Neurophysiological bases of tremors and accelerometric parameters analysis

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Abstract—Physiologic tremor is caused by three different generators with two frequency peaks that act together. A mechanical-reflex slower oscillator, that resemble the viscoelastic properties of muscle-joint complex and a faster oscillator that is the compound of loop reflex-composed by the spinal loop and supraspinal reflex loop and central neurogenic oscillator. Central neurogenic tremors seem to be generated by nerve networks in the Central Nervous System (i.e. cortico-basal ganglia-cortical loops/olivocerebellar pathways). Such disorders are mainly represented by Essential tremor and Parkinson’s tremor and are characterized by a frequency independent of reflex loop time, joint inertia, and joint stiffness. Even if tremor can be easily characterized describing its frequency, amplitude and relation with muscle, rest or activity, an universal method for movement disorder diagnosis and follow-up of the symptom is still missing. Among the technological tools for tremor analysis triaxial accelerometer are able to offer low invasiveness and high reliability. This paper introduces the neurophysiological substrate of tremor and offers a proof of concept of tremor evaluation for diagnostic support and drug-efficacy in Parkinsonian and subjects affected by essential tremor. It is achieved through a self-assembled wireless, low cost and wearable device, designed for operating in patient ecological environment.

I. INTRODUCTION

An involuntary back and forth movement of a body segment with the characteristic to be repetitive and stereotyped and composed by rhythmic oscillation of almost sinusoidal shape resemble the qualities of a tremor [1]. Even if it is intrinsically a nonlinear phenomenon it can be well approximated by few parameters such as its frequency and amplitude. Clinically tremor is qualified by the anatomical location that it interests and by the class of tasks that let it to be evidenced. From the last point of view tremor could be static or rest tremor, that occurs if the part is relaxed, postural and isometric tremor, occurring when the body part is contracted against gravity or an obstacle, kinetic tremor that occurs in the accomplishment of an action and task-specific tremor limited only during the execution of specific task such as writing or playing instruments. Moreover healthy subjects present a physiological tremor. For comprehensive review see [2].

Tremor is considered the most frequent movement disorder, but it is present in a wide spectrum of entities such as the classical essential tremor (ET) and Parkinson tremor (PT) but also orthostatic tremor, dystonic tremor, cortical tremor, and thalamic tremor.

Different mechanisms have been considered as underlying tremor production in the CNS, the so called central neurogenic oscillator, but except for few tremors strongly characterized by frequency (i.e. Holmes tremor, cerebellar tremor and orthostatic tremor), there is no universally recognized neurophysiologic method to definitely discriminate the different centrally produced tremors [3].

Many interesting issues emerged by the research in physiologic tremor, which, in fact, seems to be composed by three different generators with two frequency peaks that act together. A mechanical-reflex slower oscillator that is due to the movement of the mass and springs that model the viscoelastic properties of muscle-joint complex in a similar manner as Hill’s model does for the muscle, and a faster oscillator that is the compound of two systems: 1) loop reflex- composed by the spinal stretch reflex loop and supraspinal reflex loop and 2) central neurogenic oscillator [4]. The effects of those oscillators are superimposed upon a background of irregular fluctuations in muscle force and limb displacement.

Tremor due to peripheral mechanical oscillator decrease its frequency when a load is added to the body segment while
increase its frequency going proximo-distal (i.e. from the arm to the hand). When analysing this component alone, despite limb tremor, electromyographic recordings show no motor unit discharge. The oscillation frequency of the peripheral mechanical component (ω) is indeed, directly proportional to the square root of joint stiffness (K), inversely upon the joint inertia (I) according to the equation: ω = √(K/I). The mechanical-reflex component is a passive oscillator. Joints present underdamped inertial, visco-elastic properties that generate oscillations in response to irregularities in subtetanic motor unit firings (contraction) and cardiac-transmitted vibrations produced by cardiac systolic ejection of blood (Eble 1996). Stretch reflex involvement occurs only when physiologic tremor is enhanced by fatigue, anxiety, hyperthyroidism, or drugs (enhanced physiologic tremor) [5]. The cerebellum is abnormally active in tremorogenic parkinsonian patients, but it is not necessary for the production of rest tremor. Even if basal ganglia and cerebellum are traditionally considered as anatomically and functionally distinct, direct interactions between them have been shown; in fact Hoshi et al. [6] have demonstrated that the cerebellum has a strong disynaptic projection to the putamen, by way of the thalamus, specifically targeting indirect pathway neurons of the putamen. As a consequence, the two systems could interact leading to an increased complexity in the computational modelling of tremors. The cerebello-thalamo-cortical pathway is probably involved in all tremors, but for each subtype it is not well understood the specific role of the cerebellum in suppressing or generating tremor. Coherence analyses of tremorogenic EMG and simultaneously recorded electroencephalography and magnetoencephalography have revealed involvement of the ipsilateral cerebellum, contralateral sensorimotor cortex and other neuronal Basal Ganglia pools. It seems that oscillatory networks that underlie the various tremor disorders partially overlap in space, and show distinct features with regard to oscillation frequencies, oscillatory power and/or oscillatory coupling. Those “simple” descriptions underline the real complexity in searching for pathophysiological models of tremors in the clinical context. From this point of view, many (but partial) advances have been done in measuring tremors that do not allow a clear picture. Within this frame, the implementation of motion transducers for measuring tremor is an integral part in the study of motor control and in clarifying the different pattern of diseases that the conventional clinical scales could not be able to disentangle.

