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Central Tremor Oscillators – a Directionality Study

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Abstract

This study investigates the relation of causality between the two central putative oscillators of the bilateral postural hand tremor. For this, we used a photic driving paradigm that induced at the visual cortical level a specific oscillatory activity. Having the particular functional relation between the hand motor system and the visual system, we assumed that changes in the last one were reflected in the central tremor oscillatory activity too. The stimuli frequencies were particularly chosen out of the alpha frequency band (7 Hz, 19 Hz), thus preventing the cortical driven oscillations to interfere with the spontaneous cortical rhythm. Physiological postural hand tremor was recorded bilaterally while the visual stimuli were delivered – either concurrently, either alternatively –, in the two visual hemifields. To track the causal functional interdependence between the two tremor central oscillators accompanying the corresponding changes induced in the cognitive state, we applied the partial directed coherence analysis.

1. Introduction

Even now, the origins of the physiological and/or pathological hand tremors continue to represent a matter of debate. Moreover, the study of the last ones could also bring new insights on the processes underlying the physiological tremor (PT). Regarding the origin of the PT, there are some papers whose results sustain the central hypothesis (the existence of cortical and/or sub-cortical oscillators driving the hand tremor). A review of these researches could be found in [1]. Also, there are studies like [2] in which the authors concluded that a pathological tremor like Parkinson tremor has, for example, its basis in the thalamic processing of basal ganglia outputs (here, the sub-cortical oscillator resides in the motor thalamus); additionally, this thalamic processing is considered to be influenced by sensory inputs and/or changes in attentional level elicited by external stimulation.

Related to the central hypothesis of the PT, it was additionally suggested [3] that in normal subjects there are two central oscillators that independently drive the corresponding hand tremor signal. Nevertheless, these central oscillators in the right and left brain seem not to be entirely independent of each other in both, normal and pathological conditions as it is the case of patients with essential tremor [4], for example. The authors likely ascribed in [4] this dynamical synchronization to the interhemispheric coupling via the corpus callosum. In fact, in [5] an increased interhemispheric coherence, due to a normal functional coupling of the right and left sensorimotor cortex, was experienced during the learning and/or execution of a bimanual voluntary task.

Being aware about the existence of such an interhemispheric functional coupling as well as about the tight relation that exists between the visual and the hand motor system (for eg., eye-hand coordination), we investigated, in the following, the causal interrelations induced between the two tremor central oscillators in two different external visual stimulation conditions. Rather, in this paper we analyzed the interdependence between the two putative central oscillators proposed in [3] using for this the tremor signals acquired simultaneously from the both hands during the visual stimulation. A solution to uncover the causal mechanisms between these tremor oscillators – mechanisms that characterize the dynamics following the external visual stimulation –, is given by the path diagrams. Recently used as a feasible technique in the causal analysis of the multivariate time series [6], this tackling of graph type is essentially based on the global Markov properties. These last ones give graphical conditions [13] for the dependent/ independent relations investigated anytime when the sub-processes are taken into account instead of the entire global process. This is our case in which latent variables of the process – like those modeling motor unit firing properties, mechanical resonances and reflex loop resonances – are not considered in the analysis. Based on the vector autoregressive models and the concept of Granger causality, we explored the causal relations mentioned above using a function defined in the frequency domain, namely partial directed coherence (PDC). Increasingly used today in the assessment of cortical connectivity patterns [7] [8], the PDC function has, beside coherence and partial coherence functions, the advantage of detecting not only the linear direct and/or indirect interdependences present in multivariate time series but also the information of causality.

