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The Hurst exponent of heart rate variability in neonatal stress, based on a mean-reverting fractional Lévy stable motion

Matej Šapina, MD^{a,b,c,*}, Matthieu Garcin, PhD^{d,*}, Karolina Kramarić, MSc^{a,b,c},
Krešimir Milas, MD^{a,b}, Dario Brdarić, PhD^e, Marko Pirić, MD^b

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Abstract

We aim at detecting stress in newborns by observing heart rate variability. The heart rate variability features nonlinearities. Fractal dynamics are a usual way to model them and the Hurst exponent summarizes the fractal information. In our framework, we have observations of short duration, for which usual estimators of the Hurst exponent, like DFA, are not adapted. Moreover, we observe that the Hurst exponent does not vary much between stress and rest phases, but its decomposition in memory and underlying probability distribution leads to satisfactory diagnostic tools. This decomposition of the Hurst exponent is in addition embedded in a mean-reverting model. The resulting model is a mean-reverting fractional Lévy stable motion. We estimate it and use its parameters as diagnostic tools of neonatal stress: the value of the speed of reversion parameter as well as the evolution of both parameters in which the Hurst exponent is decomposed are significant indicators of stress, whereas the Hurst exponent itself does not bear useful information.

Keywords – fractals, heart rate variability, mean reversion, stable process, Hurst exponent

1 Introduction

In the evolutionary context, acute stress is life-saving when evading a predator. However, exposure to chronic stress is harmful [32]. Stressors are various nonspecific stimuli which cause a stress response variety [51]. What does not seem to be stressful to adults, might have significant effects on a term-, moreover, on a preterm newborn [30, 20].

If exposed to acute stress, like a simple heel prick blood drawing, the newborn goes through significant physiological changes. The infants start crying, but in behind the curtains the activation of the hypothalamic-pituitary-adrenocortical (HPA) system goes on [21, 10]. Serum catecholamine and glucocorticoid levels rise, the sympathetic of the autonomic nervous system rises, both the heart and blood pressure increase, the heart rate variability, respiration rate and respiration movements change etc. [20, 38, 49, 45, 29].

Much effort is given towards the prevention of stress in human term and preterm newborns [6]. Due to their immaturity, preterm infants are more vulnerable than term infants to acute stress. Having already a compromised autoregulation of cerebral blood flow, its fluctuations caused by various stressors might disturb normal neurodevelopment [30, 55].

The long-term effects of stress exposure are related to the prolonged effects of glucocorticoids on every body

*These authors contributed equally to this study. Corresponding author: matthieu.garcin@m4x.org.

^a University hospital Osijek, Pediatric Clinic, J. Huttlera 3, 31000 Osijek, Croatia.

^b Medical faculty Osijek, Cara Hadrijana 10E, 31000 Osijek, Croatia.

^c Faculty of Dental Medicine and Health, Crkvena 21, 31000 Osijek, Croatia.

^d Léonard de Vinci Pôle Universitaire, Research center, 92916 Paris La Défense, France - LabEx ReFi

^e Institute of Public Health for the Osijek-Baranya County, Drinska 8, 31000 Osijek, Croatia.

system [32]. Abnormal perinatal conditions have also been associated with various behavioral and emotional deviations, lower cognitive capabilities, and might cause epigenetic modifications [45, 53, 16, 22].

In this paper, we propose a new method to detect stress in newborns. This method is based on statistical properties of the heart rate variability (HRV). We focus on the fractal scaling properties of the HRV, in particular its Hurst exponent in the framework of a new model: a mean-reverting fractional Lévy stable motion. We show how to interpret the parameters of this model in the case of neonatal stress.

