DYNAMICS DAYS SOUTH AMERICA 2010
International Conference on Chaos and Nonlinear Dynamics

INPE – National Institute for Space Research
São José dos Campos – SP – Brazil – July 26-30, 2010

MULTISCALE ENTROPY ANALYSIS OF SPONTANEOUS BLINKING TIME SERIES

Denny Marcos Garcia[1], *Carolina Trindade Pinto*[2] *e Antonio Augusto Velasco e Cruz*[3]

[1] School of Medicine of Ribeirão Preto – USP, Ribeirão Preto, Brazil, dmgarcia@fmrp.usp.br
[2] School of Medicine of Ribeirão Preto – USP, Ribeirão Preto, Brazil, carolinatpinto@yahoo.com.br
[3] School of Medicine of Ribeirão Preto – USP, Ribeirão Preto, Brazil, aavecruz@fmrp.usp.br

Abstract: We compare the complexity of spontaneous blinking of healthy subjects and of Graves' orbitopathy patients. Using a multiscale entropy algorithm which may provide a way to measure complexity over a range of scales, we observed no difference between groups in either time series analyzed, interblink intervals and amplitude. This finding leads to the conclusion that Graves' orbitopathy does not interfere with the central control of spontaneous blinking.

keywords: Time series analysis, multiscale entropy, spontaneous blinking, Graves' orbitopathy.

1. INTRODUCTION

The upper eyelid, has an important role in the protection and lubrication of the ocular surface.[1] Graves' orbitopathy is an autoimmune condition characterized by upper eyelid retraction, restrictive myopathy of the extraocular muscles and proptosis[2]. The coexistence of lid retraction and proptosis is especially dangerous for the ocular surface and the affected patients often develop exposure keratitis.

Usually, spontaneous blinking activity is assessed by simple measurements such as the blink rate and the distribution of time intervals between blinks. To the best of our knowledge, there are no studies on the structure of the event sequence. Entropy-based algorithms for measuring the complexity of physiologic time series have been widely used[3,4] to discriminate disease states.[5,6]

2. PURPOSE

To apply multiscale entropy algorithms to the analysis of the complexity and regularity of time series of spontaneous blinking in healthy subjects and Graves' patients.

3. METHODS

3.1. Subjects

We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research.

Two groups of subjects were prospectively studied. The control group (G1) consisted of 6 healthy subjects (4 women and 2 men) with no history of systemic or ocular diseases ranging in age from 30 to 67 years (mean ± SD, 44.8±13.5). The Graves group (G2) consisted of 5 patients (3 women and 2 men) with Graves' orbitopathy ranging in age from 39 to 67 years (52.8±11.0). In the control group the lid was randomly chosen. In the Graves patients we selected the lid with the greater retraction.

3.2. Data collection

Eyelid blinks were recorded using the magnetic search coil technique.[7] The subject is comfortably positioned in a weak magnetic field and watches a movie for 60 minutes. The signal generated by the coil is pre-processed, digitized by an AD converter NI PCI-6220 and the data are saved in ASCII text format.

The detection of spontaneous blinks was performed by the method based on derivatives, using custom software developed in Python 2.6. We considered the temporal position of the maximum amplitude to determine the moment of each event. Two series were obtained from this process, one with the interblink intervals in seconds (ITBI) and the other with their respective amplitudes in degrees (AMP).

3.3. MSE method

Given a time series, $\{x_1,...,x_i,...,x_N\}$, a consecutive coarse-grained time series is first constructed by averaging a successively increasing number of data points. Each element of the coarse-grained time series, $y_j^{(\tau)}$, is calculated by (1):

$$y_j^{(\tau)} = \frac{1}{\tau} \sum_{i=(j-1)\tau+1}^{j\tau} x_i \,, \quad 1 \le j \le N/\tau \qquad (1)$$

where τ represents the scale factor. The N/τ length of each coarse-grained time series is N/τ. For scale 1, the coarse-grained time series is simply the original time series. Sample entropy[5] (SampEn) is then calculated for each coarse-grained time series.

SampEn quantifies the regularity of a time series. It reflects the conditional probability that two sequences of m data points which are similar to each other will remains similar when one more consecutive point is included. The sequences are considered to be similar when a specific distance measure is less than r. Therefore, SampEn is a function of m and r parameters.[8]

3.4. Data analysis

For each time series ITIB and AMP were obtained as shuffled time series ITIBs and AMPs. A routine was developed using Matlab 7.0® to reorder randomly the sequence of data points. Therefore, four time series were studied in each subject. The MSE was calculated by the PhysioToolkit[9] software using parameters m = 2, r = 0.2 and 20 scales, since this configuration is more common.

4. RESULTS

Overall, a total of 9574 blinks were record for G1 and 8110 for G2. The means (±SD) were 26.2±7.2 (G1) and 22.6±5.1 (G2) for AMP and 2.40±0.61 (G1) and 2.43±0.80 (G2) for ITIB.

The MSE results are presented as the group mean for each time series on 20 scales (Figure 1).

