TIME-FREQUENCY CHARACTERIZATION OF DEEP EEG SIGNALS IN MICRORECORDING-GUIDED NEUROSURGERY

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Abstract: Some encephalic pathologies are associated with neuronal activity alterations. Diagnosis can be carried out acquiring deep EEG signals by means of microrecording-guided neurosurgery. It is necessary to know exactly the neuronal zone where electrode is located, it can be solved through neuronal sound listening. The goal of the present work is to apply time-frequency techniques in order to characterize thalamus and sub-thalamus from deep EEG signal. The present study was accomplished in 7 patients who underwent Parkinson's disease surgery. Signals were classified by neurophysiologist while microelectrode was covering the previously planned trajectory to get sub-thalamus. Three time-frequency distributions were calculated: Choi-Williams distribution (CWD), conic distribution (ZAM) and spectrogram with different window length (SPwl). Reduced interferences distributions (CWD and ZAM) identify better deep EEG brain signals. However functions calculated from spectrogram are better than CWD and ZAM for quantifying neuronal signal. Sub-thalamus has a significant lower bandwidth average (564±27 Hz) than thalamus (601±30 Hz). Energy and frequency parameters calculated from spectrogram also reaches significant differences ($p<0.05$) between thalamus and sub-thalamus. Thus, time-frequency local functions and parameters could be used in order to identify neuronal response in different areas while microrecording-guided neurosurgery is being carried out.

Introduction

Studies have shown that several encephalic pathologies are associated with changes in neuronal bioelectric activity [1]. Specifically, Parkinson's disease is related with neuronal activity variations in the sub-thalamus [2]. In physiological conditions sub-thalamic neurons discharge irregularly. However, under pathological conditions, they show a high and anomalous activity (tremor-cells and bursts).

Microrecording-guided neurosurgery is used to assess the precise location of some specific deep brain areas. A map based on patient cerebral images is insufficient due to brain shifts during surgical intervention and the small size of the targeting areas. Thalamus is a small brain region deeply located. On the other hand, sub-thalamus is even smaller and deeper than thalamus.

Microelectrodes, which only record the activity of few surrounding neurons, are introduced in steps of millimetres towards the target. Bioelectric activity is recorded simultaneously during the electrode course. Some signal processing must be carried out to identify the cerebral area. Traditionally, the sound of the recordings is listened by neurophysiologist. Actually, in order to analyze encephalic signals, some authors have studied other properties of direct signals recorded by the electrodes [3, 4]. Some authors prefer to study bioelectric activity of individual neurons, with techniques based on spike retrieval and its analysis. This is possible applying wavelets techniques [5] or classifying by means of neural networks [6].

Figure 1 shows signals acquired from thalamus and sub-thalamic nucleus (upper and middle traces respectively). It can be observed irregular peaks, specifically in thalamic signal. Therefore, it can be assumed that neuronal activity, recorded from microrecording-guided surgery, produces a non-stationary signal.

The aim of present study is to analyze signals acquired from two cerebral areas: sub-thalamus and thalamus. A third signal will be studied, corresponding to neurophysiologist classification as non-activity (lower trace in figure 1). Time-frequency analysis will be carried out in order to know the exact area where electrode is placed.

Materials and Methods

This study was accomplished in 7 patients who underwent Parkinson's disease surgery. The trajectory to reach the target (sub-thalamus) was studied and fixed before surgical intervention, with the information obtained from medical images.

Five fine tungsten micro-electrodes were introduced through trephine hole [7]. It is used five electrodes, 2 mm separated, for increasing the probability of finding the sub-thalamus. Electrodes are 0.5 millimetres in diameter and 25 millimetres long. Ends are sharpened until reaching less than 50 micrometers of diameter.