In the literature, the autocorrelation of HRV has been depicted by several models and statistical methods [1], like spectral analysis [50, 4, 44, 15], entropy measures [42, 43, 46] and tools of the chaos theory such as the correlation dimension [37, 3], Poincaré plots [26, 11, 49], recurrence plots [36, 35] or Lyapunov exponents [2, 54]. Fractal dynamics are another popular family of models of HRV. For these dynamics, the most relevant parameter is the Hurst exponent, which quantifies the time scaling of the stochastic process or time series: by definition, if we note H the Hurst exponent of a stochastic process S_t , an increment of duration d , $S_{t+d} - S_t$, has the same probability distribution as $d^H(S_{t+1} - S_t)$, for all time t . The Hurst exponent can be estimated by several methods. For the analysis of the HRV, it has been estimated by the method of absolute moments [9], rescaled range analysis (R/S) [31, 34] and detrended fluctuation analysis (DFA), in which the HRV signal is detrended by a piecewise linear trend [41, 40, 13, 52, 48] or by a moving average [5]. Among these three techniques, our preference goes to the method of absolute moments [39, 18] because it does not need a dataset as big as for computing R/S analysis or DFA, which are based on regressions on many subsamples.

But Hurst exponent is not only a statistical indicator. It can indeed be directly linked to a well-known stochastic process, the fractional Brownian motion (fBm), which is the Gaussian process consistent with the scaling rule based on Hurst exponent. However, HRV does not look like a fBm and we now introduce in this paper a dynamic featuring two other specificities: a mean-reversion and a more detailed scaling rule than the traditional Hurst exponent, based on a memory term and on a parameter of a stable distribution. These specificities enable a more accurate fit of the shape of HRV time series. They result in some additional parameters, which can easily be estimated and interpreted. These specificities of the model constitute an innovation in the description and analysis

of HRV.

The rest of the paper is structured as follows. We first present the mean-reverting fLsm model and the method for estimating its parameters. Then, we present the results of our analysis on 40 patients. Finally, we discuss these results and conclude.

2 Methodology

In this section, we present our model, a mean-reverting fractional Lévy stable motion, and we propose a method to estimate all its parameters. Afterwards, we will focus on quantifying the significance of each estimated value by the mean of a statistical bootstrap. We finish this section by presenting the study protocol.

2.1 The model: a mean-reverting fractional Lévy stable motion

2.1.1 Rationale of the model

We first focus on the two specificities introduced in this model: the mean-reversion and the decomposition of the scaling rule.

- ▷ It has been noted in the literature based on DFA that the Hurst exponent for the HRV signal is in fact scale-dependent. This implies that the fBm is not well specified for HRV. Multifractal dynamics are thus more accurate in this framework [25, 33]. But the fact that fBm is not well suited to HRV can be explained by many other model specifications than the sole multifractality of the process, like a time-dependent Hurst exponent [18] or a Lamperti transform of a fBm [19], which generalizes the mean-reverting Ornstein-Uhlenbeck process. A rapid look at some healthy and at rest HRV time series shows besides a mean reversion [12, 24]. As a consequence, we add in our model a mean reversion to the fractional process.
- ▷ In the fBm model, one can link the Hurst exponent H to the autocorrelation of the process. Thus, one usually considers that $H > 1/2$ corresponds to a long-memory feature, whereas $H < 1/2$ corresponds to a negative autocorrelation and $H = 1/2$ to an absence of autocorrelation. This is true for the fBm but not for all fractional processes. If the increments

of the process are not Gaussian, another interpretation should be made [8]. Indeed, the Hurst exponent is a scaling parameter and the scaling rule is established by two causes: the non-conditional probability distribution of the increments of the process and the dependence between these increments. In particular, if we consider symmetric α -stable increments, of which the standard Gaussian variable is a particular case,¹ we can build a much more general process called fractional Lévy stable motion (fLsm) [56]. The fLsm is characterized by two parameters instead of the sole H parameter of the fBm: the parameter $\alpha \in (0, 2]$ of the α -stable increments and a memory parameter, m . Then, the scaling parameter H , as estimated by an absolute moment method, can in fact be decomposed as:

$$H = m + \frac{1}{\alpha}.$$

It provides us with a richer interpretation of the scaling rule of the process. In particular, the fLsm is positively autocorrelated when $m > 0$, negatively autocorrelated when $m < 0$ and with no autocorrelation when $m = 0$. For instance, a standard Brownian motion has parameters $m = 0$ (independent increments) and $\alpha = 2$ (Gaussian increments), leading to $H = 1/2$.