2. Materials and methods

2.1. Materials

The tremor acquisition system was implemented with two low-g accelerometer sensors (ADXL203, Analog Devices), a National Instruments data acquisition board (AT-MIO-16E-10) and a software program that acquired simultaneously, and in synchronism with the visual stimuli, the tremor signal of both hands. On a single chip, the ADXL203 circuit embeds a high precision, low power, dual axis iMEMS (integrated Micro Electro Mechanical System) accelerometer, that measures acceleration with a full-scale range of ±1.7 g and a sensitivity of 1000 mV/g. The AT-MIO-16E-10 DAQ board was configured in the differential mode and acquired the tremor movement on 12 bits, with a sampling rate of 240 Hz. The low-pass filtering for anti-aliasing and noise reduction was implemented using the ADXL capability. The mass of the each accelerometer plus mounting plate was less than 5 g and the entire montage was positioned between the forefinger and the middle finger of the subject.

Two healthy right-handed adults, with normal or corrected-to-normal vision, served as volunteer subjects after giving informed consent. They were 29 and, respectively, 32 age old. They have been taken no kind of medication in the week previous to the recordings and, also, none of them reported a history of tremor or any other relevant medical disorders. All the recordings took place in a quiet room without any other source of light than that of the stimuli generator. The subjects were seated in front of a 17"-computer screen, the head stabilized with a chin rest at a constant viewing distance of 80 cm. Viewing was binocular and, during testing, the subjects had to maintain fixation on a central white cross while thinking at nothing and avoiding blinks or eye movements. They were instructed to use minimal effort to maintain their stretched hands in an approximately same horizontal position while having no visual control of them. For each subject and for each paradigm 40 trials were recorded, every trial taking 64 s. The elbows of the subjects were fixed and brief rests were allowed between each trial in order to avoid the arm fatigue influence.

In this study two different conditions were tested. In the *1st paradigm* two stimuli were presented against a dark background at two different locations (left visual hemifield, LVH, and right visual hemifield, RVH). The stimuli were lined up along the horizontal meridian of a computer monitor set to a resolution of 1280 x 1024 pixels, with a refresh rate of 85 Hertz. Each stimulus was a white circle changing its luminosity between a black background and a white flash. Also, the stimuli subtended a viewing angle of 2.48 x 2.48 degrees, with an eccentricity of 10°12″ representing the distance between the inner edges of the circles to the central fixation cross. The stimulus in each visual hemifield was flickered at a different frequency (with a 50/50 on/off cycle): the stimuli from the LVH was flickered at rate of 7 Hz and only in the first 32 seconds, while the stimuli from the RVH was flickered at rate of 19 Hz and only in the last 32 seconds of a 64-seconds trial. Simultaneously with the stimuli the tremor signals from the both hands were recorded. In the *2nd paradigm* the stimuli presented above were simultaneously delivered to the subject during all 64 seconds of a trial. Another difference is that after the first 32 seconds of the experiment the stimuli exchanged their frequency characteristics (now, left stimulus – 19 Hz, right stimulus – 7 Hz) and remained so until the end of the recording.

2.2. Methods

In order to analyze the interrelation pattern of the two putative central tremor oscillators that independently control the right and left physiological hand tremor movements [3] we employed the partial directed coherence (**PDC**) method. Defined as a function in the frequency domain, the PDC for a vector time series (X_V={$X_v(t)$, $t\in Z$}, with $X_V(t)$={$X_v(t)$, $v\in V$}, mean zero, weakly stationary process) is calculated based on the following autoregressive representation (eq. 1):

$$X_V(t) = \sum_{u\in N} a(u)X_V(t-u) + \varepsilon_V(t) \quad (1)$$

where: $a(u)$ is a square summable sequence of VxV matrices and {$\varepsilon_V(t)$} is a white noise process with mean zero and non-singular covariance matrix, Σ.