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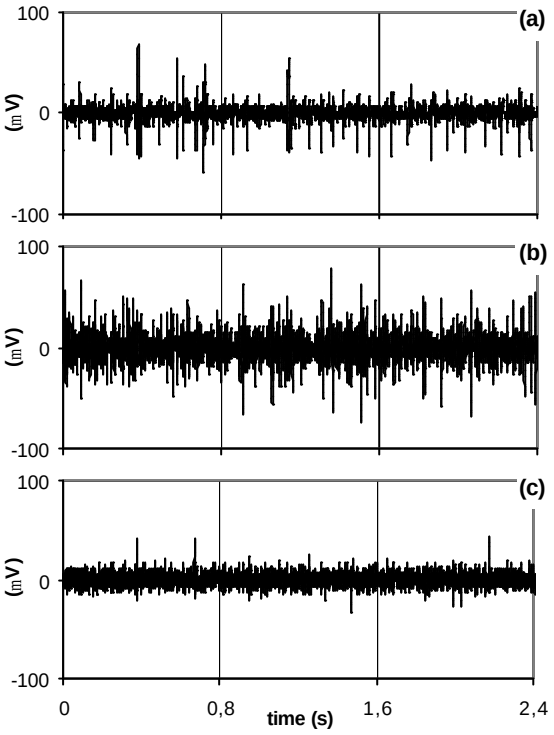

Figure 1: Deep encephalographic signals recorded in thalamus (a), sub-thalamus (b), and non-activity neuronal area (c).

Microelectrodes are introduced, along the planned trajectory, in 5 millimetre steps. Signals were amplified using the bandwidth between 100 Hz and 4 kHz, and they were acquired at 24 kHz sample frequency. After pre-processing, consisting of anti-aliasing low-pass filtering and decimating, 10 seconds of neuronal activity were saved (8 kHz sample rate) in each recording step.

This amplified, acquired and saved signal was listened by neurophysiologist, who diagnosed the cerebral area where each one of the five electrodes is located. More than 600 signals were acquired; however in the present study, 168 signals were selected from thalamus (56), sub-thalamus (56), and from non-activity cerebral area (56). These selected records were classified by neurophysiologist with high certainty rate.

Three time-frequency distributions were calculated for each one of the selected and classified recordings [8]: Choi-Williams distribution (CWD) with σ=1; Zhao-Atlas-Marks distribution (ZAM) with a=1; and spectrogram with two different window length: 50 milliseconds (SP50) and 200 milliseconds (SP200). However, as can be observed in figure 2 and figure 3, spectrogram with large time window (lower traces) had not a good time resolution, which could be negative in order to identify spikes. Therefore, only SP50 was used to quantify spectrogram distribution.

Time functions of spectral parameters and local functions were calculated from time-frequency distributions. Specifically, time marginal (Pt), local frequency (Ft) and local bandwidth (Bt) were obtained from all distributions [Cohen].

Results

Figure 2 and figure 3 shows normalized time-frequency distributions calculated from microrecording-guided when electrode is placed in thalamus (same recording as upper trace in figure 1) and sub-thalamus (recording of middle trace in figure 1). Negative terms of the non-positive distributions (CWD and ZAM) are not shown.

Specifically for thalamus recordings, energy distribution is represented with accuracy in CWD (see figure 2). Thus, noise of the original signal (trace (a) of figure 1) is converted to a diffuse and low energy distribution in CWD (trace (a) of figure 2). An increasing energy can be occasionally seen in precise time localization for higher frequencies. It corresponds to individual spikes, which are neuronal discharges.

However, sub-thalamic recordings (see trace (b) of figure 1) are characterized by a high and anomalous activity which implies that energy distribution in time-frequency is diffuse but high (figure 3). Some spikes could be observed, but they are hidden by the noise allocation in every time-frequency distribution.

Spectrograms reveal the compromise between time and frequency resolution (see traces (c) and (d) in figure 2 and figure 3). The narrowband spectrogram (SP200 in traces (d)) distinguishing spikes in frequency; however, they are not located in time. Wideband spectrogram (SP50 in traces (c)) places precisely the spikes but it loses the frequency resolution.

Several local and marginal functions were calculated from each one of the time-frequency distributions. Figure 4 shows time evolution of frequency and bandwidth in thalamus and sub-thalamus. It can be observed that frequency is higher in sub-thalamus than in thalamus, while bandwidth seems more similar.

If a global statistic study is carried out (see table 1), it can be observed statistical differences between mean values of local and marginal functions obtained from sub-thalamus, versus thalamus or non-activity. Largest differences can be observed in energy parameter, but frequency parameters also present significant differences ($p<0.05$) between values obtained from sub-thalamus and thalamus.

