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Time-frequency analysis of spontaneous pupillary oscillation signals using the Hilbert-Huang transform

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ABSTRACT

In this work a new application of the Hilbert-Huang transform (HHT) is proposed. Recordings of pupillograms were analyzed through the non-traditional HHT, in order to investigate patterns in the time-frequency parameters of the spontaneous pupillary oscillation (SPO) signals. Unlike the traditional Fourier transform, which is only useful for the analysis of linear stationary signals, the HHT was designed for the analysis of non-linear and non-stationary signals. Therefore, the HHT is a more suitable tool to study SPO signals which are fundamentally non-stationary.

The intrinsic properties of the spontaneous pupillary oscillation signals were characterized under the HHT scheme. The obtained results showed that SPO waves exhibit local and intermittent variations through the time span. From the numerical parameters that were obtained, we could observe that there is a wide inter-subject variation in the contribution of the intrinsic time-frequency parameters from each yielding mode to the total signal content.

1. Introduction

In this study it is demonstrated that the assumption that spontaneous pupillary fluctuation is stationary, it is not only an enormous simplification but a serious misconception. Complex interactions occur between the sympathetic and parasympathetic systems, the two components of the autonomic nervous system which acts as a balance between competing neural mechanisms. Under selected stimulations, the dynamics of this balance mechanism can be significantly altered. Such modifications can be studied using relevant autonomic indices [1].

The iris is a vascular structure; changes in pupil size are under the control of two smooth muscles in it [41]. The sphincter pupillae, located in the stromal layer, is under cholinergic control, mediated via parasympathetic nerves from the Edinger-Westphal nucleus; and the dilator pupillae, situated posterior to the constrictor muscle, is innervated by adrenergic fibers originating in the superior sympathetic ganglion. This set of opposing muscles exercise a fine but extensive control over the pupil [2].

The pupil is richly innervated by autonomic nerves. Its size reflects a balance in tone between the opposing sympathetic (adrenergic) dilator and parasympathetic (cholinergic) constrictor muscle [3]. Pupil diameter can range from 1.5 to more than 9 mm in man, and can react to stimulation in as little as in 0.2 s [4]. In its role of maintaining homeostasis, the autonomic nervous system is in a state of constant fluctuation [5,35]. This fluctuation, expressed by spontaneous variations in the rhythmic changes in pupil-size of around 1%, occurs with heart beats and breathing due to fluctuations in blood pressure [6]. The variance of normal pupil size is very large. It is practically impossible to establish values for normal pupil sizes. The size of the pupil under all conditions of illumination has continuous oscillatory movements. Oscillatory variations in pupil size are thought to be a charactersitic of the regulatory mechanism. These oscillations are often said to show a state of pupillary unrest. This is a physiologic phenomenon [2]. The phenomenon of spontaneous pupillary fluctuation (SPF) appears in the conditions of permanent lighting and eye fixation, and it represents a dynamic equilibrium of pupil size for which the sympathetic and parasympathetic activity modulated by the central nervous system

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is responsible [7]. A typical recording of pupil size in a constant light source shows marked spontaneous activity with an irregular pattern of aperiodic oscillations. Unrest amplitudes are higher for medium pupil sizes [8]. A better term would be spontaneous pupillary oscillations.

2. Related works

In [9] the authors used digital filtering techniques and Fourier analysis to calculate several parameters designed to report hippus and miosis. These techniques provided a quantitative way to evaluate pupillograms that will be used in the assessment of alertness. The first parameter designed to report hippus was derived from the Fourier-transformed pupillogram and was the area of the frequency spectrum in a selected band of frequencies. A second parameter to report hippus was also investigated. Spectra differed by the most at low frequencies. At higher frequencies, differences diminished.

A fast Fourier transformation was carried out as an objective test of vigilance for frequencies from 0.0 to 0.8 Hz in [10] with the purpose of detecting fatigue waves, i.e., slow pupillary oscillations. For the analysis of temporal changes in the frequency domain of pupillary oscillation, two parameters were extracted. One parameter was based on the FFT regarding only frequencies below 0.8 Hz, neglecting fast pupillary changes (>1.5625 Hz). An additional parameter referring to the pupil's tendency to instability, the pupillary unrest index (PUI), was defined by cumulative changes in pupil size based on mean values of consecutive data sequences. The power and PUI were compared using the Mann–Whitney *U* test. Both parameters showed significant differences between the two groups [43]. The main differences between an alert group of men and a sleepy one, in power and PUI, demonstrated the usefulness of this method to detect and quantify sleepiness objectively.

