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Original Research Article

# β-oscillations linked by neuronal-spiking within the STN neurons via deep brain stimulation (DBS) in parkinson disease: Part – II

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ABSTRACT

In the microelectrode recording and in the macrostimulations through DBS leads, the coupling was highest on the abaxial, i.e., dorsal- sub thalamic nucleus frontier-edge. The results proved that the larger β-high frequency oscillations and phase angle coupling is within the vicinity macro-leads contact which were clinically useful evaluated by continuing un effective-contacts, implying that PAC could prognostic of retort to STN-DBS. Neural-spiking was confined to the shape of 7Hz–30Hz oscillations(/fluctuations in the membranes), then longitudinal topography of spike-shape locking (S.S.L.)/ or spike-phase-locking(SPL) was analogous to PAC. Differences of phase amplitude coupling plus SPL indicated a lack—of spatio-temporal-correlations. β-coupled H.F.O.s and electrical-field protected (locked/fused) neurons have got unique and ideal phase-angles, i.e., signal/waveform-shapes above (+Ve) x-axis coordinates and below (-Ve) axis coordinates 2D spatio-temporal regions, did not occurred in the similar phase of modulating-oscillation. Therefore, our findings help which β – H.F.O—PAC could be key to patho physiology of Parkinson disease which suggests— locally electrical field-locked neurons are inadequate alone for the appearance of high frequency β-coupled oscillations.



## 1. Introduction

Deep brain stimulation of sub thalamic nucleus is the surgical procedure for reducing the motor symptoms of and rest orating the motor and improving the motor functioning in Parkinson's movement disorders and in other movement movement disorders, such as dystonia, Huntington diseases.[1–8] We gathered the field potentials, i.e., LFPs around the nuclei, i.e., STN to observe the spatio(area)-temporal magnitude of cross-correlation through transformed frequency domain FFT—frequency connections amongst β-fluctuations as well as high frequency oscillations. Results showed that the connections were extremely significant and very valuable at the d o r s a l sub thalamic nuclei border also, the intensity of these interfaces were linked to the experimental value of DBS stimuli. Single and multi-unit activity (SUA and MUA) of STN neurons were acquired with support vector machine (SVM) based MER system asynchronously (parallelly) and the main purpose is to study the areal point of locked electrical field potentials movement and activity. We notice that these connections or interfaces were highest at the d o r s a l STN border. We largely observed the co-existence of cross-correlation frequency also local electrical-field-spikes contacts and found no evidence of a causal relationship in bilateral subthalamic nucleus deep brain stimulation Parkinson's disease motor symptoms at the cortico and subcortical levels i.e., sub thalamic nucleus and pallidal neurons.[9–19]

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## 2. Objectives

To study the interconnections of the stimulating micro and macro electrodes implanted by DBS surgical procedure. To acquire the concurrent spike recordings of the electrically local field potentials and also single and multi-unit activities of the parallelly connected basal ganglion circuitry in the nervous system, i.e., MER with bilateral sub thalamic nucleus deep brain stimulation in Parkinson's. Phase of the amplitude through the stimulus intensity by the micro and macro electrodes by microelectrodes stimulations and macrostimulations coupling in the sub thalamic nuclei which was precise to β-phase plus high frequency oscillations stimulus amplitudes, followed by the coupling at the abaxial sub thalamic nucleus border.

## 3. Materials and Methods

The following methods were applied in this study. Microelectrodes for microelectrode signal recording of bilateral sub thalamic nucleus neurons, macrostimulations for the deep brain stimulation with macro lead electrodes for the acquisition of β-oscillations of bilateral sub thalamic nuclei in Parkinson son's, could be uniquely identified by its absolute depth in few millimeters with regard to the pre op target. To collective data for heap across all the route paths, i.e., trajectories' in every signal (data) acquisition gathering and followed by diagonally and/or transversely every session and also the Parkinson-subjects(patients), we, standardized with regard to the acquired sub thalamic nuclei neural (neuronal) distance measurement in every path trajectory through conversion of the absolute depth of every neural recording into pragmatic depth, through 0% and hen 100% demonstrating the tangentially dorso-lateral and ven tro-medial borders, characteristically, of the STN-neurons see Figure 1 part 9A) left side-brain hemisphere (in Part I article of this edition in IP IJN July – Sept 2022). We designated relative depths <0% (dorsal to the sub thalamic nucleus) as pre-STN, 0% –50% as dorso- lateral sub thalamic nucleus, 50% –100% as ventromedial STN, and >100% (ventral to the STN) as post-STN.