Rewriting the equation 1 in spectral terms gives the subsequent formula (eq. 2):

$$dZ_{X_V}(\lambda) = A(\lambda)dZ_{X_V}(\lambda) + dZ_{\varepsilon_V}(\lambda) \quad (2)$$

where: $dZ_{X_V}(\lambda)$ and $dZ_{\varepsilon_V}(\lambda)$ are random processes on [-π,π], with values in C^V, mean zero and orthogonal increments indicating the frequency components of the time series X_i, ε_i at frequency λ; $A(\lambda)$ is the Fourier transform of the autoregressive coefficients $a(u)$. Here, the complex value coefficient $A_{ij}(\lambda)$ is a measure of the direct causal effect of X_j on X_i at frequency λ, $A_{ij}(\lambda)$ uniformly vanishing for all $\lambda \in[-\pi,\pi]$ if and only if X_j is Granger-noncausal for X_i with respect to X_V. Defined by Baccala and Sameshima [9] as a normalized measure within the range [0, 1], the PDC function from X_j on X_i is given by eq. 3:

$$\pi_{ij}(\lambda) = \frac{\left|\tilde{A}_{ij}(\lambda)\right|}{\sqrt{\sum_{k\in V}\left|\tilde{A}_{kj}(\lambda)\right|^2}} \tag{3}$$

Here, $\tilde{A}(\lambda) = I - A(\lambda)$, with I representing the identity matrix. If the value of PDC is non-zero then one can say that there is an influence of X_j process on X_i process.

To achieve our goal we used the bivariate Granger causality analysis. Largely used in the literature, this type of analysis allows the study of causal relationships among multiple time series by separately analysing pairs of time series. For any $\{i,j\}\in V$ the corresponding bivariate subprocess $X_{\{i,j\}}$ is also a weakly stationary process. In time domain its autoregressive representation is given by eq. (4):

$$\begin{cases} X_i(t) = \sum\limits_{u\in N}\tilde{a}_{ii}(u)x_i(t-u) + \\ \qquad + \sum\limits_{u\in N}\tilde{a}_{ij}(u)x_j(t-u) + \tilde{\varepsilon}_i(t) \\ X_j(t) = \sum\limits_{u\in N}\tilde{a}_{ji}(u)x_i(t-u) + \\ \qquad + \sum\limits_{u\in N}\tilde{a}_{jj}(u)x_j(t-u) + \tilde{\varepsilon}_j(t) \end{cases} \tag{4}$$

The meaning of the terms in eq. (4) are alike to those in eq. (1). In time domain, one can say that X_j process do not Granger cause X_i process if and only if the coefficients $\tilde{a}_{ji}(u)$ are zero for all lags $u\in N$ (the corresponding frequency domain relations are $\pi_{ij}(\lambda)=0$, for all λ).

3. Results

The tremor signals were first pre-filtered with a FIR 45 Hz low-pass filter and de-trended, using a polynomial 2nd order for removing slow drifts introduced by the tremor acquisition system.

Assuming that the two tremor central oscillators are functional (dynamically) coupled and regarding the bilateral hand tremor signals as corresponding outputs of these oscillators (see Figure 1), we determined, by using the PDC function, their preferential direction of coupling. For this, the autoregressive representation was used for the bivariate process given by the pairs of hand PT signals, $X_{\{i,j\}}$, as in eq. (4). The bivariate Grange analysis was applied for the both paradigms presented in the first part of this paper. The obtained results are those presented in graphical mode, in Figure 3.A and Figure 3.B.