The aim of the study reported in [11] was to assess whether, and to what extent, LF and HF rhythms contribute to spontaneous pupil diameter fluctuations at rest and during sympathetic activation [42]. To investigate the statistical properties of the SPDF, a parametric spectral and cross-spectral estimation was used. The spectral coherences were used to quantify the statistical link among rhythms in different signals. A rhythmic respiratory component (HF) was clearly found at 0.25 Hz in the pupillogram spectrum in all the subjects. Cross-spectral analysis showed significant coherence in this band between pupil and respiration, pupil and tachogram and pupil and systogram [33]. In conclusion, the analysis of the SPDF showed the contribution of two specific harmonic components, which have been found to correspond to the well-known LF and HF rhythms of the heart rate and blood pressure variability signals [34]. Additionally, the authors concluded that the apparently stochastic behavior of the spontaneous PDF hides specific harmonic components reflecting the autonomic activity [40].

In [7] the authors developed a new method for the variability description of the spontaneous pupillary fluctuation (SPF) signals based on the time-frequency analysis. They studied the variability of the SPF signal spectrum. The application of fast pupillometry for recording the SPF allowed them to expand the analyzed frequency band to 20 Hz. The proposed method of analysis and the introduced measures of SPF variability enabled them for the detection and quantitative description of short-lasting time-frequency and time-amplitude variations that remain obscured by the overall spectral analysis [37]. The authors mentioned that the Fourier transform (which requires a stationary signal and is commonly used in the spectral analysis of SPF) has limitations in that signal testing. It was concluded that the SPF signal is non-stationary, i.e., its spectrum varies in time. Thus, it was demonstrated that the previous assumptions are no longer valid [12].

For some time it has been believed that the fluctuations in pupil diameter arose from random processes but new results from chaotic time series have shown that they may also arise from deterministic systems [8]. The accumulated evidence supports the notion that the dynamics of pupil size are governed by deterministic chaos rather than a linear or stochastic process. This has been demonstrated by analyzing the pupil size versus time from six subjects using pupillography and nonlinear techniques [8]. The examined values of the correlation dimension, the Hurst exponent, the flat power spectra, the values of the Lyapunov exponent, and phase plane analyses indicated a chaotic system as the origin of the phenomenon. In addition, it has been reported that the pupil activity showed repetitive complex patterns which could be explained by a chaotic system instead of a random one [8].

As mentioned previously, the analysis of the SPF signal has been used for monitoring the level of alertness in clinical conditions, for diagnosing sleep disorders, for assessing how the different rhythms of the SPS contribute to spontaneous pupil diameter fluctuations at rest and during sympathetic activation, and for assessing the efficacy of therapeutic interventions [42,13–16,11,17–19,10]. These analyses have been usually performed thanks to spectral indices computed from standard spectral analysis techniques (such as the fast Fourier transform). Such methods have generated comparable results but cannot account for the unavoidable inter-individual variability that naturally occurs in pupillary fluctuation signals. There are some crucial restrictions of these techniques: the system must be linear and the data must be strictly stationary; otherwise, the features extracted via the Fourier transform do not have any physiological significance [13,31].

Physiological signals are non-linear and non-stationary waves, for which the Fourier transform is unsuitable [20]. It is desirable to employ quantitative methods which do not assume stationarity [31]. The Hilbert-Huang transform (HHT) was developed initially for natural and engineering sciences and now is applied to financial data [21]. The HHT method is specially developed for analyzing non-linear and non-stationary data.

Nowadays, several methods are available for the time-frequency analysis of non-stationary signals. For instance, the short-time Fourier transform (STFT) can be used when the signal is piece-wise stationary whereas the wavelet transform can be used for linear non-stationary signals. One drawback of the wavelet transform is that a *priori* knowledge about the signal to analyze is needed in order to choose a suitable wavelet. Another drawback is that its time-frequency resolution is limited by the Heisenberg-Gabor uncertainty principle. In contrast, the HHT can be used to analyze nonlinear and non-stationary signals with excellent resolution in both time and frequency [22,23].

3. Hilbert-Huang Transform

The development of the HHT was motivated by the need to describe non-linear and non-stationary distorted waves in detail [38]. It was developed at the National Aeronautics and Space Administration's (NASA's) Goddard Space Flight Center (GSFC), and pioneered by [21,24–28]. Since its introduction, it has shown the ability to analyze non-linear and non-stationary data in many areas of research (bio-signal, chemistry and chemical engineering, financial applications and others). In comparison with other common transforms like the Fourier transform, the HHT is more like an algorithm (an empirical approach) that can be applied to a dataset, rather than just a theoretical tool. It has also been called *data-driven method*, which means that the function is derived from the data itself. This decomposition method is adaptive, and therefore, highly efficient. As indicated by [29], one of the advantages of the HHT is that its data-driven criteria is not fully dependent on a theoreti-