In this paper, we show that the sole Hurst exponent is not relevant for detecting stress in newborns. On the contrary, it is shown that a stress situation is linked to a diminution in the parameters m and α . It thus fully justifies the decomposition of the Hurst exponent in both m and $1/\alpha$. However, for some patients in our study, the dataset of HRV is too restricted in size to observe significant changes in m and α . In these cases, we can rather base our analysis on the parameter of our model which depicts mean reversion. Indeed, whatever the size of the dataset, we always observe a strong rise in this parameter and we can even define a threshold for this parameter, discriminating stress and rest.

¹ The α -stable distribution is particularly relevant since the sum of two independent α -stable variables of scale parameter σ is an α -stable variable of scale parameter $2^{1/\alpha}\sigma$. Therefore, in this i.i.d. setting, $1/\alpha$ plays a role of scaling parameter in the same manner as does the Hurst exponent in the fBm.

² Indeed, with no stochastic part, the standard Ornstein-Uhlenbeck process is a deterministic function of time, described by the differential equation $x'(t) = -\theta x(t)$, whose solution is $x(t) = Ce^{-\theta t}$, for a constant C . On the contrary, equation (1) becomes $x''(t) = -\theta x(t)$, whose solution is $x(t) = C_1 \cos(\sqrt{\theta}t + C_2)$, for constants C_1 and C_2 .

³ The unit of θ is in beat^{-2} . This is consistent with the fact that X_t is in time/beat, dX_t/dt in time/beat² and $\int_{\tau}^t X_s ds$ in time.

2.1.2 Definition of the model

We observe the interbeat interval process B_t between time 0 and time T . We translate it first to get a centred process X_t :

$$X_t = B_t - \frac{1}{T} \int_0^T B_s ds.$$

We assume that X_t is the solution of the following equation, which defines our mean-reverting fLsm:

$$dX_t = -\theta \left(\int_{\tau}^t X_s ds \right) dt + \sigma dW_t^{\alpha, m}, \quad (1)$$

where $\theta \geq 0$ is the speed of reversion, $\tau \in [0, T]$, $\sigma > 0$ is a scale parameter and $W_t^{\alpha, m}$ is a fLsm with underlying distribution parameter α and memory parameter m . The fLsm is defined by the integral

$$W_t^{\alpha, m} = \int_{-\infty}^{\infty} ((t-s)_+^m - (-s)_+^m) dW_s^{\alpha, 0}, \quad (2)$$

where $W_s^{\alpha, 0}$ is a symmetric Lévy α -stable motion, that is to say a stochastic process with i.i.d. increments of symmetric Lévy α -stable distribution [56].

In equation (1), the mean-reversion part is introduced by the mean of an integral $-\theta \int_{\tau}^t X_s ds$ instead of simply $-\theta X_t$ as it is the case in a fractional Ornstein-Uhlenbeck model. This is a consequence of the observation of real HRV time series, in which, when the signal decreases below (respectively increases above) the mean, it progressively decreases (resp. increases) less rapidly until to suddenly increase (resp. decrease). The mean reversion thus occurs after a certain time spent by X_t below (resp. above) the mean. On the contrary, in a more traditional fractional Ornstein-Uhlenbeck model, the mean-reversion effect is activated as soon as the time series crosses the mean. The value of the parameter θ can be interpreted as a speed of reversion towards the average value of the process. More specifically, if we get rid of the stochastic part of the process, a peak of X_t will be followed by an exponential decay in the standard Ornstein-Uhlenbeck model, with a half life equal to $\ln(2)/\theta$, whereas it will generate sinusoidal oscillations around 0 for equation (1), with a period equal to $2\pi/\sqrt{\theta}$.² In the HRV framework, it means that when $\theta = 0.001$,

a peak in the beat-to-beat intervals (without fluctuations) will be followed by oscillations of the following intervals with a period equal to 199 beats.³ We interpret that these oscillations should correspond to a very low-frequency HRV, whereas the stochastic part should represent a high-frequency HRV. We found some papers introducing a mean-reversion in a model of HRV, but it corresponds to the traditional Ornstein-Uhlenbeck model [12, 24]. The main differences with the present paper are thus: the activation of the mean-reversion by an integral of X_t or by X_t ,⁴ the presence or not of a fractional aspect in the underlying stochastic process and therefore the presence or not of an autocorrelation in it.