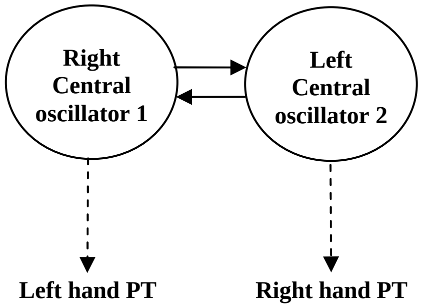

Figure 1. Bivariate system used to analyze the PT causal mechanisms

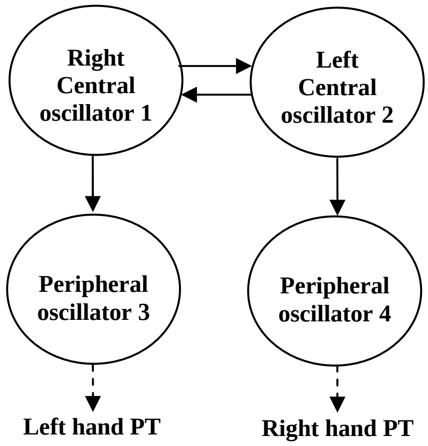

Figure 2. Multivariate system proposed to analyze the PT causal mechanisms

4. Discussion

A significant coherence was obtained for a frequency value around 4 Hz, for both paradigms and for both parts of the recordings, this indicating a dependence of the processes driving tremor activity on both sides. From the results presented in figure 3 and from the conceptual significance of them (presented above in the theoretical part of the paper) one can say that the two tremor central oscillators are dynamically linked, with a predominant direction from the right to the left oscillator.

Why does a significant partial directed coherence appear at 4 Hz when we use 7 and 19 Hz for the photic stimulus? Up to now we do not have any pertinent answer for this question. After an extensive analyze of the bibliographic sources we did not find any information regarding a similar behavior observed by other researchers. The answer for this subject remains an open research field.

Nevertheless there are some aspects that have to be discussed. One of them consists in the fact that the vector autoregressive process used to

A)

B)

