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Noise and poise: Enhancement of postural complexity in the elderly with a stochastic-resonance–based therapy

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Abstract – Pathologic states are associated with a loss of dynamical complexity. Therefore, therapeutic interventions that increase physiologic complexity may enhance health status. Using multiscale entropy analysis, we show that the postural sway dynamics of healthy young and healthy elderly subjects are more complex than that of elderly subjects with a history of falls. Application of subsensory noise to the feet has been demonstrated to improve postural stability in the elderly. We next show that this therapy significantly increases the multiscale complexity of sway fluctuations in healthy elderly subjects. Quantification of changes in dynamical complexity of biologic variability may be the basis of a new approach to assessing risk and to predicting the efficacy of clinical interventions, including noise-based therapies.

The development of predictive tests for falls, a major cause of disability and death in older individuals, is a challenging and important task. Postural instability in elderly people and in patients with certain pathologies [1–5] is a major contributor to such falls. Recently, a novel intervention [6–10] was proposed to increase postural stability that is based on the principle of stochastic resonance —enhancing signal transmission by introducing noise into the system.

The search for new therapeutic interventions designed to improve postural stability underscores the need to develop reliable non-invasive methods to test for beneficial effects.

Previous studies [11–14] have shown that the time series generated by a variety of free-running healthy physiologic dynamics exhibit complex fluctuations that are not simply due to uncorrelated random errors. This is also true for physiologic systems whose main purpose seem to be reducing variability and maintaining a steady state, as for example, the postural control system [15]. Previous studies [16] suggested[1] that the complex fluctuations in the time series of the center of pressure (COP) position during quiet standing result from the interactions among the somatosensory, vestibular and the visual systems feedback mechanisms.

The purpose of this study is to quantify the complex dynamics of postural control in healthy subjects and compare these dynamics to those from elderly people at risk of falls. Furthermore, we purpose to determine whether loss of postural complexity is reversible through a noise-based intervention aimed at enhancing sensory feedback from the feet.

We assume that the postural regulatory mechanisms control two fundamental variables related to balance: the

[1]Previous studies [16] of postural control in humans using stabilogram-diffusion analysis indicate that over time intervals shorter than approximately one second, the body sways as a positively correlated random walk, while over larger time intervals it resembles a negatively correlated random walk.

position of the center of pressure and the velocity at which the center of pressure changes its position.

Accordingly, to probe the dynamical properties of postural control, we quantify the complex variability of the COP position and velocity time series for both the anteroposterior (AP) and mediolateral (ML) directions. Following ref. [7], the AP and ML directions refer, respectively, to the front-to-back and side-to-side changes in the center of pressure distribution underneath the feet during postural sway. Our underlying conceptual framework includes the notions that: i) healthy systems with intact regulatory mechanisms, which have the highest capacity to adjust to an ever-changing environment, generate the richest outputs, *i.e.*, signals with the highest information content over multiple temporal/spatial scales; ii) due to the degradation of the control mechanisms and/or the coupling among them, aging and pathologic systems generate less complex (either more ordered or more random) outputs; and iii) interventions that enhance postural balance control also enhance dynamical complexity.

Recently, a mathematical method, termed multiscale entropy (MSE) [14,17–19], was introduced to measure the complexity of physical as well as physiologic time series with a limited number of data points. The MSE method quantifies the information content of a signal over multiple scales.

Briefly, the method comprises two steps. First, we construct consecutive coarse-grained time series by averaging a successively increasing number of data points in non-overlapping windows. Each coarse-grained time series captures the system's dynamical behavior on a given time scale. Second, we quantify the information content of all coarse-grained time series by measuring their entropy. Finally, we plot the entropy values as a function of scale and analyze the profile of the obtained MSE curves.

In this paper, we use the MSE method to test the following specific hypotheses: i) the time series of both the COP position (displacement) and velocity obtained from elderly fallers are less complex than those obtained from either healthy young or healthy elderly subjects; and ii) the complexity of both the COP sway and velocity time series will increase with a stochastic-resonance–based intervention that enhances postural stability.

The time series presented here were derived from signals recorded for 30 s at either 100 Hz or 60 Hz. Due to the short duration of the available recordings, in this study we focus exclusively on the COP fluctuations that can be accounted for by previously described [16] regulatory mechanisms operating over short time scales (< 1 s).