### *3.1. Phase angle/amplitude coupling and phase shift locking*

For evaluating the spatio-temporal connection amid β-coupled high frequency oscillations as well as local electric field potentials plus local electric-field locked neurons, we investigated the acquisitions/(recordings) through both substantial phase(shape of the signal/waveform) angle/amplitude coupling also noteworthy spatio-temporal/(spatial) phase-shift locker. And for every hidden (i.e.,isolated)neuron- units (i.e., MER signal multi-units activities), it is found that the peri spike log transformed higher frequency β-power be in the zone of beyond each and every spike-durations, by applying a spatio-temporal windowing of 100microseconds, that links to two signals/wave lengths of a 8Hz-30Hz oscillations, i.e., beta-oscillations.

The phase/or shape of the MER signals waveform-angle and amplitude couplings strengths were matched amongst inside vs. outside the sub thalamic nucleus. Spatio-temporal/(spatial) phase (phase-shift) locker strengths were evaluated amongst the dorso lateral vs. the ventro medial sub thalamic nuclei (two-tailed 't'-test; †p<0.1; †p<0.05).

Therefore, in support of the same and identical set—of microelectrodes signal recording showing significant phase angle coupling and spatio-temporal locking, additionally we also verified by testing whether β-coupled oscillations (higher-frequencies) dependably or reliably heralds or trails locally electrical-field locked-neurons. And we also did the data binning (while bin is at the center) in every MER-recording session by applying the two different signal-epochs (temporally) through higher (upper +Ve) lash – to – upper lash and/or lower lash to lower lash (-Ve) cycles of the 8Hz –30Hz filtered with band pass filter beta oscillations (i.e.,LFPs) figure 5. (D), upper. In every MER signal epoch, the power of the high frequency oscillations plus the occurrence of confounding-activities discovered in the course of their corresponding frequency cycles (hertz) for half cycles only but not a complete full cycle (hertz). For every sample signal recording, we graded the beta-power of higher frequencies oscillations transversely time-based sequential singal-epochs obsessed by q u i n t i l e s also computed the corresponding likelihoods occurrences of discovering and detecting the confounding activity-movement in the interior of the same signal temporal-epoch(s). And we computed the alterations in these likelihood-possibilities transversely uninterrupted higher frequency oscillations followed by quintiles and then linked them related them for all sample recordings of the microelectrodes sub thalamic nuclei neurons signal recording.

Following this, we analyzed the tspatio-emporal diminuendos like dynamic ranges of spatial and spatio phase (angle shapes) lockers, i.e., spatial-phase shift lockers followed by the phase amplitude couplings inside the specific mer with stn-dbs recording's by way of splitting every sample recording into non-intersecting (not overlapping) period (retro) segments of more than or equal to 6seconds plus more than or equal to 60spiking-events. And we have incorporated the STN signal recordings along with no less than 7 such-type-of-epochs (absolute complete period more than equal to 35seconds) for the conclusions purposes for deducing and drawing the inferences. Because each temporal epoch did not contain a sufficient number of spikes to quantify Enorm, Then we have computed the intricate mean-of allocation of direct phases(shape of signals) throughout spiking—events, $\bar{\mu}$, averaging across 500random—samples of fifty-spikes in all epochs this is

