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Biomagnetic activity and non linear analysis in obstetrics and gynecology in a Greek population

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Summary

This article reports the application of non-linear analysis to biomagnetic signals recorded from fetal growth restriction, fetal brain activity, ovarian lesions, breast lesions, umbilical arteries, uterine myomas, and uterine arteries in a Greek population. The results were correlated with clinical findings. The biomagnetic measurements and the application of non-linear analysis are promising procedures in Obstetrics and Gynecology.

Key words: Biomagnetic activity; SQUID; Non-linear analysis; Obstetrics; Gynecology.

Introduction

The Superconducting Quantum Interference Device (SQUID) is a diagnostic tool capable of measuring the exceedingly weak magnetic fields emitted by the living tissues. The higher the concentration of living cells in the test area, the higher the biomagnetic fields produced and recorded from it. The method is a non-invasive procedure, well tolerated by the women, rapid, and simple to interpret.

Materials and Methods

Biomagnetic signals were recorded using a single-channel SQUID with a sensitivity of 95 pico-Tesla/volt at 1,000 Hz (DC SQUID model 601, second-order gradiometer) in an electrically shielded room of low magnetic noise. Ultrasound scanner Doppler examination assessed prior to the procedure, the exact placement of the target area in order to ensure that biomagnetic signals from nearby vessels were excluded. The SQUID probe was placed three-mm over the target area to allow the maximum magnetic flux to pass through the coil with little deviation from the vertical direction. Thirty-two consecutive measurements of one-second duration each were taken. The sampling frequency was 256 Hz with a band width between one and 128 Hz. The average spectral densities from the 32 records of magnetic field intensity were obtained after Fourier statistical analysis. The signals were related to measurements of background magnetic activity (noise). The duration of the above signals was justified because the chosen time interval was enough to cancel out, on average, all random events and to record only the persistent ones. In addition to the Fourier power spectrum estimation of the biomagnetic activity and in order to investigate if there was any differentiation in the complexity underlying the dynamics that characterized the activity, dimensional analysis of the existing strange attractors was applied, using a chaotic analysis approach.

The theory of non-linear analysis

According to the Grassberger and Procaccia [1, 2] method, the dynamics of the system can be experimentally reconstructed from the biomagnetic signals. Thus for a discrete time series $B_i=B_{(ti)}$ (i=1,2...N) the vector construction of V_i is given by the following equation:

$$V_i=\{B_i,B_{i+(k+1)\tau},...,B_{i+(m-1)(k+1)\tau}\} \qquad (1)$$

This equation, taking into consideration Theilert's correction [3] by rejecting the k closest neighbors, that are temporally but not dynamically correlated, gives a smooth embedding of the dynamics in a m-dimensional space and the resulting phase trajectory in the phase space is topological equivalent to the original phase space. The reconstruction time τ is a suitable delay parameter, which may be chosen arbitrary. If the dynamics of the physical system is chaotic, the evolution of the system in the phase space, once transients die out, settles on a submanifold which is a fractal set, called the strange attractor. The concept of strange attractors is of a great importance in chaotic dynamics, since its existence or absence is related to the behavior of the system as chaotic or deterministic. If a strange attractor exists, it can be described by a geometrical parameter, the correlation dimension or fractal dimension D. This parameter is related to the number of variables required to define the space of the attractor within the phase space. The Grassberger-Procaccia method [1, 2] is essentially a computational mathematical method of estimating the fractal dimension D from an experimental time series by means of the correlation integrals C(r,m) defined as:

$$C(r,m)= \Theta(r-|V_i-V_j|) \qquad (2)$$

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where $\Theta(u)$ is the Heaviside function defined as ($\Theta(u)=1$ for $u>0$ and $\Theta(u)=0$ for $u \leq 0$), m is the embedding dimension and n is the number of vectors constructed from a time series with N samples, given by the formula $n=N-(m-1)\tau$. The resulting correlation integral C(r,m) measures the spatial correlation of the points on the attractor and it is calculated for different values of r in the range from 0 to r_{max}, where r_{max} is the maximum possible distance of two random selected points of the attractor of the time series. The r_{max} is equal to $(m)^{1/2} (x_{max}-x_{min})$, (assuming that x_{max} and x_{min} are the maximum and the minimum recorded values in the time series). For a chaotic system the correlation integrals should scale as $C(r,m) \sim r^{D(m)}$.Thus, the correlation dimension D of the attracting submanifold in the reconstruction phase space is given by:

$$D = \lim_{n\to\infty} \frac{2}{n(n-1)} \sum_{\substack{i=1 \\ i\neq j}}^{n-1} \sum_{j=1+i}^{n} \Theta(r-|V_i-V_j|) \tag{3}$$

In the case of a chaotic signal exhibiting a strange attractor, there is a saturation value, indicated as a plateau in a graph of these slopes v's ln(r) which remains constant, although the signal is embedded in successively higher-dimensioned phase spaces. The saturation value of the slopes, gives an estimation of the correlation dimension of the attractor.