Two technical issues need to be taken into consideration when applying the MSE analysis to COP sway time series: i) data length and ii) stationarity. Since MSE is a statistical measure, the length of the data has to be substantially larger than the scales we study to ensure enough samples for the analysis [18,20]. Typically, time series of the length used here with either 1.8×10^3 or 3×10^3 data points can be coarse-grained up to scale 6, in which case the shortest coarse-grained time series comprises 300 or 500 data points, respectively.

Sample entropy examines a time series for similar epochs of a pre-determined length m. Briefly, it calculates the negative natural logarithm of the conditional probability that sequences similar for m points remain similar when one more point $(m+1)$ is added to those sequences. In our analysis, $m = 2$ and $m + 1 = 3$. In the case of the time series sampled at 60 Hz, we analyze temporal structures whose characteristic scales range from 0.05 s for scale 1, to 0.3 s for scale 6. This upper time scale is within the range where the COP displacement has been reported [7] to fluctuate like a positively correlated random walk.

Nonstationarities defined on scales larger than those considered for the MSE study may also substantially alter the results. Such nonstationarities may lead to a spurious increase in the apparent degree of irregularity of a time series for the shortest scales. To overcome this problem, prior to performing the MSE analysis, the original COP sway time series need to be detrended beyond the scales of interest. We applied two different methods for detrending the data in order to verify that our results are independent of the algorithm used (see appendix). The parameters for both detrending algorithms were selected such that they remove slow-varying trends on scales larger than the upper time scale limit of the MSE analysis.

By definition, the COP velocity time series is the first derivative of the COP position time series. The velocity time series were obtained by calculating the differences between consecutive data points of the sway time series. To the extent that the derivative time series are much more stationary than the original time series, there is no need to detrend the velocity time series before calculating their MSE curves.

In order to study the effects of aging and pathology on the complexity of postural dynamics, we analyzed COP sway and velocity time series derived from signals continuously recorded for 30 seconds from 15 healthy young (age: mean $\pm$ SD, 27 ± 3 years), 22 healthy elderly (75 ± 4 years), and 22 elderly faller (74 ± 6 years) subjects, using the experimental protocol described in [7]. Ten trials per subject were obtained. Figure 1 shows representative COP sway and velocity time series in the AP direction for the three groups of subjects. Note that the sway time series show high frequency fluctuations superimposed on the low frequency trends (red line in the on-line version). These trends were obtained by summing the 5 intrinsic mode functions of lowest frequency as described in the appendix.

The MSE curves were calculated for all subjects for all trials. For each MSE curve we calculated the complexity index C_I, defined as the area under the curve [14]: $\sum_{i=1}^{6} \mathrm{SampEn}(i)$.

The complexity indexes (see table 1) for the position and the velocity of the COP time series from both the

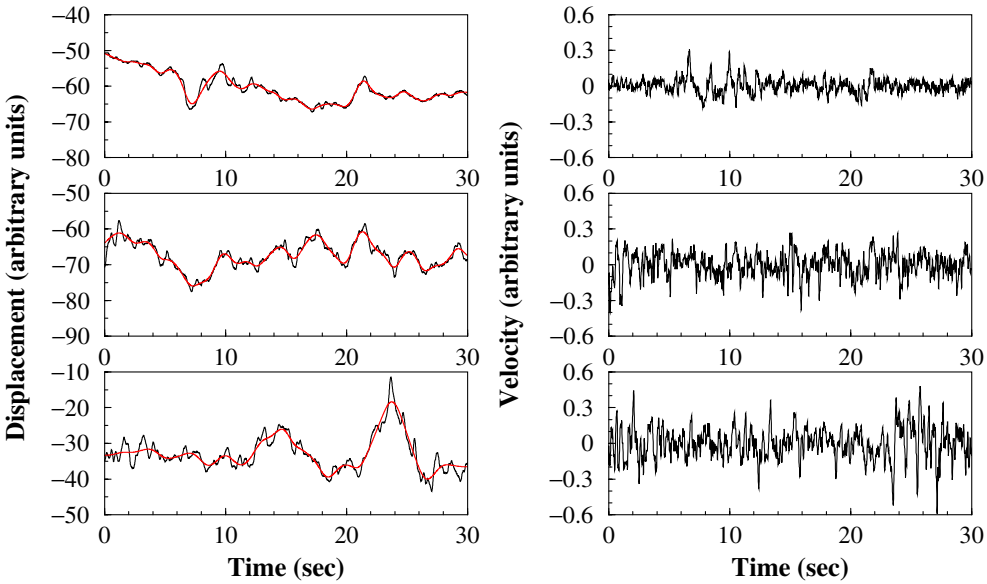

Fig. 1: (Colour on-line) Time series of the center of pressure displacement (left panels) and velocity (right panels) in the anteroposterior direction for representative: healthy young (top panels), healthy elderly (middle panels) and elderly faller (bottom panels) subjects. For each displacement time series the trends obtained by summing the 5 intrinsic mode functions of lowest frequency are shown in red in the on-line version (see appendix.)