2.2 Estimation method

The mean-reverting fLsm has five parameters, θ , τ , σ , α and m . In the analysis of the HRV, we will focus on three of them, for which the interpretation is clearer: θ , α and m . We now explain how to estimate all the parameters. First, it has to be noted that the observed signal is not in continuous time. We thus observe it at times $\{0, 1, \dots, T\}$. In this framework, the equation (1) is thus discretized and the parameters are estimated in the same order as follows:

1. Let $Y_t^{(\tau)} = \text{sgn}(t - \tau) \sum_{s=\min(t, \tau)}^{\max(t, \tau)} X_s$ be a discretized version of $\int_{\tau}^t X_s ds$. The absolute value of the mean-reversion term $-\theta Y_t^{(\tau)}$ should be minimal when X_t reaches a maximum or a minimum and it should be maximal when $X_t = 0$. Moreover, we assume that the mean-reversion mechanism works similarly in both directions, up and down. Therefore, we estimate τ by the value $\hat{\tau}$ minimizing the variance of $|Y_t^{(\hat{\tau})}|$ when $X_t = 0$:

$$\hat{\tau} = \underset{s \in \{0, 1, \dots, T\}}{\text{argmin}} \left\{ \frac{1}{|\Theta|} \sum_{t \in \Theta} |Y_t^{(s)}|^2 - \left(\frac{1}{|\Theta|} \sum_{t \in \Theta} |Y_t^{(s)}| \right)^2 \right\},$$

where Θ is a discretized approximation of the zeros of X_t : $\Theta = \{s \in \{0, 1, \dots, n-1\} | X_s X_{s+1} \leq 0\}$.

⁴ A random θ allows the authors of one of these papers to circumvent the limitations of the standard Ornstein-Uhlenbeck model [24].

⁵ In the literature, the estimation of parameters of a characteristic function often relies on a set of several transform variables [58] and, in the particular case of stable distributions, on linear regressions for several values of u [28, 27]. To make the estimation more direct, we choose a specific u . However, an arbitrary choice of u may lead to numerical errors in equations (3) and (4). Two numerical errors are possible: if u is too large in absolute value, the cosines may have negative values and make the calculation of the logarithm impossible; when u goes to zero, the numerical estimation of the cosines is close to 1 and imprecise, so that the estimate of alpha converges towards 0. The first error is avoided when $|2u(\hat{Z}_t - \hat{Z}_{t-1})| \leq \pi/2$ and the second by choosing the largest possible value for $|u|$. Therefore, $u = \pi(4 \max |\hat{Z}_t - \hat{Z}_{t-1}|)^{-1}$ seems a reasonable choice. Nevertheless, for sharply leptokurtic distributions, like the Cauchy distribution, we can choose a larger u , based for example on the inverse of high quantiles of the increments instead of their maximum. Indeed, for these distributions, extreme increments are much larger than others and, if u is not big enough, most of the increments $|\hat{Z}_t - \hat{Z}_{t-1}|$ will play no significant role in equation (3).

⁶ Some do not have any moment at all, like the Cauchy variable, for which $\alpha = 1$.

2. In order to estimate θ , we extend a standard estimator of the Ornstein-Uhlenbeck model [23]:

$$\hat{\theta} = - \frac{\sum_{t=0}^{T-1} Y_t^{(\hat{\tau})} (X_{t+1} - X_t)}{\sum_{t=0}^{T-1} \left(Y_t^{(\hat{\tau})} \right)^2},$$

which is a discretized version of $-\int_0^T Y_t^{(\hat{\tau})} dX_t / \int_0^T \left(Y_t^{(\hat{\tau})} \right)^2 dt$.

