Effective deep brain stimulation co-modulate cross-frequency coupling at gamma frequencies

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The disruption of pathological signals in the cortico-basal ganglia- network has been hypothesised as a mechanism of action of deep brain stimulation (DBS). The induced decrease of pathologically prolonged beta bursts within the subthalamic nucleus (STN) through DBS could therefore permit the preferential processing of physiological activity. Similarly, a modulation of physiological and pathological oscillations of other distinct frequencies, e.g in the gamma range, occurs. However, a comprehensive model for DBS modulating gamma oscillations is still missing. Besides considering gamma as physiologic and pro-kinetic, it has been suggested that finely tuned gamma oscillations between 60-90Hz reflect dynamic processing, possibly by inducing local inhibition or facilitation. Most studies investigating gamma focused on oscillations within the STN, motor cortex (M1), supplementary motor area (SMA), and the pallidum. Only a limited number of studies examined more than two regions at the same time. Furthermore, elements of the BG-thalamo-cortical network like the premotor (PMC) or prefrontal cortices (PFC) have been neglected to date. We hypothesised that clinically effective high-frequency-DBS of the STN modifies beta and gamma oscillations in wide cortical-subcortical network of interconnected regions. We aimed to reveal that network during resting state EEG recordings. We recorded resting state high-density 256-channels EEG of 31 PD-patients during DBS at the clinically most effective frequency (i.e 130Hz or 160Hz). We compared spectral power and cross-frequency coupling (frequency to power) of cortical and subcortical regions using a beamformer algorithm for coherent sources. Two clinically ineffective frequencies (i.e +20 and -20 Hz) have been tested as control experiments. We demonstrated that clinically effective STN-DBS alters oscillatory activity in a wide-spread network of cortical and subcortical regions. A reduction of beta and increase of gamma power is attested in the cortical (M1, SMA, PMC, PFC) and sub-cortical network nodes (STN). Additionally, we found increased cross-frequency coupling of narrowband gamma frequencies to the stimulation frequency in the same nodes of the cortico-subcortical network. No such dynamics were revealed within control regions (i.e. posterior parietal cortex). Furthermore, stimulating at lower or higher frequencies did not significantly alter the networks' source power spectra or cross-frequency coupling. We were able to show a modulation of beta- and gamma-power and cross-frequency coupling during DBS with HD-EEG in a cortical-sub cortical network. DBS does not exclusively influence motor-function but also the physiological processing related to facilitation and dynamic adaptation, in line with the proposed function of gamma oscillations.