**Table 1:** The frequency thoroughness of phase-angle/amplitude coupling vs. spatio-temporal/phase-locker

| **Phase-angle-coupling (PAC, (macro stimuli/microstimuli or macrostimulation vs. micro stimulation))** | | | | |
|---|---|---|---|---|
| | **Tiny-β** | **High-β gamma** | **Broadband-β** | **higher-frequency oscillations** |
| $\theta$ | t (45)=0.97 | t (45)=0.91 | t(45)=0.75 | t (45)=0.80 |
| t | (35)= -0.50 | t(35)= -0.23 | t(35)= -0.62 | t(35)= -0.34 |
| $\alpha$ | t (45)=1.71 | t (45)=1.78 | t(45)=1.17 | t(45)=1.17 |
| | t (35) = -1.15 | t (35) = -1.94 | t (35) = -0.66 | t (35)=0.62 |
| Low-β | t (45)=0.63 | t (45)=0.95 | t (45)=0.15 | t (45)=2.12†† |
| | t (35) = -0.09 | t (35) = -0.05 | t (35) = -0.12 | t (35)=1.20 |
| Higher-β | t (45)=0.93 | t (45)=0.85 | t (45)=0.71 | t (45)=2.40†† |
| | t (35)=0.09 | t (35) = -0.20 | t (35)=0.26 | t (35)=2.00† |
| | Spatial(spatio)-temporal -phase locker (macro-stimuli/micro-stimuli) | | | |
| | 4Hz–8Hz | 8Hz–20Hz | 20Hz–30Hz | 30Hz–40Hz |
| | t (258)=0.97 | t (258)=2.59†† | t (258)=2.07†† | t(258)=0.63 |
| | t (258)=1.24 | t (258)=1.83† | t (258)=2.25†† | t (258)=1.18 |

Phase-angle/amplitude coupling strengths were matched amongst within vs. out-side sub-thalamic-nuclei. Spatio-temporal/(spatial) strengths were contrasted amongst dorso-lateral vs. the ventro-medial sub thalamic nucleus (two-tailed and student 't'—test; Pearson's correlation, †p<0.1;††p<0.05).

because of spatio-temporal epochs had not consisted an adequate and numerous spikes to determine the epochs normalization.

As well as higher frequencies-bands oscillations and then extrapolated stimulus intensity amplitudes/signal strengths, pulse-widths and phase-angle (phase-shift) information by applying the Hill Bert transformations to build the complicated time domain/time—series, z (t) = real part of the signals Amplitudes-of $_{hfo}$ (t) $e^{i,\varphi}\beta$ (t). For every sample mer signal recording, we identified the ideal phaseof β-coupled frequency oscillations higher as the phase-angle of center mean of z (t).

### *3.2. Deep brain stimulations – post op*

Thirty days after the macro leads of the deep brain macro stimulations, i.e., through macrostimulations techniques, every Parkinson patient experienced a preliminary training session on DBS-programming/coding. The mono polar assessment was accomplished for every contact and for all contacts, where- by the stimulus intensity-amplitude and pulse-width was progressively and slowly amplified, plus the current-voltage (electric-current), v, compulsory (obligatory) and mandatory to obtain clinical-diagnostic-benefit (where the windowing-access) as well as side-effects (exiting the windowing) were determined. A restorative (curative) windowing, w, for every-link was created or determined by estimating the distinction amongst the windowing-exiting and windowing-entry current-voltagesFigure 1 . (A), plus link through major restorative windowing was chosen as the stimulating-link. In cases in which higher than one single link showed huge restorative windowing's, in which one single was taken indiscriminately or randomly. The then dynamic and effective programming, i.e., coding dynamically were set and the settings were achieved on or after the very latest post op measurement-evaluation right from the 8.5±1.8months with effect from the electrode-implantations for the assessment study purposes.

## 4. Results and Discussion

With reference from the study of part I paper, in this part II study, it is ambiguous and uncertain that in what means and what method the high frequency local electrical field potentials that are more than or equal to 85 Hz oscillations of local field potentials ascend, through a one likelihood leeway being that they are electro graphic noise distortions through instrument noise, apparatus, acoustics, user interfered, etc. occurring from phantom,i.e,-spectral faults of the local electrical field potential's via electromyograph electrical action potentials, i.e., EMG potentials due to the jerking or yanking by the Parkinson's disease patients during surgery.

Studies also shows that phantom (spectral) leakage be able to lead to deceptive and hence fallacious hippo campus coupling amongst $\theta$- phase-angle plus superior $\gamma$ stimulus-amplitude intensity, pulse-width amplitude etc. which can be differentiated on or after real authentic and accurate phase angle / phase shift coupling. Though we observed the spiking effects and phase shift oscillations with higher gamma frequency power in micro electrode recording (MER) signals of sub thalamic nucleus neurons, the data in this study advocate that the experimented β-higher frequency oscillations together with phase shift angle couplings was an unaffected system of fractious(cross or crisscross)-frequency interface for the reason that the modifying and modified frequency—bands were bounded and limited, while contrasting to the wideband (wide brand or broad band) nature of counterfeit and false-coupling. We investigated the likelihood that power of higher frequency-oscillations might be associated in the