3. The parameters α and σ of the underlying probability distribution are estimated with the help of the characteristic function of a symmetric centred α -stable variable of scale parameter σ , which is $u \mapsto \exp(-\sigma|u|^\alpha)$. The α -stable variable is the increment of $\sigma W_t^{\alpha, m}$. This process, $\sigma W_t^{\alpha, m}$, is estimated by Z_t , iteratively defined by:

$$\begin{cases} \hat{Z}_0 &= 0 \\ \hat{Z}_t &= \hat{Z}_{t-1} + (X_t - X_{t-1}) + \hat{\theta} Y_{t-1}^{(\hat{\tau})}. \end{cases}$$

We can then estimate α by:

$$\hat{\alpha} = \frac{1}{\ln(2)} \ln \left(\frac{\ln \left(\frac{1}{T} \sum_{t=1}^T \cos \left(2u(\hat{Z}_t - \hat{Z}_{t-1}) \right) \right)}{\ln \left(\frac{1}{T} \sum_{t=1}^T \cos \left(u(\hat{Z}_t - \hat{Z}_{t-1}) \right) \right)} \right) \quad (3)$$

and the parameter σ by:

$$\hat{\sigma} = -|u|^{-\hat{\alpha}} \ln \left(\frac{1}{T} \sum_{t=1}^T \cos \left(u(\hat{Z}_t - \hat{Z}_{t-1}) \right) \right), \quad (4)$$

where the transform variable u has to be chosen carefully, for example $u = \pi/4Q_p$, where Q_p is the quantile of the absolute increments $|\hat{Z}_t - \hat{Z}_{t-1}|$ for a high level p , say 90%.⁵

4. Finally, we estimate H by the method of absolute moments [39, 18]. We focus on the first moment because some α -stable variables do not have higher moments:⁶

$$\hat{H} = \frac{1}{\ln(2)} \ln \left(\frac{\frac{2}{T} \sum_{t=1}^{\lfloor T/2 \rfloor} |\hat{Z}_{2t} - \hat{Z}_{2(t-1)}|}{\frac{1}{T} \sum_{t=1}^T |\hat{Z}_t - \hat{Z}_{t-1}|} \right).$$

As a consequence, the estimate for m is simply:

$$\hat{m} = \hat{H} - \frac{1}{\hat{\alpha}}.$$

2.3 Significance of the estimated values

For assessing the statistical significance of the variations of parameters, we must build the probability distribution of the estimator of each parameter. More specifically, we consider two phases in the experiment: an at-rest phase followed by a stress phase. As there are less observations in the second phase than in the other, say T_2 observations, the estimates in this phase are less accurate. We want to determine if the variation of the estimated parameters between the two phases is significant. The null hypothesis of this statistical test is that the parameter estimated in phase 2, say $\hat{\theta}_2$, is equal to its base value estimated in phase 1, $\hat{\theta}_1$. We thus analyse for each parameter of the second phase its p-value in the distribution of the estimator for this parameter in the case of trajectories of size T_2 generated for the parameter $\hat{\theta}_1$. In other words, if we consider that the base value $\hat{\theta}_1$ is accurate and so that it is the true parameter of the dynamic, we want to determine how likely an estimate on only T_2 observations can be equal to $\hat{\theta}_2$. We obtain the p-values by a statistical bootstrap. More precisely, for each set of estimated parameters, we simulate 1,000 mean-reverting fLsm with the base parameter estimated in phase 1 and with as many observations as in the second phase. We then infer the parameters of interest for each simulated trajectory and we build a discrete distribution for each estimator. The estimate $\hat{\theta}_2$ is thus equal to $\hat{\theta}_1$ up to a p-value equal to:

$$G_{\hat{\theta}}(\hat{\theta}_1 - |\hat{\theta}_1 - \hat{\theta}_2|) + 1 - G_{\hat{\theta}}(\hat{\theta}_1 + |\hat{\theta}_1 - \hat{\theta}_2|),$$

where $G_{\hat{\theta}}$ is the cumulated distribution function of the estimator of θ in the 1,000 simulations of length T_2 . The lower this p-value, the more significant the variation of parameters.

