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Autonomic maturation from birth to 2 years: normative values

Hugues Patural, Vincent Pichot, Sophie Flori, Antoine Giraud, Patricia Franco, Patrick Pladys, Alain Beuchée, Frédéric Roche, Jean-Claude Barthelemy.

Abstract

Background: While heart rate variability (HRV) constitutes a relevant non-invasive tool to assess the autonomic nervous system (ANS) function with recognized diagnostic or therapeutic implications, there is still a lack of established data on maturation of autonomic control of heart rate during the first months of life. The Autonomic Baby Evaluation (AuBE) cohort was built to establish, the normal autonomic maturation profile from birth up to 2 years, in a healthy population of full-term newborns.

Methods: Heart rate variability analysis was carried out in 271 full-term newborns (mean gestational age 39 wGA + 5 days) from reliable polysomnographic recordings at 0 (n = 270) and 6 (n = 221) months and from a 24-hour ambulatory electrocardiogram (ECG) at 12 (n = 210), 18 (n = 197), and 24 (n = 190) months. Indices of HRV analysis were calculated through the ANSLabTools software.

Results: Indices are dissociated according a temporal, geometrical, frequency, Poincaré, empirical mode decomposition, fractal, Chaos and DC/AC and entropy analysis. Each index is presented for five different periods of time, 0, 6, 12, 18
and 24 months and with smoothed values in the 3rd, 10th, 50th, 90th and 97th percentiles. Data are also presented for the full cohort and individualized by sex to account for gender variability.

**Discussion & conclusion:** The physiological autonomic maturation profile from birth to 2 years in a healthy population of term neonates results in a fine-tuning autonomic maturation underlying progressively a new equilibrium and privileging the parasympathetic activity over the sympathetic activity.

**Keyword:** Neuroscience

### 1. Introduction

Whatever the age [1, 2], heart rate variability (HRV) referring to beat-to-beat variations of the RR interval length constitutes a relevant non-invasive tool to assess the autonomic nervous system (ANS) function with recognized diagnostic or therapeutic implications [3, 4, 5, 6, 7, 8, 9].

For the neonatologist, the interest in HRV lies in the perception of the status of congenital or acquired autonomic dysregulation, particularly the cardiorespiratory control as objective risk factor of Sudden infant death syndrome (SIDS) [10, 11, 12, 13, 14]. In the triple risk model of SIDS involving “vulnerable child, exogenous stress and critical developmental period”, the cardiorespiratory autonomic immaturity and abnormal awakening responses appear to be critical [11, 14]. The cardiorespiratory modulations observed during arousal are mediated by the cortico-hypothalamic pathways and cardiorespiratory nuclei of the brainstem, including the solitary tract, ambiguous and dorsal nucleus of the pneumogastric nerve. Kato et al. provided an epidemiological link between central abnormalities of cardiorespiratory response during awakening and sudden death, in a large survey including 20,000 children [15]. The links with molecular research analyzes contributions of inhibitors neurotransmitters of cardiorespiratory control, in the genesis of both apnea and bradycardia as GABA γ aminobutyric acid, adenosine, serotonin, endorphins and prostaglandins [16, 17] with the identification of an abnormal serotonergic response in the bulbar and arcuate nucleus of the hypothalamus in as much as 50% of the cases, presumably linked to genetic polymorphisms [18, 19, 20, 21]. In that view, overexpression of cardiac muscarinic receptors as well as an increased enzymatic acetylcholinesterase activity have been reported [22]. Regardless of the fetal risk associated with autonomic dysfunction, the study of the child autonomic status is also of great interest in many clinical situations as frequent as infections, sepsis [23, 24], chronic inflammatory [25] diseases or type 1 diabetes [26] in which impaired autonomic control and increased risk for cardiovascular disease are reported.
While there are advances on the biological regulations, there is still a lack of established data on maturation of autonomic, particularly during the first months of life. It has been established that at least 37 weeks of in utero maturation are needed to achieve full autonomic maturation at birth [2, 27, 28, 29, 30]. As a matter of fact, both cardiac autonomic responsiveness and baroreflex loop are altered in preterm infants regardless of gestational age (GA) and remain very low at theoretical term when compared with full-term newborns [27, 28]. In a recent review about ANS in newborns, an increasing postnatal age is related to a significant rise of HRV parameters, particularly for the high frequency (HF) parameter, recognized as a relevant representative of parasympathetic maturation [31].