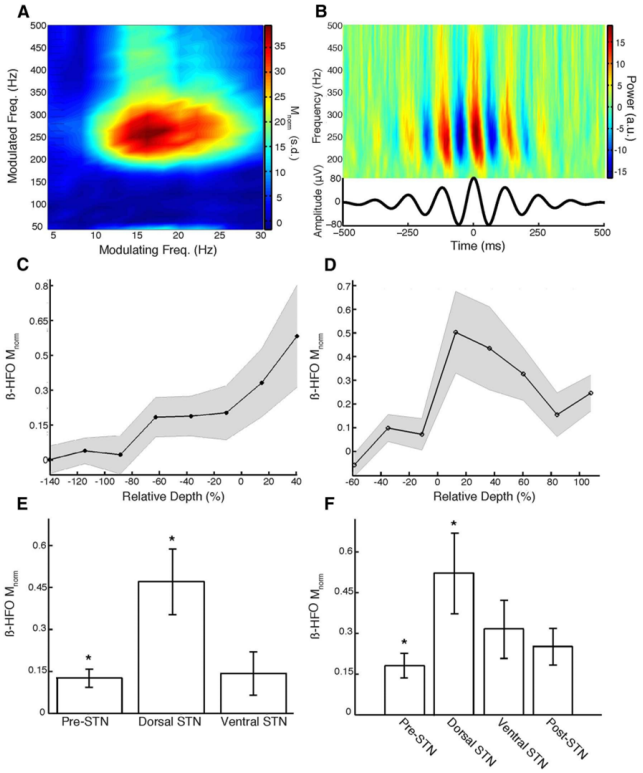


**Fig. 1: A:** MER signals normalizations∀sequences of modulating-frequencies 4Hz –30Hz as well as modified 40Hz–500Hz frequencies of local electrical field potentials signals/waveforms as of a gathering (though MER acquisition) made within the field dorsal lateral sub thalamic nucleus; **B:** Visualization of phase angle coupling amongst beta β-phase as well as higher-frequency oscillations; **C:** MER progress in β-oscillations higher frequencies; **D:** MER progression similar in C in phase angle phase-shft amplitude couplings phase-shift at the dorsal-border; **E:** as well as **F:** Macro stimulations through deep brain stimulations macro lead electrodes as well as micro electrodes recording (MER through the DBS microelectrodes β-higher frequencies phase angle phase amplitude coupling and phase shift locking.

direction of multi-unit activity. Therefore, it is observed that the gathered frequency oscillations of higher frequency components in the frequency domain in the STN neurons of Parkinson's were not connected to numerous uncategorized (not separated) spikes which might impact the MER signals generated via DBS local electrical field potentials. Likewise, we also encountered that the spatio-temporal topo graph (topography) of microelectrodes phase shift angle couplings which were very eminently analogous following the removal of group-wise-clustered spikes noises, distortions and user-artifacts, apparatus instrument and other noises emerging due to the science of acoustics. Considerably, that β-coupled oscillations' i.e., higher-frequency oscillations as well as β-locked neurons had drastically distinct desired phases/phase-angles and phase-shift alongside the varying fluctuations.

## 5. Conclusions

In our study, the data showed that the β-oscillations within the sub thalamic nucleus of Parkinson's neurons attune or drag (and/or entrains) and regulates the high frequency oscillations also confounding spiking—activity by a spatially (STN area or region wise) exact topo graph, nevertheless, the two electro physio logic phenomenon whitethorn unswervingly unrelated. Comparatively and fairly also the constant β-oscillations accustom and adjust the sub thalamic nucleus neurons in such a way that the examined spike phase lockers in the offing possibly and expectedly point towards group of clusters (or a cluster) of neurons confined to the causal β-oscillations. On the contrary or other hand, equally we propose that β-coupled high-frequency oscillations may possibly be arise on or after a greater collection of de synchronized neuronal/neural clusters which collectively lead to nonstationary and nonlinear high-frequency oscillations with different frequencies and different phase frequencies in the locally electrical field potentials, i.e., local field potentials.

## 6. Conflict of Interest

The authors declare no relevant conflicts of interest.

## 7. Source of Funding

None.

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