However, this global study does not consider the non-stationary characteristic of the signals. So, other local functions calculated from SP50 could be more interesting. As for example figure 5, where time evolution of a bandwidth rate is shown. Another example is the bandwidth decomposition in a frequency modulated effect (69%) and an amplitude modulated effect (31%).

Table 1: Mean and standard deviation of parameters obtained from local and marginal functions (n=56).

	thalamus	sub-thalamus	non-activity
Et ($\mu V \cdot s$)	480±308	3045±1740	333±205
Ft (Hz)	1205±84	1126±87	1167±152
Bt (Hz)	601±30	564±27	610±34

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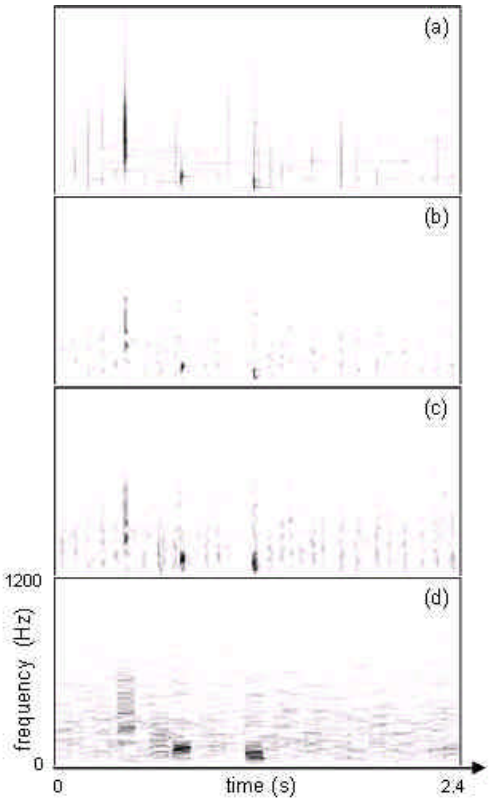

Figure 2: Time frequency distributions calculated for signal recording at thalamus (upper trace in figure 1): CWD (a), ZAM (b), SP50 (c) and SP200 (d).

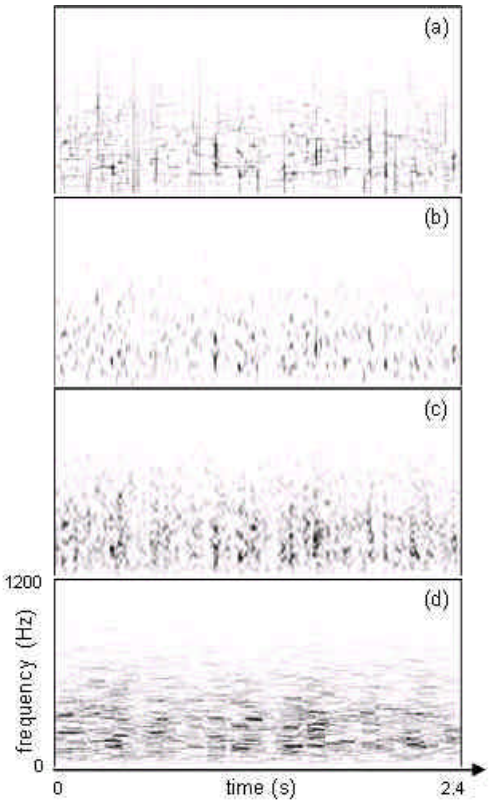

Figure 3: Time frequency distributions calculated for signal recording at sub-thalamus (middle trace in figure 1): CWD (a), ZAM (b), SP50 (c) and SP200 (d).

Discussion

An advantage of the deep EEG signals recordings is the possibility to analyze the neuronal activity in order to characterize these areas. It is an alternative to studies of the individual neuron discharge pattern supported by some authors [6]. Furthermore, in the cerebral areas is possible to analyze the resulting activity of neuronal interactions and their possible variations, relating them with pathological conditions.

Time-frequency was chosen due to signals are non-stationary. Reduced interference distributions are the best distributions for identifying and interpreting the signal object of the present study [8]. So, individual spikes can be observed in CWD when thalamus activity is recorded (figure 2); in contrast with diffuse and high energy distribution shown in sub-thalamus (figure 3).

