Imaging Coherent Sources of Tremor Related EEG Activity in Patients with Parkinson's Disease

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Abstract—**The cortical sources of both the basic and first "harmonic" frequency of Parkinsonian tremor are addressed in this paper. The power and coherence was estimated using the multitaper method for EEG and EMG data from 6 Parkinsonian patients with a classical rest tremor. The Dynamic Imaging of Coherent Sources (DICS) was used to find the coherent sources in the brain. Before hand this method was validated for the application to the EEG by showing in 3 normal subjects that rhythmic stimuli (1-5Hz) to the median nerve leads to almost identical coherent sources for the basic and first harmonic frequency in the contralateral sensorimotor cortex which is the biologically plausible result. In all the Parkinson patients the corticomuscular coherence was also present in the basic and the first harmonic frequency of the tremor. However, the source for the basic frequency was close to the frontal midline and the first harmonic frequency was in the region of premotor and sensory motor cortex on the contralateral side for all the patients. Thus the generation of these two oscillations involves different cortical areas and possibly follows different pathways to the periphery.**

I. INTRODUCTION

IN Parkinsonian tremor we do not only see an oscillation at the (basic) tremor frequency but also at its first harmonic frequency. Previous findings [10, 11] on the oscillatory network of the Parkinsonian tremor have given first hints that the two oscillations could have different origins in the brain. Firstly, it has been proved in [12] with scaling analysis that both these oscillations are not simple harmonics due to existence of different scaling patterns. Secondly, the estimated delays measured by the maximizing-coherence method [14] was significantly larger for the first harmonic frequency compared to the basic frequency, which also indicates that they have different origins in the brain and have different ways of interaction between the brain and the muscle [14]. Thirdly, the dynamics of these two oscillations were estimated with the dynamical-coherence analysis which indicated independent prevalence in the coherence over time. Based on these three findings it has been postulated that the two oscillations involve different areas in the brain. The relatively new method of dynamic imaging of coherent sources (DICS) uses a spatial filter to localize brain activity that is coherent with a peripheral tremor signal [6]. However it has never been applied separately for both frequencies in Parkinsonian tremor, and all previous studies with DICS [7-11] were performed with MEG signals. In this study, we look for the sources of both the frequencies separately by applying DICS for the first time to a 64-channel EEG system, and the results were validated by a preliminary surrogate experiment.

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II. METHODS

A. Power and Coherence

The spectra for the EEG and EMG signal are estimated using the multitaper method. In this method the data is multiplied with several orthogonal tapers (sliding time windows) for calculating the power spectrum by discrete Fourier transformation. If $x(t)$ is the signal, then the spectrum is defined as [1]:

$$S_{MT}(f) = \frac{1}{K} \sum_{k=1}^{K} \left| \tilde{X}_k(f) \right|^2$$

where $\tilde{X}_k(f)$ is the Fourier transform of the windowed signal $x(t)$ which can be formulated as

$$X_k(f) = \sum_{t=1}^{N} w_t(k) x(t) \exp(-2\pi i f t)$$

the $w_t(k)(k = 1, 2....K)$ are the K orthogonal tapers.

As K orthogonal windows with good leakage and spectral properties, the discrete prolate spheroidal sequences (DPSS) are applied. The linear time-invariant relationship between the two signals is estimated by coherence as follows:

$$\hat{C}(\omega) = \frac{\left| \hat{S}_{xy}(\omega) \right|^2}{\hat{S}_{xx}(\omega) \hat{S}_{yy}(\omega)}$$

where S_{xy} is the cross spectrum and S_{xx}, S_{yy} are the individual power spectra; the overcap indicates the estimate of that quantity [2]. The coherence is a linear measure between 0 and 1, where 0 indicates absolutely independent signals and 1 the opposite. The power spectrum and the coherence spectrum of a Parkinsonian patient are shown in Fig.1.