II. MATERIALS AND METHODS

A. Experimental setup and protocol

Ten subjects affected by pathological tremor were involved in this study. The subjects were recruited by the Neurology unit of the “Policlinico Universitario Campus Bio-Medico” in Rome. The subjects were clinically evaluated by an expert physician, and grouped by tremor characteristics: six of them showed to be affected by PT and the other four by ET.

This paper aim at presenting a proof of concept, thus statistical analysis is outside its scope.

Subject were asked to wear a glove instrumented with a tri-axial digital accelerometer (ADXL345 by Analog Devices, Inc.), placed into a pocket on the back. Accelerometer data were acquired at 100 Hz by an embedded microcontroller (PIC18F46J50, by Microchip Technology) and transmitted to a remote PC via a Bluetooth communication. The whole device was powered by a standard nine-volts alkaline battery, which was placed together with the Bluetooth module for data transmission into a second pocket fastened on the subjects’ upper arm (see fig. 1).

![Glove setup](image)

**Fig. 1** - The experimental setup for the analysis of PT and ET composed by: a glove instrumented with a tri-axial accelerometer and a separate unit with the power supply and the Bluetooth module.

The experimental protocol was designed to elicit the different characteristics of the tremor (rest, postural and kinetic) and was composed by 5 trials, in which subjects were asked:

1. To sit down in a rest position with their hands laid down on their legs;
2. To stand up and spread their arms forward against gravity;
3. To stand up and bring their arms to their chest, with the back of the hands turned up;
4. To draw a spirogram;
5. To draw a series of parallel lines.

In all the phases we recorded data from the accelerometer for at least 30 seconds. Each subject repeated the whole protocol twice (once each hand) before and after one hours since drugs administration. Parkinson’s Disease suspected subject receive the acute administration of 250mg of LevoDOPA + 25mg of CarbiDOPA, while subjects grouped as ET were treated with 50 ml of a solution of 40% ethanol.
B. Data analysis

For each trial, data acquired by the accelerometer were filtered by a second-order low-pass butterworth filter, with a cut-off frequency of 25 Hz. The norm of the acceleration vector was calculated for each time sample, and the signal mean was subtracted to the resulting dataset.

We then performed a spectrum analysis on the acceleration magnitude using a Fast-Fourier Transform algorithm to calculate the signal spectral density of each trial.

III. RESULTS

Figure 2 shows the spectrum analysis performed on a subject affected by PT, before pharmacological treatment. Upper row shows the power spectral density during rest trial for both left and right hand, while the lower plots are relating to the postural trial with subject’s arms spread forward.

![Graphs showing spectrum analysis](image)

**Fig. 2** - Spectrum analysis of accelerometer signals on a subject affected by PT, before pharmacological treatment. Upper row shows the power spectral density during rest trial for both left and right hand, while the lower plots are relating to the postural trial with subject’s arms spread forward.

Further is presented the analysis of the response of tremor parameters to specific treatments. Figure 4 shows the power spectral density relating to a subject with PD, before and 1 hour after the administration of LevoDOPA. Subject’s positive response to drug administration is clearly shown by the strong reduction of the rest tremor component at 5-6 Hz.

In ET, as can be seen in fig.5, the higher frequency component of tremor at 12Hz disappeared one hour after the ethanol administration.