While an autonomous imbalance in the first year of life implies inappropriate cardiorespiratory reactions to internal or environmental stress [11, 12, 13, 14], the lack of references data at that age makes clinical studies unrelated to the others. This may concern up to the premature adolescent, but focusing up the two first years of age may help monitoring the most at risk infants [32, 33, 34]. Therefore, describing the natural evolution of autonomous maturation in the first years of life may bring useful data to clinicians in search for a better interpretation of autonomic status and its clinical relationships. The Autonomic Baby Evaluation (AuBE) cohort was built to establish, for the first time, the normal autonomic maturation profile from birth. We here publish the first results of the cohort, up to 2 years, in that healthy population of full-term newborns [35].

2. Methods

2.1. Design

Autonomic Baby Evaluation (AuBE) study is a prospective single-center observational study conducted at the University Hospital of Saint-Etienne (France), a level III Maternity managing 3,500 births annually. The cohort of the consecutive full-term newborns was performed over a 24 months’ period, from September 2009 to September 2011 to assess the autonomic maturation profile during the first two years of life.

For the Heart rate variability analysis, polysomnographic recordings were realized at 0 and 6 months and due to the growing motor ability of children, the recordings were then performed through a 24-hour ambulatory electrocardiogram (ECG) at 12, 18, and 24 months. The first two-year follow-up of the cohort ended in September 2014. All the design of the study with the approval by our institute’s ethics committee, the inclusion and exclusion criteria and the technical procedure for acquiring recorded data have been published in a previous review [35]. The study was registered in the International Clinical Trials Registry under the label ClinicalTrials.gov ID NCT01583335 [29].
Among the 302 children recruited, we kept 271 (89.7%) of them as being full-term, excluding the 31 (10.3%) preterm born before 37 weeks of gestational age (wGA). They were recruited continuously according to the availability of the recorders independently of ethnicity, and sex. For term newborns \( (n = 271) \), the median gestational age was 39 wGA + 5 days [37 wGA, 41 wGA + 6 d]. The ratio M/F was 1.22 (149/122). We did not retain alcohol exposure during fetal life, but 86 (31%) newborns were probably exposed to nicotine in utero without precision of intensity [35].

No child presented a dysmorphic syndrome. At birth the mean term newborn weight was 3256 g (2640–4410), the mean length was 49.6 cm (44–55), and the mean head circumference was 34.2 cm (33.0–38.5). The mean Apgar score was 9 at one, 10 at two, and 10 at ten minutes. The mean CRIB score [36] was 0. One child received a brief resuscitation in the delivery room requiring a short cardiac massage with immediate hemodynamic recovery. No child presented neonatal lung disease, or hemodynamics, gastrointestinal or neurological troubles. One child (0.2%) had been treated for a suspected neonatal infection. Hospital stays lasted an average of 3 days [2, 5] and 100% of the children were considered clinically normal. No home monitoring was recommended at discharge. In this cohort of 271 infants, one child (0.03%) died in the third month of life, probably because of asphyxiation in bed without further explanation despite an extensive research of etiologic factors and an autopsic procedure. As a result, he was not excluded from the first recording. We note an early loss to follow-up before two years of age for 68/271 (25%) infants. Reliable HRV recordings were 270 polysomnographic recordings (M0) 210 polysomnographic recordings and 11 Holter 24 hours ECG (M6) and 210, 197 and 190 Holter ECG recordings at, respectively M12, M18 and M24.

2.2. Materials

The 24-hour ECG recordings were obtained from the polysomnographic recordings (Dream® Medatec, Belgium), or from ECG Holter (Vista®, Novacor, Rueil Malmaison, France). The sampling frequency was 200 Hz for both materials. HRV calculations were performed through the ANSLabTools software [37].

First, ECG tracings were resampled at a frequency of 1000 Hz and each R peak was detected to provide the R-R interval series with a precision of 1 ms. Then, missing beats, isolated premature heart beats and artifacts were corrected using a spline cubic interpolation [38, 39].