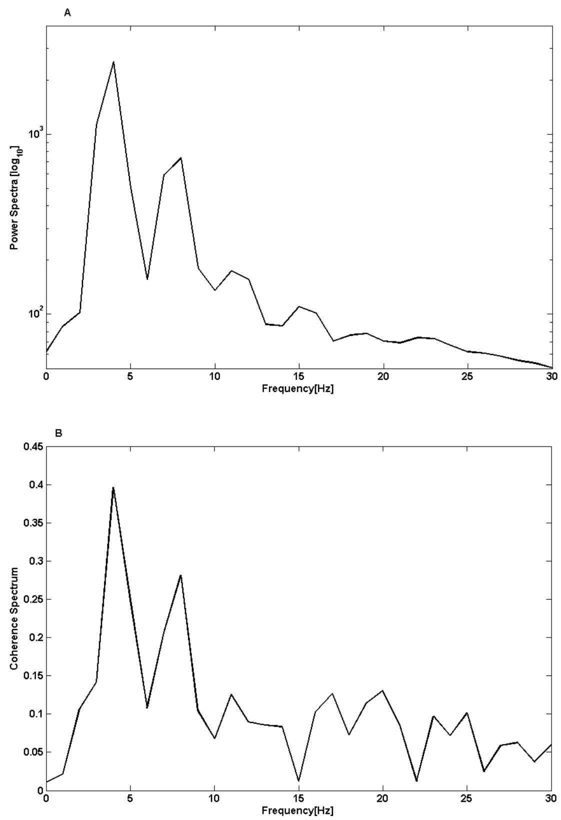


Fig. 1. A shows a typical EMG electrode (M3) power spectrum of Parkinson patient where the power values are higher at the basic frequency 4 Hz, and the first harmonic frequency 8 Hz. Fig. 1. B shows the coherence spectrum between the EEG and EMG signal of the same patient for a single electrode C3 with M3 which is clearly coherent at these frequencies.

B. Model and Lead- field Matrix

Inorder to project the coherence calculated on the surface of the head to the cortex a volume conduction model is used with a boundary element method [3]. The well known single sphere model is used. The head is modeled by giving in the radius and the position of the sphere with the electrode locations. The linear Poisson equation defined as:

$$\nabla \cdot (\sigma \nabla \varphi) = \nabla \cdot J^{s}$$

where σ is the electrical conductivity, ϕ is the electric potential, J^{s} are the electric current sources, gives the distribution of the electromagnetic field in the head [4]. The lead field matrix is used for the mapping of electric sources within the cranium to the scalp recordings outside of the scalp. The relation between the sources, s, the resultant recordings, ϕ_r, and the noise, n, with the lead-field matrix L can be written as,

$$\phi_r = Ls + n$$

In this model the lead-field matrix, L, contains the information about the geometry and the conductivity of the model. From the above relation given a set of recordings, ϕ_r, calculating L, and making some assumptions for the noise, n, the solution for the sources, s, which gave rise to these recordings, can be estimated by inverting the lead-field matrix L. In this paper we assume a single sphere model where L is easy to construct from simple sphere geometries.

C. Spatial Filter

The power and coherence at any given location in the brain can be computed using a linear transformation which in our case is the spatial filter. The spatial filter relates the underlying neural activity to the electromagnetic field in the surface. The neural activity is modeled as a current dipole or sum of current dipoles. Let us assume x to be a length N vector containing the potentials measured at the N different electrode sites. The potential due to a single dipole with location vector q is given as [5]

$$x = H(q) \cdot m(q)$$

where $H(q)$ is an N by 3 matrix which is the transfer function and $m(q)$ is a length-3 vector which contains the x, y, z components of the dipole moment. If x is due to the potentials of R active dipole sources at locations $q_i, i = 1,2,...R$ and noise n. It can be expressed as the superposition of all active neurons

$$x = \sum_{i=1}^{R} H(q_i) \cdot m(q_i) + n .$$

The spatial filter is designed using the covariance matrix of the data x. The dipole moment is modeled in terms of mean and covariance $C(q_i)$. We assume that noise is zero mean and covariance matrix Q and the moments associated to the different dipoles are not correlated. The covariance matrix $C(x)$ of measured potentials can be written as [5]

