy [1)].

Togawa et al. evaluated phase-amplitude coupling (PAC), which reflects neuronal coding in information processing, using ECoG in 11 patients with intractable focal epilepsy. PAC was observed between slow waves of 0.5-0.6 Hz and gamma activities, not only during light sleep and slow-wave sleep (SWS) but even during wakefulness and rapid eye movement (REM) sleep. While PAC was high over a large region during SWS, it was stronger in the posterior cortical region around the temporoparietal junction than in the frontal cortical region during REM sleep. PAC tended to be higher in the posterior cortical region than in the frontal cortical region even during wakefulness. The findings suggest that the posterior cortical region has a functional role in REM sleep and may contribute to the maintenance of the dreaming experience [2)].

Both phase-amplitude coupling (PAC) and beta-bursts in the subthalamic nucleus have been significantly linked to symptom severity in Parkinson's disease (PD) in humans and emerged independently as competing biomarkers for closed-loop deep brain stimulation (DBS). However, the underlying nature of subthalamic PAC is poorly understood and its relationship with transient beta burst-events has not been investigated. To address this, we studied macro- and micro electrode recordings of local field potentials (LFPs) and single unit activity from 15 hemispheres in 10 PD patients undergoing DBS surgery. PAC between beta phase and high frequency oscillation (HFO) amplitude was compared to single unit firing rates, spike triggered averages, power spectral densities, inter spike intervals and phase-spike locking, and was studied in periods of beta-bursting. We found a significant synchronisation of spiking to HFOs and correlation of mean firing rates with

HFO-amplitude when the latter was coupled to beta phase (i.e. in the presence of PAC). In the presence of PAC, single unit power spectra displayed peaks in the beta and HFO frequency range and the HFO frequency was correlated with that in the LFP. Furthermore, inter spike interval frequencies peaked in the same frequencies for which PAC was observed. Finally, PAC significantly increased with beta burst-duration. Our findings offer new insight in the pathology of Parkinson's disease by providing evidence that subthalamic PAC reflects the locking of spiking activity to network beta oscillations and that this coupling progressively increases with beta-burst duration. These findings suggest that beta-bursts capture periods of increased subthalamic input/output synchronisation in the beta frequency range and have important implications for therapeutic closed-loop DBS. SIGNIFICANCE STATEMENT: Identifying biomarkers for closed-loop deep brain stimulation (DBS) has become an increasingly important issue in Parkinson's Disease (PD) research. Two such biomarkers, phase-amplitude coupling (PAC) and beta-bursts, recorded from the implanted electrodes in subthalamic nucleus in PD patients, correlate with motor impairment. However, the physiological basis of PAC, and it relationship to beta bursts, is unclear. We provide multiple lines of evidence that PAC in the human STN reflects the locking of spiking activity to network beta oscillations and that this coupling progressively increases with the duration of beta-bursts. This suggests that beta-bursts capture increased subthalamic input/output synchronisation and provides new insights in PD pathology with direct implications for closed-loop DBS therapy strategies [3].

Beta band power and phase-amplitude coupling within the subthalamic nucleus correlated positively with severity of motor impairment. This effect was more pronounced within the low-beta range, whilst coherence between subthalamic nucleus and motor cortex was dominant in the high-beta range.

Beta band might impede pro-kinetic high-frequency activity patterns when phase-amplitude coupling is prominent. Furthermore, results provide evidence for a functional subdivision of the beta band into low and high frequencies [4].

1)
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