Table 1: Complexity indexes (C_I) and p values obtained using one-tailed t-test with unequal variance. AP and ML are the abbreviations of anteroposterior and mediolateral directions, respectively. n. s. indicates not significant.

C_I (mean $\pm$ SD)	Position		Velocity	
	AP	ML	AP	ML
Young	5.8 ± 2.0	3.8 ± 1.3	9.3 ± 1.6	8.9 ± 1.4
Elderly	5.4 ± 1.6	3.8 ± 1.3	8.9 ± 1.6	8.3 ± 1.6
Fallers	4.5 ± 1.2	3.4 ± 0.9	7.9 ± 1.2	7.6 ± 1.4
p values				
Young *vs.* Fallers	4×10^{-3}	n. s.	2×10^{-3}	7×10^{-4}
Elderly *vs.* Fallers	4×10^{-3}	n. s.	4×10^{-3}	4×10^{-2}

AP and ML directions were, on average, higher for the healthy group of subjects than for the group of fallers. To test whether these differences were statistically different or not we used a one-way analysis of variance (ANOVA) (table 1).

From the analysis of the COP displacement time series, we found that the complexity indexes for the three groups of subjects were significantly different for the AP but not the ML direction. *Post hoc* analysis of the AP complexity indexes, using a one-tailed t-test with unequal variance, indicated that the complexity indexes for both the young and the elderly groups were significantly higher than for the elderly faller group.

From the analysis of the COP velocity time series, we found that the complexity indexes for the three groups of subjects were significantly different in both the AP and ML directions. *Post hoc* analysis of the AP and ML complexity indexes, using a one-tailed t-test with unequal variances, indicated that the complexity indexes for both the young and the elderly groups were significantly higher than for the elderly faller group.

These results are consistent with the hypotheses that the postural sway dynamics of healthy individuals are the most complex and that the control system's complexity degrades with disease.

Recently, Collins and colleagues [6–8] showed that the application of subsensory vibratory white noise to the feet of young and elderly subjects enhances sensory and motor function, possibly via a stochastic-resonance–type of mechanism. Using stabilogram-diffusion analysis, the authors of ref. [8] found that, in the presence of input vibratory noise, the values of two postural sway parameters (the ML range and critical mean square displacement) for elderly subjects approached the values for young subjects. Based on the concept that healthy systems exhibit the most complex fluctuations and that complexity analysis can be used to assess the health status of a physiologic system, we hypothesized that input noise would enhance the complexity of COP dynamics of elderly subjects. Therefore, the MSE algorithm was next used to analyze the time series of both the position and the velocity of the COP fluctuations derived from 15 young (age, mean $\pm$ SD: 23 ± 2 years) and 12 elderly (age, 73 ± 3 years) healthy subjects under baseline conditions and with subsensory noise stimulation, as described in [8]. The original data are available at `http://physionet.org/physiobank/database/nesfdb/`. Briefly, young subjects did 20 trials: 10 with mechanical noise applied to the sole of each foot, and 10 without;