In this bootstrapping procedure, the simulation of fLsm is made possible by the simulation of independent standard symmetric stable random variables, which are then weighted and summed as in the integral definition of the fLsm presented in equation (2). In other words, we simulate first the increments of the fLsm. However, the simulation of stable random variables is not straightforward. For this purpose, we use Chambers-Mallows-Stuck method, in which

we simulate first two independent random variables: P is uniform in $(-\pi/2, \pi/2)$ and Q is exponential of parameter 1. Then, the random variable R , defined by:

$$R = \frac{\sin(\alpha P)}{(\cos(P))^{1/\alpha}} \left(\frac{\cos(P(1-\alpha))}{Q} \right)^{\frac{1-\alpha}{\alpha}},$$

is a standard symmetric α -stable random variable, when $\alpha \neq 1$ [14, 57].

This method is used in section 3.4, in which, for each patient, we determine if the variation of the value of a parameter between two phases is significant.

3 Application

3.1 Study protocol

By using simple random sampling, 40 (21 females and 19 males, birth weight 3542.05 ± 339.09 g, 72 hours old) subjects were included in this study.⁷ The study involved only full-term infants, without prenatal and perinatal risk factors, ready for discharge from the maternity ward. The subjects were naive for iatrogenic stress stimuli.

A high-resolution (1024 Hz) heart rate monitor (Firstbeat Bodyguard 2, Firstbeat Technologies Ltd, Jyväskylä, Finland) was used to obtain RR interval data. After visual inspection and artifact correction, the raw data were further used for analysis. A third-degree polynomial detrending was used to eliminate existing trends in the obtained signal, before the data analysis.

Infants were fed and placed in supine position before the procedure to diminish external artifacts. The research was conducted in the maternity ward, by ensuring no interruptions and excessive noise pollution.

The protocol included three parts: a) dummy stimulation phase, b) the heel stick phase, c) the treatment phase. Only phases a) and b) are used in this work, each consisting of two subphases. Phase a) starts with the first baseline phase lasting 10 minutes (phase 1), followed by simulating the heel stick procedure (phase 2), by intermittently pressing the heel in a way the standard heel stick blood drawing is performed. The duration of phase 2 was chosen to be 90 seconds, which is the average time to perform the actual blood drawing. At the end of the second subphase is the start of phase b). It contains

⁷ The research was accepted by the institution's ethical committee, and informed consents were obtained from all research participant's parents or guardians.

two subphases as well, the first subphase being the second baseline (phase 3), followed by the heel stick blood sampling (phase 4), which ends as the beginning of phase c).

3.2 Results

After having estimated the parameters for each phase and for each patient, we answer two questions.

1. Does a parameter indicate by its sole value if patients are in stress or at rest?
2. Does the stress phase imply an increase in the value of a given parameter, a decrease, or non-characterizing variations with some up and some down, depending on patients?

For the first question, we focus on the value of the estimated parameters averaged over all the patients. The second approach is devoted to the significant variations of the values of the estimated parameters between two phases.

3.3 Discriminant value of the parameters

In this paragraph, for a given parameter in a given phase, we constitute a sample of 40 estimates corresponding to the 40 patients. Each sample thus leads to an empirical distribution of the parameter in each phase. The data were analyzed with the R software (version 3.3.2). The normality of the distributions of numerical variables was assessed by the Kolmogorov-Smirnov test. Normally distributed data are descriptively presented with means and standard deviations, along with 95% confidence intervals, with corresponding confidence intervals. Otherwise, medians, along with 95% bias corrected bootstrap confidence intervals and interquartile ranges were used. Group differences were assessed with one-way ANOVA or Friedman's test. The results are gathered in Table 1. Considering variables τ and θ , statistically significant differences were found between the distributions of estimates in the baseline phases and in the intervention phases, while no significant changes were found for H , α , m and σ .