2.3. Analysis of heart rate variability

Indices of HRV analysis were calculated through the ANSLabTools giving several types of indices according to the litterature [37, 38].
- **Time domain analysis.** They are based on means and standard deviations calculated on short-term to long-term variations in RR intervals. The standard deviation of normal-to-normal intervals (SDNN), the standard deviation of the mean of all normal RR intervals for 5-min segments (SDANN) and the mean of the standard deviation of all normal RR intervals for all 5-min segments (SDNNIDX) represents global and long-term variations [37, 38], and the percent difference between adjacent normal RR intervals greater than 50 ms (pNN50), the square root of the mean of the squared differences between adjacent normal RR intervals (rMSSD) represents fast changes linked to the parasympathetic activity. The geometrical indices calculated on the sample density distribution of the RR intervals, corresponds to the assignment of the number of equally long RR intervals to each value of their length.

Poincaré plot is a graphic tool using SD1 and SD2 index, calculated as the standard deviation of the distances of the RR intervals from they $x = x$ line and the $y = -x + 2$ mean (RR) line respectively. SD1 represents short-term and SD2 long-term RR intervals variability.

- **Frequency domain analysis.** For those analyses, the RR signal was resampled at 4 Hz and the high frequency (HF) bandwidth was extended up to 2 Hz as recommended for newborns and children analyses [37, 38, 39]. Whereas total power (Ptot) represents the global variability, ultra-low frequencies (ULF), very low frequencies (VLF), low frequencies (LF), and high frequencies (HF) represent specific bands of interest. HF power is modulated by parasympathetic modulation, LF power is controlled by both sympathetic and parasympathetic activity, and normalized indexes (LFnu, HFnu) or the LF/HF ratio (calculated has the mean of the LF/HF values of all successive 5-min epochs of the entire RR serie) are used to estimate sympathetic modulation and autonomic equilibrium.

- **Geometrical analysis.** The indices calculated are HRV triangular index (the integral of the density distribution divided by the maximum of the density distribution) and the TINN index (triangular interpolation of the RR interval histogram i.e. the baseline width of this triangle). These measures quantify overall HRV mainly influenced by slow, but not by rapid, oscillations of RR intervals.

- **Non-linear analysis.** The indices arising from nonlinear approach provide information on the complexity of the autonomic regulations. In this context, the fractality of heart rate variability consist in quantifying the repetition of patterns display at different scales. These indices were calculated using detrend fluctuation analysis ($\alpha_1, \alpha_2, H$), Hurst exponent, 1/f slope, Higuchi and Katz and largest Lyapunov exponent algorithms. In addition, entropy indices are an estimation of the regularity and complexity of pattern at different length. Many indices have been calculated as the Shanon entropy and its derived indices, conditional entropy, corrected conditional entropy, normalized corrected conditional entropy, the sample entropy and approximate entropy.
- **Deceleration and Acceleration Capacities.** In this last non-linear approach, these two indices are used to estimate the vagal and sympathetic capacities by analyzing heart deceleration capacity (DC: detection of sequences of two successive RR beats that increase) and acceleration capacity (AC: detection of all sequences that decrease).

### 2.4. Statistical analysis

A preliminary analysis showed that many HRV indices did not follow a Gaussian distribution even when log-transformed. Thus, to construct the centiles for 24h HRV indices from 0 to 24 months, we first search for the distribution that better fits the data. For each index, we evaluated the goodness of fit of various distribution using maximum likelihood estimates of the parameters and by visual inspection of the quantile-quantile plots of sample data versus theoretical quantiles of the distribution. The analysis showed that the best fit was made by a generalized extreme value distribution. Such a distribution is often used to model the smallest or largest value among a large set of independent, identically distributed random values representing measurements or observations. It combines three simpler distributions into a single form, allowing a continuous range of possible shapes that include all three of the simpler distributions. The three distribution types correspond to the limiting distribution of block maxima from different classes of underlying distributions: distributions whose tails decrease exponentially, such as the normal distribution; distributions whose tails decrease as a polynomial, such as Student’s $t$ distribution; distributions whose tails are finite, such as the beta distribution.