However, spectrogram is the best distribution for quantifying the signals, due to window effect which implies smoothing. Spectrogram is a non-negative distribution and local functions as time evolution of the frequency (upper traces in figure 4), which could be considered as instantaneous frequency [9], does not get paradoxes like other distributions (CWD) does. SP50 seems more appropriate than SP200, since the difference between thalamus and sub-thalamus is, essentially, the individual spikes manifestation. At present study, only time function calculated from SP50 are presented in figure 5, since they show best results.

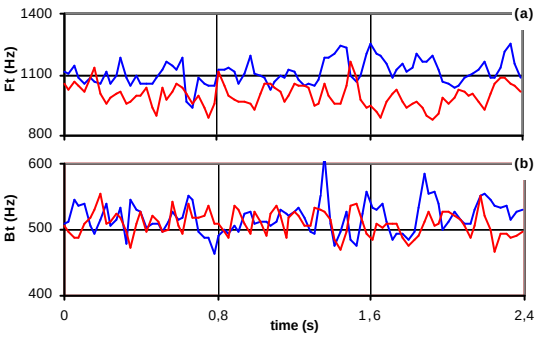

Figure 4: Time evolution of frequency (upper traces) and bandwidth (lower traces) calculated from SP50 of neuronal signal (traces (a) and (b) in figure 1) recorded from thalamus (blue), and sub-thalamus (red).

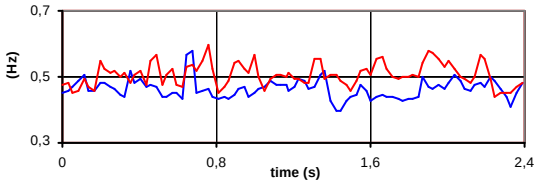

Figure 5: Time evolution of bandwidth ratio (Bt/Ft) calculated from SP50 of neuronal signal (traces (a) and (b) in figure 1) recorded from thalamus (blue), and sub-thalamus (red).

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Local and marginal functions reveal important information about the signals [9]. Figure 4 shows that frequency is higher in thalamus than in sub-thalamus. But this appreciation can be made studying the table 1. Global statistic results are in agreement with other authors who analyzed recordings in spectral studies but considering stationary signals [10].

Another important characteristic is that local functions calculated from sub-thalamus (red traces in figure 4) are more uniform (without high variations) than from thalamus (blue traces). So, parameters as standard deviation of the frequency evolution in time (58 Hz in thalamus vs. 50 Hz in sub-thalamus for upper traces of figure 4) could be used in order to distinguish cerebral areas. The same analysis was carried out for non-activity recordings, and deviation standard of the frequency evolution in time results even superior (more than 90 Hz).

With local functions several studies can be defined as it is shown in figure 5. Rate between time evolutions of bandwidth and frequency is lightly higher to 0.5 in sub-thalamus, while is minor to 0.5 in thalamus recordings. This is due to sub-thalamus frequencies are more distributed than individual spikes of the thalamus.

Spectral energy is the parameter with more significant differences between sub-thalamus and thalamus (see table 1), which is in agreement with some authors [10]. Energy in frequency bands can be calculated with the aim of determining which frequency band gives the best results [10]. However, energy parameters can be modified by the surgical and recording procedure, and normalization must be considered. So, frequency and bandwidth, which are normalized parameters [8,9], can be used for distinguishing cerebral areas because they also present significant differences between sub-thalamus and thalamus or non-activity.

Conclusions

Time-frequency analysis could be used in order to identify and quantify deep EEG signals. Specifically, reduced interference distributions identify precisely spikes and signal patterns of neuronal discharges. On the other hand, spectrogram could be used for quantifying signals. Local functions calculated from spectrogram, as bandwidth evolution in time, contribute to know the deep EEG signals.

In microrecording-guided surgery an important problem is to know exactly the trajectory of the electrodes and the target position. Therefore, local functions obtained from time-frequency distributions, which has been shown at present study, could be used in order to distinguish the cerebral area (sub-thalamus or thalamus) where electrodes are located.

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