![Graphs showing spectrum analysis](image)
In physiological condition tremor is present, but is barely visible to the unaided eye and it is symptomatic only during activities that require extreme precision. Despite this it can be evaluated through accelerometers.

Moreover the exploitation of accelerometer goes above the simple classification of tremors and can sustain the diagnosis of the movement disorder responsible for the tremor.

Parkinson tremor is the most common rest tremor, increases with walking and it is decreased by posture holding or action. It is felt by the patients as a social mark. Usually it is asymmetrical and its frequency range is 3–6 Hz.

The analysis presented in Fig 2 shows the presence of rest tremor with a 5–6 Hz frequency peak, that strongly improves when the patient holds a position or executes a task-oriented movement. Also the strong prevalence of tremor in right hand, compared with the contralateral, reinforces the diagnosis.

Typically, Essential tremor is an action tremor, either postural or kinetic in character, mainly affecting the hands. It can also affect the head and the speech. It usually appears in adulthood, even if appearance in old age or in childhood is not rare, and has a strong impact upon the quality of life of the affected subjects. ET has a strong dominant inheritance with 90% of concordance in monozygotic twin. It is usually bilateral and the fundamental electrophysiologic mark is an abnormal entrainment of motor unit activity at the frequency of tremor, which is typically 4 to 12 Hz.

Hence, Fig 3 shows bimodal distribution of Power Spectral Density with a lower frequency slightly above 5 Hz and an higher peak at about 12 Hz in a patient affected by ET. Such tremor is mainly represented in postural and kinetic tasks while disappears at rest.

Nigrostriatal cell loss, with the related dopamine depletion, in Parkinson’s disease is probably sufficient to produce Parkinson tremor, causing tremorogenic neuronal oscillation in the motor cortex, ventrolateral thalamus, globus pallidus, and subthalamic nucleus. Thus the main therapy adopted in
PD is based upon LevoDOPA, the precursor molecule for dopamine. Exploiting the accelerometer for therapy follow-up Fig 4 shows the strong reduction in 4-6Hz peak at rest after LevoDopa acute administration. This testifies the efficacy of medication and increase the reliability of diagnosis if the LevoDOPA acute administration is used as diagnostic tool. In ET mechanical oscillator is responsible of the lower frequency peak, while a higher peak in the range of 8-12 Hz, is dependent from motor unit entrainment, not from inertial load, from joint stiffness nor from stretch reflex length. This last component seems to be probably due to an oscillator located in the supraspinal structure of the CNS [10]. A large bulk of evidence (pathological and clinical) found the thalamocortical and olivocerebellar pathways as the source of oscillation. This tremor is attenuated by ethanol suggesting that essential tremor is primarily a functional disturbance of motor pathways and not a consequence of selective cerebellar lesion/degeneration. In accordance with the literature Fig 5 shows a clear reduction of 12Hz peak after ethanol administration, while the lower 4-6Hz peak is almost unaffected, in an ET patient.

V. CONCLUSION

In parallel with clinical scales and neurological objective exams, that still remains the gold standard for tremor differential diagnosis, the study of tremors can exploit electromiographic recording, spirogram with digitalized Archimed spiral [11] and kinematic sensors such as accelerometers, gyroscopes [12] or video-motion detecting systems [13]. Piezoelectric, piezoresistive or capacitative, monaxial to triaxial accelerometers fixed upon a body segment are cheap, reliable and low-weight sensors that can, from the measures of the acceleration forces that move the part, reconstruct the motion parameters of tremors. Accelerometry has been recently widely involved in the analysis of essential tremor [14] parkinsonian tremor [15] psychogenic tremor [16].

These transducers have the quality to make tremors parameters evaluation more objectively [17]. Moreover the amplitude and frequency of tremor, usually spectrally computed thought Fourier or Wavelet transformation present a good correlation with clinical ratings. According to Weber’s law of psychophysics, the smallest discernible change in tremor $\Delta T$ is $\Delta T = K \cdot T_1$, if $T_1$ is the initial amplitude of tremor and $K$ is Weber’s constant and it is logarithmically related with a five point tremor rating scale [18]. In other words an objective evaluation of tremor together with the knowledge of its relation with patient perception, with a ratio of 1:10, it’s fundamental for the evaluation of the gravity of the disease or the efficacy of the therapy.

REFERENCES