$$C(x) = \sum_{i=1}^{R} H(q_i) \cdot C(q_i) \cdot H^{T}(q_i) + Q$$

The spatial filter can be defined for a narrow band volume element Q_0 centered at location q_0 as the N by 3 matrix $W(q_0)$ and the three component filter output y can be written as the inner product of $W(q_0)$ and x

$$y = W^{T}(q_0) \cdot x$$

The linear constraint for an ideal narrowband filter is given as:

$$W^T(q_0)\cdot H(q) = \begin{matrix} I - q \in Q_0 \\ 0 - q \notin Q_0 \;\&\; q \in B \end{matrix}$$

then in the absence of noise the filter output is $y = m(q_0)$ were complete attenuation in the stop band is impossible. The optimal $W(q_0)$ satisfies these two conditions:

$$\min_{w(q_0)} tr\{C(y)\} \text{ subject to } W^t(q_0).H(q_0) = I$$

where $C(y)$ is given as follows:

$$C(y) = W^T(q_0).C(x).W(q_0)\,.$$

By solving the above equation using the Lagrange multipliers,

$$W(q_0) = (H^T(q_0).C^{-1}(x).H(q_0))^{-1}.H^T(q_0).C^{-1}(x)$$

this is the LCMV spatial filter W as a function of the transfer function H and data covariance matrix C.

The main aim of the LCMV method is to design a bank of spatial filters that attenuates signals from other locations and allows only signals generated from a particular location in the brain.

III. Preliminary Surrogate Experiment

To assess the validity of the source analysis method (DICS) with our 64-channel arrangement of the EEG we performed a surrogate experiment. The median nerve in the right hand of normal subjects was stimulated, with pulses which had a Gaussian distribution of the interpulse interval with the frequency ranging between $[1-5Hz]$. Due to these pulses the abductor pollicis brevis muscle (APB) is activated in a frequency centered around $3Hz$ and the other frequencies seen in the EMG power spectrum of Fig. 2.A are simple harmonics of this basic frequency. The EEG is recorded on the surface of the head with a 64 channel cap, and the EMG of the APB is recorded simultaneously.

The recording duration was 10 minutes. The power spectrum of the EMG is shown in Fig. 2.A. The coherence spectrum Fig. 2.B shows clear peaks at the basic and the first harmonic of the stimulation frequency. We know from everyday clinical neurophysiology that the median nerve stimuli evoke time locked brain activity in the sensorimotor cortex. Thus we expect the brain activity coherent with the stimulus frequency also in this region, and this should be the same for the basic and the first harmonic frequency of the stimulus-evoked muscle response.

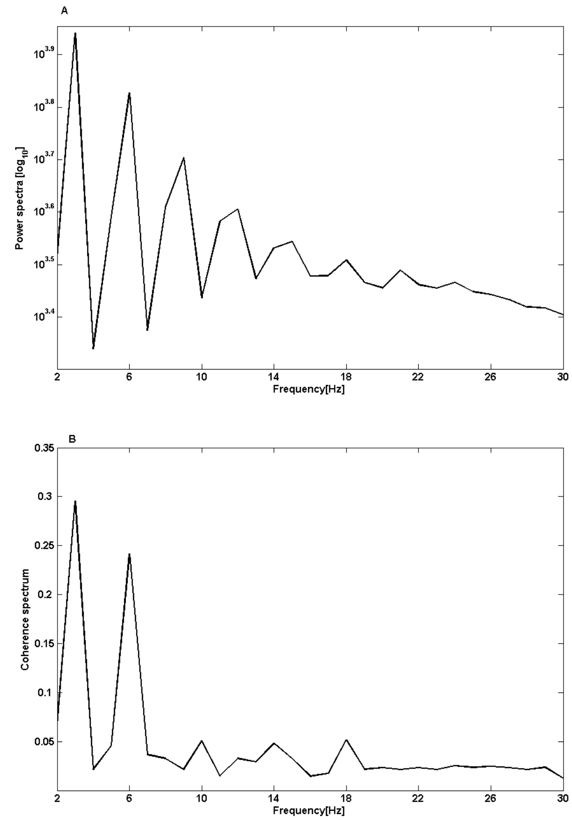
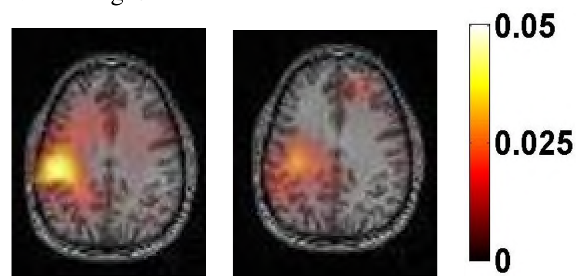