Specifically the correlation integrals are used to determine whether or not a space of sufficient dimensions, the aforementioned m-dimensional space, exists so that a geometrical area can be defined to enclose the whole of the given signal. It has been proven that if such an m-dimensional space exists, then the value of this embedding dimension m, along with the fractal dimension D are measures of the complexity of the underlying dynamical system.

Fetal growth restriction

Anastasiadis *et al.* [4] studied how chaotic and periodic heart rate dynamics differ between normal fetuses ($n = 19$) and intrauterine growth restricted fetuses (IUGR) ($n = 11$) at 34 to 37 weeks of gestation. They quantified the chaotic dynamics of each heart rate time series obtained by fetal magnetocardiography (FMCG) using correlation dimension. The correlation dimension was significantly lower in IUGR than in normal fetuses ($p < 0.001$). The periodic dynamics were also obtained by fMCG and measured by power spectrum. The low-frequency components and therefore the periodicity of the low-frequency range were significantly higher in IUGR than in normal fetuses ($p < 0.001$).

Fetal brain activity

Anninos *et al.* [5] investigated the fetal biomagnetic brain activity obtained in normal and pre-eclamptic pregnancies. Using the application of non-linear analysis and dimensionality calculations, they observed a clear saturation for the dimension of the fetal biomagnetic brain activity from pre-eclamptic pregnancies and no saturation for normal pregnancies.

Breast lesions

Anninos *et al.* [6] investigated the biomagnetic activity obtained in benign and malignant breast lesions. Magnetic recordings were taken from 21 patients with palpable breast lumps. Of these 11 were invasive carcinomas and ten were benign breast lesions. They used non-linear analysis to investigate whether there was any biological differentiation in the dynamics in these two types of lesions. High amplitudes characterized the waveform of a malignant breast lesions, whereas in benign ones the corresponding amplitudes were low. Using the application of non-linear analysis they observed a clear saturation value for the dimension of malignant breast lesions and no saturation for benign ones.

Ovarian lesions

Anninos *et al.* [7] investigated the biomagnetic activity measured in benign and malignant ovarian lesions. Using the application of non-linear analysis in the ovarian lesions, they observed a clear saturation value for the dimension of malignant ovarian lesions and non-saturation for benign ones.

Umbilical arteries

Anninos *et al.* [8] investigated the hemodynamics of the feto-placental circulation in normal and pre-eclamptic near term pregnancies. Thirteen abnormal and 25 normal pregnancies were included in the study. The application of non-linear analysis revealed a clear saturation value for pre-eclamptic and non-saturation for normal pregnancies. These findings were statistically significant and were correlated with fetal heart rate monitoring, pH, and Apgar score: high biomagnetic cases (140-300 $fT/\sqrt{Hz}$) were related with normal patterns, $pH > 7.25$ and $Apgar > 7$, while low biomagnetic recordings (50-110 $fT/\sqrt{Hz}$) were connected with abnormal patterns, $pH < 7.25$ and $Apgar < 7$.

Uterine myomas

Kotini *et al.* [9] determined if there was any non-linearity in the biomagnetic recordings of uterine myomas. Twenty-four women were included in the study. Sixteen of them were characterised with large myomas and eight with small ones. Uterine artery waveform measurements were evaluated by use of pulsatility index (PI) (normal value $PI < 1.45$). Applying non-linear analysis to the biomagnetic signals of the uterine myomas, they observed a clear saturation value for the group of large ones and no saturation for the small ones.

Uterine arteries

Anninos *et al.* [10] investigated the hemodynamics of uteroplacental circulation in normal and pre-eclamptic pregnancies. Fifteen pregnancies complicated with pre-eclampsia and 37 normal ones were included in this study. All were near term. Applying non-linear analysis to the biomagnetic activity recorded from the uterine arteries in pre-eclamptic pregnancies and using dimensionality calculations, they observed a clear saturation value for pre-eclamptic pregnancies and non-saturation for normal ones. These findings were statistically significant and were correlated with fetal heart rate monitoring, pH, and Apgar score at one and five minutes. High amplitude cases were related to normal fetal heart rate patterns, pH > 7.25 and an Apgar score > 7, whereas low amplitude recordings were correlated with abnormal fetal heart rate patterns, pH < 7.25, and an Apgar score < 7.

Conclusions

Biomagnetic measurements and non-linear analysis are promising procedures in Obstetrics and Gynecology. Therefore, more studies and further technological innovation of the equipment used need to be performed before the method can be established as a screening procedure in clinical practice.

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