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# Cross frequency coupling in Parkinson disease patients during deep brain stimulation

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**Background:**

The aim of this study was to identify if cross frequency coupling is present in Parkinson disease (PD) patients during the ON state of deep brain stimulator (DBS). Also, to understand the influence of the DBS frequency on other frequency oscillations present in the brain of the PD patients. The source analysis method used here is the dynamic imaging of coherent sources (DICS) (Gross et al. 2001) with a realistic boundary element method forward model (Fuchs et al. 2002). Finally, to describe the cross frequency coupling in the identified sources using the measure frequency to frequency coupling (Jirsa et al. 2013).

**Data and Methods:**

DICS was applied to EEG segments recorded for duration of 120 seconds in five patients with PD during deep brain stimulation. The parameters of the stimulating electrodes were according to the clinical setting unipolar configuration for all the patients. The pulse width was 60 µs, the amplitude varied between (1.0 and 3.0 V) and the frequency varied between (130 and 180 Hz). The EEG recording was from a 256-channel system with a sampling frequency of 1000 Hz. Power spectrum analyses were performed to identify the predominant stimulation frequency. The brain area with the strongest power in the analyzed frequency (130 or 180Hz) range was defined as the reference region (primary motor cortex). DICS was used to compute the coherence between this reference region and the entire brain. We then find five more sources which are coherent with the reference region. Cross frequency coupling in the identified sources was estimated for the frequency range (1-200 Hz).

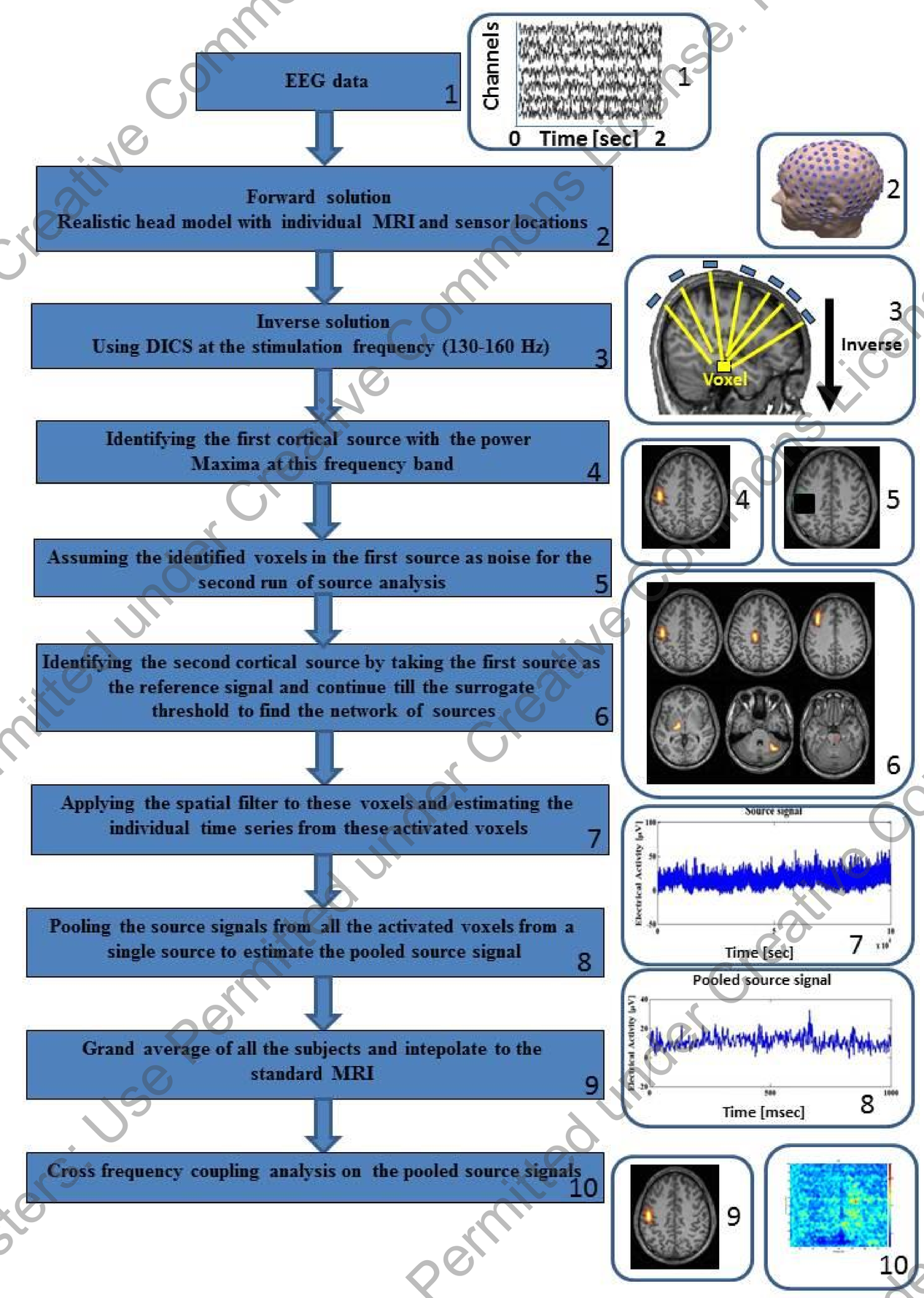


**Figure 1:** The flowchart explaining the step by step procedure for the beamformer source analysis and followed by the cross frequency coupling analysis on the pooled source signals obtained from the coherent source analysis DICS for each of the source separately both cortical and sub-cortical.