Fig. 2. A shows the power spectrum of an EMG electrode M1 with log scale Fig. 2. B shows the coherence spectrum between the EEG and EMG signal of the same subject for a single electrode C5 with M1 which is clearly coherent at these frequencies.

The DICS [6] was applied on this simulated data, and sources for the basic frequency $3Hz$ and first harmonic $6Hz$ were projected using the homogenous transformation matrix and interpolating the source coherence on a standard MRI. Indeed we saw the same center of coherence in the contralateral region of the sensorimotor cortex for the basic and the higher harmonic frequency. Only the coherence at $3Hz$ is stronger than at $6Hz$ as to be observed in Fig. 3.



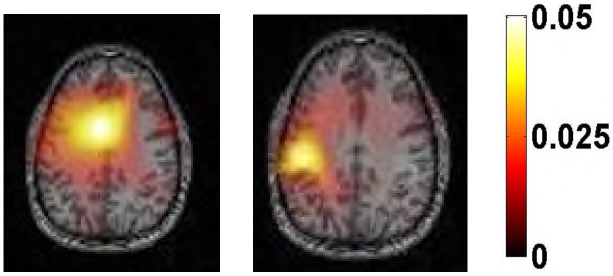
A B

Fig. 3. A shows the single slice of the basic frequency 3Hz. Fig. 3. B shows the single slice of the first harmonic frequency 6Hz.

IV. Application to Parkinsonian Patients

In the next step the DICS method was applied to 6

Parkinson patients all of whom had clear peaks in the power spectrum, cross spectrum and coherence spectrum at the basic and first harmonic frequencies of their tremor as seen in Fig.1. The average basic frequency for all the patients was $4.6Hz$ and the average first "harmonic" frequency was $9.5Hz$. In all the patients the source for the basic frequency was in the centre of the brain and for the first harmonic frequency in the contralateral side of the brain as to be seen in the example of Fig.4. For this patient the flexor right muscle M1 was taken as the reference. This finding supports the hypothesis and is the first direct evidence that the two frequencies are not simply harmonics but have different origins in the brain.



A B

Fig. 4. A shows the single slice of the basic frequency 5Hz. Fig. 4. B shows the single slice of the first harmonic frequency 10Hz. In this patient the reference was flexor right muscle M1.

V. DISCUSSION

The issues of the real physiological background of the first harmonic frequency of the Parkinsonian patients were addressed in this paper. The previous findings [7-11] with MEG signals have given some first hints supporting these results. However, in [15] they made it evident that it is a harmonic component by analyzing the cross spectrum. The fact that a real harmonic of the tremor frequency can also activate different sources will remain unchanged.

VI. CONCLUSION

In conclusion we were able to show in our preliminary surrogate experiment that the DICS applied to 64-channel EEG data leads to plausible results. Specifically the sources of the basic and higher harmonic frequencies of a single generated signal are projected to the same plausible region of the cortex. Thus our findings in Parkinson disease patients using the same method do not reflect a methodological artifact but likely indicate that the two peaks at the tremor frequency and around the double value are not simply harmonics but reflect independent oscillations involving separate cortical sources. In future, the first step will be to increase the number of Parkinsonian patients and the normal subjects with the surrogate experiment and the next step is to simulate EEG data by incorporating two sources at different locations for both the oscillations and testing the results from Parkinsonian patients using the DICS algorithm.

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