	Phase 1		Phase 2		Phase 3		Phase 4		
	μ (s.d.)	95%C.I.	μ (s.d.)	95%C.I.	μ (s.d.)	95%C.I.	μ (s.d.)	95%C.I.	p*
H	0.34 (0.25)	0.26;0.42	0.39 (0.19)	0.33;0.45	0.38 (0.21)	0.31;0.44	0.38 (0.23)	0.31;0.45	0.593
α	1.73 (0.18)	1.67;1.79	1.68 (0.23)	1.61;1.75	1.77 (0.15)	1.72;1.81	1.68 (0.25)	1.60;1.76	0.138
m	-0.25 (0.23)	-0.32;-0.17	-0.22 (0.21)	-0.29;-0.15	-0.19 (0.19)	-0.25;-0.13	-0.24 (0.26)	-0.32;-0.15	0.574
τ	630.1 (375.7)	509.9;750.3	115.9 (71.9)	92.9;138.9	687.4 (421.9)	552.5;822.4	210.8 (191.9)	149.4;272.1	<0.001
	mdn (IQR)	95%C.I.	mdn (IQR)	95%C.I.	mdn (IQR)	95%C.I.	mdn (IQR)	95%C.I.	p**
θ	0.0006 (0.0003;0.0010)	0.0004;0.0008	0.0073 (0.006;0.013)	0.0064;0.0094	0.0004 (0.0002;0.0010)	0.0003;0.0005	0.0029 (0.0017;0.0060)	0.0021;0.0041	<0.001
σ	50.42 (17.40;102.72)	30.44;57.52	19.63 (8.13;42.67)	13.39;28.91	38.21 (23.32;92.51)	29.91;53.95	16.29(8.91;47.47)	10.95;34.42	<0.001

Table 1: p* - p-value for one-way repeated measures ANOVA, p** - p-value of Friedman's test, μ - mean, s.d. - standard deviation, C.I. - confidence interval (in the non-normal case, bias-corrected bootstrap confidence interval), IQR - interquartile range.

A ROC curve analysis was used to test the diagnostic properties of the variables where significant differences were found, by comparing intervention phases with baselines. To test the discriminant thresholds, p-values less than 0.05 were considered statistically significant.

Table 2 contains the results of the ROC analysis using only the variables which were statistically different in

3.4 Significant variations of the parameters

We now try to build another diagnostic indicator based on the variation of the parameters instead of an analysis of the value of the parameters compared to

Table 1. The variables θ and τ are statistically significant compared to an area under the ROC curve (AUC) of 0.5. The diagnostic capabilities of the parameters based on a threshold discriminating rest and stress is described by an AUC close to its maximum possible value, which is 1. A significant difference was found in the AUC of θ between the Phase 2/Phase 1 (AUC=0.998) and Phase 4/Phase 3 (AUC=0.91). Figure 1 shows the ROC of θ .

a universal threshold. The underlying idea is that a given parameter can have very different values in the same phase depending on the patient but, when going from a rest phase to a stress phase, the parameter should vary in the same direction for all the patients. As the time series are not very long in our experi-

	Phase 2/Phase 1		Phase 4/Phase 3		
	AUC	95%C.I.	AUC	95%C.I.	p
θ	0.998	0.951 ; 1.000	0.910	0.825 ; 0.962	0.005
τ	0.966	0.900 ; 0.994	0.844	0.745 ; 0.915	0.009
σ	0.687	0.574 ; 0.786	0.669	0.555 ; 0.770	0.811

Table 2: Comparison of ROC curves. C.I. - binomial confidence interval, p - p-value [17].

Figure 1: ROC curve for θ .

ment, our estimation of the parameters is not always accurate and we thus filter first the variations of parameters between phases 1 and 2 and between phases 3 and 4 in order to only keep the significant variations. The method for determining the significance by the

mean of a p-value is described in section 2.3. Then, among the patients passing the significance test, we determine the proportion of those for which the parameter increases between two phases. The results are gathered in Table 3.