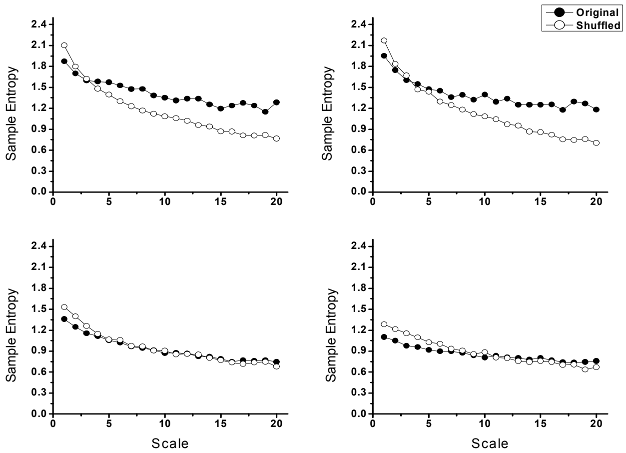

Figure 1 – Top: AMP and AMPs. Bottom: ITIB and ITIBs. Left: Control Group. Right: Graves Group.

Table 1 shows how the standard deviation varied throughout the time series.

Table 1. Mean SD (min-max) of each time series along scales.

	G1	G2
AMP	0.16 (0.05 - 0.29)	0.14 (0.05 - 0.26)
AMPs	0.06 (0.02 - 0.13)	0.09 (0.05 - 0.14)
ITIB	0.36 (0.30 - 0.43)	0.34 (0.28 - 0.49)
ITIBs	0.17 (0.07 - 0.38)	0.25 (0.12 - 0.53)

5. DISCUSSION

Numerical simulation shows that the entropy for white noise time series decreases monotonically with the scale factor while the entropy for 1/f noise remains constant for all scales.[9]

First, we can see that the time series showed similar behavior in the two groups. The AMP time series had a greater entropy than the ITIB time series. This suggests that there was a smaller number of repetitions in the AMP pattern. Generally, higher entropy values are related to white noise, or uncorrelated series. However, when AMP is compared with its shuffled time series, AMPs, we see that both groups had higher entropy in the first 3 scales while the others had lower entropy. This characteristic, as mentioned above, is related to the fact that shuffling the series broke possible dependencies between events, which are in a temporal order. Finally, we can say that although the AMP time series behaves like white noise in the first scales, it keeps a trend in the entropy for larger scales, suggesting a degree of dependence in the long term.

ITBI time series have low entropy values, with consequent greater similarity in their temporal pattern. The constant behavior of the entropy value across scales also suggests the presence of 1/f noise. Time series which have 1/f noise tend to keep their entropy values even with increasing scales. This noise has been found in various neural activities[10] and the blink activity probably is related to the dopaminergic system[11].

Probably due to the presence of spikes in the ITIB, its shuffled series, ITIBs, showed no major differences from the original series, since these spikes interfere significantly with the standard deviation, increasing the degree of tolerance of the r parameter. However, by analyzing the standard deviation of the mean entropies (Table 1), we notice that the standard deviation is lower for the shuffled series. The breaking of the temporal correlation of the series causes the entropy to vary less among individuals. This result argues for the existence of temporal dependence between blinking events throughout the series.

6. CONCLUSION

Entropy-based algorithms have been used to quantify complexity and regularity in biological time series. The ITBI and AMP may be used to compare groups with different eye conditions. Although the time series analyzed show degrees of temporal dependence between events, no difference was detected between groups. Since Graves' orbitopathy is a peripheral disease, probably there is no modification in the central control.

References

[1] M.G. Doane, "Blinking and the mechanics of the lacrimal drainage system", Ophthalmology, Vol. 88, pp. 844-851, 1981.

[2] G.B. Bartley, C.A. Gorman, "Diagnostic criteria for Graves' ophthalmopathy", Am J Ophthalmol, Vol. 119, pp. 792-795, 1995.

[3] J.S. Richman, J.R. Moorman, "Physiological time-series analysis using approximate entropy an sample entropy", Am J Physiol Heart Circ, Vol. 278, pp. H2039-2049, 2000.

[4] M. Costa, A.L. Goldberger, C.K. Peng, "Multiscale entropy analysis of biological signals", Phys Rev E, Vol. 71, 021906, 2005.

[5] S.M. Pincus, "Assessing serial irregularity and its implications for health", Ann N Y Acad Sci, Vol. 954, pp. 245-267, 2001.

[6] M. Costa, A.L. Goldberger, C.K. Peng, "Multiscale entropy to distinguish physiologic and synthetic RR time series", Comput Cardiol, Vol. 29, pp. 137-140, 2002

[7] D.A. Robinson, "A method of measuring eye movement using a sclera search coil in a magnetic field", IEEE Trans. Biomed. Eng., Vol. 10, pp. 137-145, 1963.

[8] M. Costa, C.-K. Peng, A.L. Goldberger, J. M. Hausdorff, "Multiscale entropy analysis of human gait dynamics", Physica A, Vol. 330, pp. 53-60, 2003.

[9] PhysioTookit, "Open source software for biomedical science and engineering", http://www.physionet.org, accessed in April 2010.

[10] P. Grigolini, G. Aquino, M. Bologna, M. Lukovic, B.j. West. "A theory of 1/f noise in human cognition", Phisica A, Vol. 388, pp. 4192-4204, 2009.

[11] C.N. Karson, "Spontaneous eye-blink rates and dopaminergic systems", Brain, Vol. 106, pp. 643-653, 1983.