**Results:**

The power spectral analysis on all the EEG channels showed a clear peak at the stimulation frequency followed by its harmonics. The stimulation frequency source analysis in all the subjects was associated with bi-lateral sources in the primary motor cortex (CMC), pre-frontal cortex (PFC), secondary motor area (SMA), sub-thalamic nucleus (STN), cerebellum (CS) and brain stem (BS). There was significant frequency-frequency synchronization present, in all these sources, between the stimulation frequency and the gamma frequency (30-100) Hz. At the same time, there was de-synchronization between the stimulation frequency and the beta frequency (15-30) Hz. In order to verify whether the frequency-frequency coupling was only present in the identified sources, the posterior parietal cortex with the MNI co-ordinates [8, -77, 38] was chosen. In this area there was no significant synchronization with the gamma or de-synchronization with the beta frequency. The grand average and the cross frequency coupling for all the sources are shown in figure 3 A.

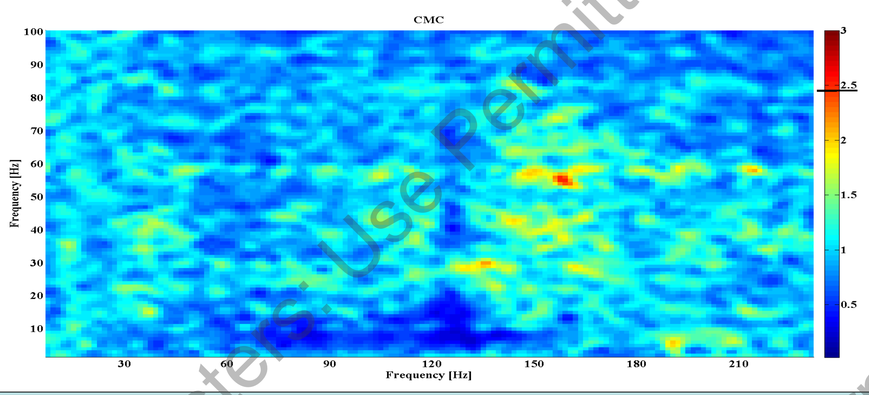


**Figure 2: B)** Depicts the cross frequency coupling for contralateral motor cortex till the frequency 160 Hz. The black line in the colour bar indicates the significance threshold for the modulation index.

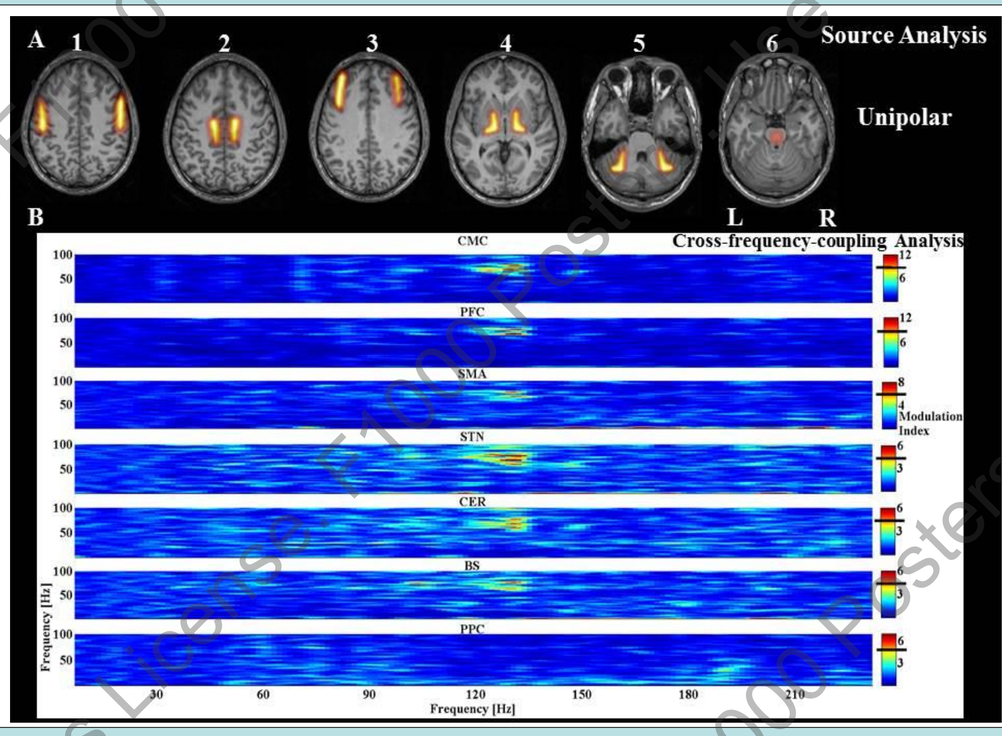


**Figure 3: A)** Shows the grand average of the network of sources of all the patients for the unipolar configuration during the deep brain stimulation. **B)** Depicts the cross frequency coupling for all source signals and the posterior parietal cortex. The black line in the colour bar indicates the significance threshold for the modulation index.

## Conclusion:

- The source analysis revealed the networks influenced during the deep brain simulation in the PD patients. The existing frequency-frequency coupling revealed that this could be one reason in solving a larger puzzle of why deep brain stimulation affects only the involuntary and not the voluntary actions in the PD patients.

## References:

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Gross J, Kujala J, Hamalainen M, Timmermann L, Schnitzler A, Salmelin R (2001) Dynamic imaging of coherent sources: Studying neural interactions in the human brain. Proc Natl Acad Sci U S A 98 (2):694-699.

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