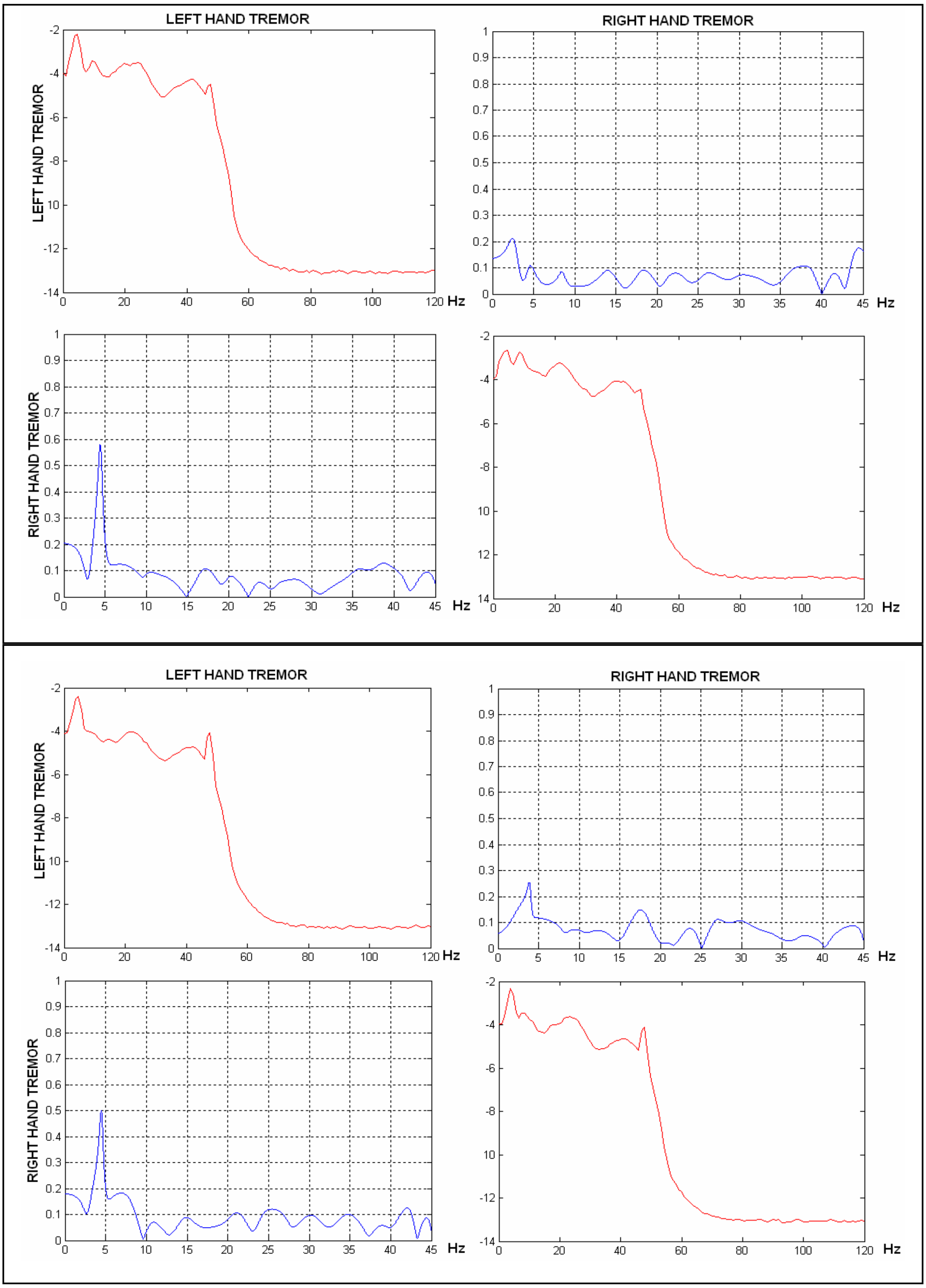

Figure 3. The results for: **A**) paradigm 1, B) paradigm 2. The power spectrums of both hand PT signals are represented on the 1st diagonal of each of the two figures (Fig. 3.**A**, Fig. 3 **B**) while the PDC calculated for these signals are shown on the second diagonals.

model the global system and presented in Figure 1 could be inconsistent with the real system; that is because it does not include the all important variables (the so-called latent variable). This is one major challenge when we want to calculate a reliable PDC measure, because spurious results could be obtained in this case. For these reasons, in our future research we also will take into account other models like, for example, the one presented in eq. (5).

The proposed model [10] that also includes the so-called latent variables is given below:

$$\begin{cases} c(t) = b_1 c(t-1) + b_2 c(t-2) + \varepsilon(t) \\ r(t) = \alpha f(x(t-\delta t)) \\ EMG(t) = c(t) + r(t) + \eta(t) \\ x(t) = a_1 x(t-1) + a_2 x(t-2) + EMG(t) \\ ACC(t) = \ddot{x}(t) \end{cases} \quad (5)$$

where: $c(t)$ denotes the central inputs, $r(t)$ represents the reflex contribution, and $f(.)$ is the nonlinearity of the reflex that is modeled by the tangens hyperbolicus. The central input is given by an order two autoregressive process, AR[2].

Another challenge in estimating consistent partial directed coherences is given by the parameter estimation of multivariate, autoregressive processes, which has to provide a reliable solution. A last important aspect is related to a major drawback of the autoregressive models, namely their unsuitability to cope with observation noise [11]. Thus, a significant underestimation of the process parameters is obtained when the observation noise is neglected [12].

5. Conclusions

As we already presented above, within the analysis of causal relations between the two hand PT central oscillators, the bilateral hand tremor signals were interpreted as being the outputs of the central oscillators that were assumed to be coupled. Actually, the things are a little bit more complex. That is, the PT signal has multiple origins, with central as also peripheral influences (for eg., reflex loops). In this case a more appropriate representation of the entire system could be that presented in Figure 2, in which the tremor signal is the output of a peripheral oscillator that is driving, in turn, by the central corresponding oscillator. Consequently, in our model we faced a frequently encountered problem, namely the omission of some relevant variables, especially because these ones can not be directly measured but by invasive methods. Hence, in our analysis the omitted variables are the outputs of the two central oscillators whose causal relations have to be determined having for this only the bilaterally acquiered tremor signals. For this reason, in order to get further a pertinent causal Grange analysis we have to look for another, more suitable model for the entire system (central oscillator coupled to the peripheral oscillator who has as output the PT signal). From this model we will derive the ouput signals of the central oscillators and then we will apply the bivariate causal Grange analysis to find out the direction of the causal relation between them.

6. References

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