p	Phase 1 → Phase 2				Phase 3 → Phase 4			
	0.05	0.01	0.005	0.001	0.05	0.01	0.005	0.001
H	71.4% (7)	75.0% (4)	50.0% (2)	50.0% (2)	20.0% (10)	14.3% (7)	0.0% (3)	0.0% (1)
α	20.0% (15)*	11.1% (9)*	14.3% (7)	0.0% (5)*	11.8% (17)**	7.7% (13)**	0.0% (11)**	0.0% (8)**
m	37.5% (8)	20.0% (5)	0.0% (4)	0.0% (3)	26.7% (15)	0.0% (6)*	0.0% (6)*	0.0% (4)
θ	100.0% (38)**	100.0% (32)**	100.0% (31)**	100.0% (23)**	100.0% (34)**	100.0% (28)**	100.0% (24)**	100.0% (16)**

Table 3: Proportion of increased parameters between rest and stress phases and, in parenthesis, number of patients. The variable p indicates the threshold of p-value below which a variation is considered as significant. Only the patients with significant variation are taken into account for each parameter. The proportion of increasing estimates is tested against the hypothesis of a proportion of 50%, thanks to a binomial test ; we highlight the significant proportions of increase and of decrease with * (p-value lower than 0.05) and ** (p-value lower than 0.01).

Significant variations of parameters in one direction are observed for θ , α and m but not for H . When going from a rest phase to a stress phase, the patients in general see an increase of their parameter θ , a decrease of α and m , whereas H can change in an unpredictable way. The most significant variations are observed for θ and, to a lesser extent, for α . The strong significance of the variation of θ is perfectly consistent with our findings about a discriminant value for this parameter.

4 Conclusion and discussion

We have introduced a new model describing the HRV in a fractal manner. Existing literature on fractal scaling analysis of HRV only relies on the estimation of one or two Hurst exponents. Here, the Hurst exponent H is one parameter among others since we model the dynamic of HRV by a mean-reversion of speed θ . Moreover, we decompose H in two components, as $m+1/\alpha$. The parameter m is the memory of the dynamic whereas α is linked to the kurtosis of the underlying distribution of HRV. Other parameters (σ et τ) complement the model but are not interpretable.

Our model has thus two components: a fractal dynamic and a mean-reversion, which account for high-

and low-frequency HRV. This is consistent with the findings of papers estimating Hurst exponent in HRV, in which a crossover phenomenon is described, with different scaling properties in a short range and in a longer range [41, 7], or with different scaling properties for accelerations and decelerations of heart rate [48]. This depicts the complexity of the HRV and of the autonomic nervous system.

In the framework of stress diagnostic, our model gives promising insights. First, observing the sole value of θ indicates quite accurately if the patient is suffering. We can consider 0.0015 as a good threshold. If θ is above it, it indicates a stress situation, with a false positive rate of 13%. If it is below, it indicates a rest phase, with a false negative rate of 12%.⁸ The interpretation is the following : when the patient is suffering, the oscillations of his HRV become more frequent and the part of the mean-reversion effect becomes overriding compared to the random fluctuations. This last observation is consistent with the fact that entropy also decreases during stress phases of neonates, which indicates a lower uncertainty in HRV [47]. It is also consistent with the increase of the Hurst exponent of decelerations in the asymmetric scaling approach, during stress phases [48]. Indeed, such an increase smooths the fluctuations and thus makes the HRV more predictable.

⁸ We considered the estimates of θ in the 4 phases. We observed 82 values above the threshold, among which 11 (so 13% of 82) are in phase 1 or 3, thus corresponding to a false positive error with respect to a test of stress detection. Symmetrically, we observed 78 values of θ below the threshold, among which 9 (so 12% of 78) are in phase 2 or 4, thus corresponding to a false negative error regarding the same test of stress detection.

The variation of the value of the parameters is also insightful. It may be surprising that no characterizing variation is observed for H . However, our decomposition as $H = m + 1/\alpha$ is relevant since we observe that both m and α decrease during a stress situation. The variation in different directions of m and $1/\alpha$ is not visible when observing only H . The interpretation of these variations is that the global scaling properties are non-significantly affected by a stress but the autocorrelation of the series decreases and the variations of the heart rate are more frequently extreme. This depicts how the autonomic nervous system reacts in case of stress.

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