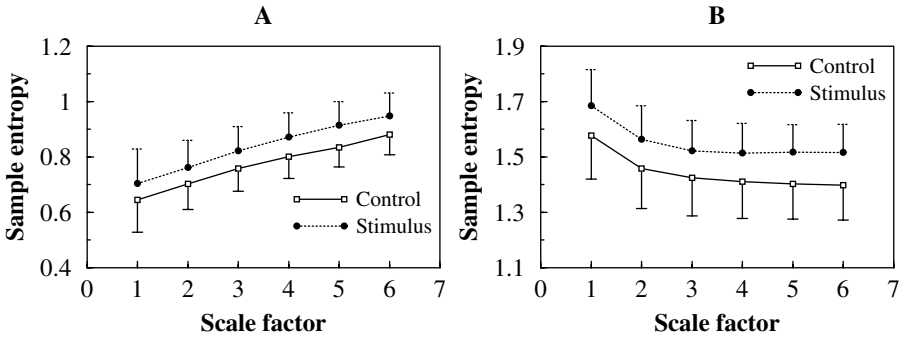

Fig. 2: MSE analysis of: A) anteroposterior and B) mediolateral postural displacement sway time series recorded under free-running (control) conditions and with subsensory noise stimulation (stimulus) from a healthy elderly subjects. Time series were detrended using the empirical mode decomposition method. The symbols represent mean values of sample entropy (SampEn) for all subjects and all trials and error bars represent standard errors. Parameters for the calculation of SampEn were: $m = 2$ and $r = 0.15$.

elderly subjects did 10 trials: 5 with input noise and 5 without. Each trial had a duration of 30 seconds. Signals were sampled at 60 Hz.

Figure 2 presents mean MSE values for the AP and ML sway displacement time series of healthy elderly subjects obtained with and without the application of subsensory noise. We found that noise significantly increased the values of the complexity indexes for both directions[2]. The p values obtained using a one-tailed Student's paired t-test were 0.02 and 0.03 for the ML and AP directions, respectively. In contrast, the changes in the complexity of the postural dynamics of young subjects in response to the application of noise were not statistically significant suggesting that, in the group of healthy subjects, the feedback postural control mechanisms operate at an already optimized level of control and cannot, therefore, be substantially improved.

Analysis of the time series of the velocity of the COP displacement also revealed a significant increase in the values of the complexity during the application of subsensory noise for both the AP (p value $= 0.006$) and ML (p value $= 0.01$) directions.

These results indicate, for the first time to our knowledge, that an external noise-based intervention may increase physiologic multiscale complexity and support previous reports of noise enhancement of postural stability in elderly subjects. These findings are also consistent with the prior observation of loss of multiscale complexity in cardiac interbeat interval time series with aging and disease [17,18]. Finally, the findings raise the possibility of using MSE and other complexity metrics as "dynamical assays" of therapeutic efficacy, even with relatively short time series.

[2]The increase in the complexity of sway fluctuations with white noise application is not directly attributable to the uncorrelated noise itself but to the integrated response of the postural control mechanisms to the noise. Indeed, the superposition of white noise on a time series either degrades (or leaves unchanged) the complexity of the original time series [18].

Appendix

Data detrending. – First, a detrended time series was derived from the original time series by subtracting the average value inside a window of length $L = 51$ data points (0.50 s) from the value of the window's middle data point, *i.e.* data point 25. The window is then moved one point at a time over the whole time series.

As a second independent approach, we used the empirical mode decomposition (EMD) method [21–24] to detrend the signals. The EMD method was specifically developed for decomposing nonlinear, non-stationary signals into their intrinsic frequencies components. Unlike wavelet and Fourier analyses, this method has the advantage of using a fully adaptive basis derived from each data set by means of a sifting process.

The EMD method decomposes a signal $X(t)$ into a complete set of "intrinsic mode functions" (IMFs), $X(t) = \sum_{i=1}^{n} \Psi_i(t) + r_n(t)$, where $\Psi_i(t)$ is the i-th IMF and $r_n(t)$ is a residue, which can be either the mean trend or a constant. Typically, the power spectrum of an IMF is a peaked function with predominant power over only a limited range of frequencies [22]. Although, a certain degree of overlap between the spectrum of consecutive IMFs is expected, different IMFs capture the properties of the original signal on different time scales.

The empirical mode decomposition (EMD) algorithm decomposes a signal with N data points into a maximum of $\log_2 N$ intrinsic mode functions (IMFs). For the time series analyzed here we typically obtain 10 components with characteristic frequencies given by $sample\ frequency/(2^{n+1})$, where $1 \leqslant n \leqslant 10$. The first 5 IMFs have predominant power for frequencies ranging from approximately 1 to 30 Hz, and the last 5 IMFs have predominant power for frequencies ranging from approximately 0.05 to 1 Hz. The detrended time series can then be obtained in two equivalent ways: 1) adding together

the 5 IMFs of highest frequency, or 2) subtracting the 5 IMFs of lowest frequency from the original time series.

To the extent that our study is limited to the analysis of temporal structures with characteristic scales ranging from 0.01 s (100 Hz) to 0.3 s (3 Hz), the removal of frequencies below 1 Hz assures that no relevant information for the multiscale analysis is lost with the detrending process.

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