From this chosen distribution, we extracted the median and the centiles (3rd, 10th, 90th, 97th) for each HRV index at each period (0, 6th, 12th, 18th and 24th months). Then, the curves were plotted using polynomial curve fitting technic. Values were calculated for all children and separately for girls and boys.

HRV differences between girls and boys were calculated using a Mann-Whitney U test. The Friedman test was utilized to compare the HRV indices measured at each period (0, 6th, 12th, 18th and 24th months), for all subject and separately for girls and boys. A p-value was considered as statistically significant when $<0.05$.

Statistics and graphs were computed using Statistics and Machine Learning Matlab toolbox 10.2 R2016a (The MathWorks Inc., Natick, MA, USA).

### 3. Results

The results of the HRV indices are presented according to the fields previously described as temporal (Table 1), geometrical (Table 2), frequency (Table 3), Poincaré (Table 4), empirical mode decomposition (Table 5), fractal (Table 6),
Table 1. HRV indices in the temporal domain (all 5-min segments).

| Months | n  | Smoothed centiles for Mean RR (ms) (All) | Smoothed centiles for Mean RR (ms) (Girls) | Smoothed centiles for Mean RR (ms) (Boys) |
|--------|----|----------------------------------------|------------------------------------------|------------------------------------------|
|        |    | 3rd 10th 50th 90th 97th                | 3rd 10th 50th 90th 97th                  | 3rd 10th 50th 90th 97th                  |
| 0      | 260| 420 432 466 514 542                    | 0 117 420 430 460 506 536               | 0 143 421 435 472 520 546               |
| 6      | 205| 425 442 483 533 558                    | 6 95 423 439 477 525 551               | 6 110 428 445 488 537 560               |
| 12     | 198| 434 455 505 561 586                    | 12 86 433 452 500 554 580             | 12 112 436 459 511 564 586             |
| 18     | 187| 447 473 534 599 628                    | 18 82 448 472 528 593 624             | 18 105 447 475 538 601 626             |
| 24     | 182| 464 495 567 646 682                    | 24 80 470 496 561 642 683             | 24 102 460 495 572 647 678             |
|        | Total 1032 | Total 460 | Total 572 |

| Smoothed centiles for Mean HR (bpm) (All) | Smoothed centiles for Mean HR (bpm) (Girls) | Smoothed centiles for Mean HR (bpm) (Boys) |
|------------------------------------------|------------------------------------------|------------------------------------------|
| 3rd 10th 50th 90th 97th                | 3rd 10th 50th 90th 97th                  | 3rd 10th 50th 90th 97th                  |
| 0 111.3 116.7 128.4 139.3 143.5        | 0 117 112.5 118.3 130.2 140.2 143.6    | 0 143 110.6 115.6 127.0 138.3 142.9   |
| 6 108.3 112.9 124.0 136.3 142.0        | 6 95 109.3 114.2 125.5 137.5 142.9     | 6 110 107.8 112.1 122.7 135.0 141.0   |
| 12 103.5 107.8 118.7 132.3 139.3       | 12 86 104.2 108.7 120.0 133.4 140.0   | 12 112 103.2 107.2 117.6 131.1 138.4 |
| 18 96.9 101.2 112.4 127.3 135.5        | 18 82 97.0 101.8 113.7 128.0 135.1    | 18 105 97.0 100.9 111.5 126.5 135.3   |
| 24 88.5 93.2 105.3 121.5 130.6         | 24 80 87.9 93.4 106.5 121.2 128.1     | 24 102 89.1 93.2 104.5 121.2 131.6    |
| Total 1032 | Total 460 | Total 572 |

(continued on next page)
| Months n | Smoothed centiles for pcNN20 (%) (All) | Smoothed centiles for pcNN20 (%) (Girls) | Smoothed centiles for pcNN20 (%) (Boys) |
|---------|--------------------------------------|----------------------------------------|--------------------------------------|
|         | 3rd 10th 50th 90th 97th            | 3rd 10th 50th 90th 97th                | 3rd 10th 50th 90th 97th               |
| 0       | 260 2.84 6.50 17.21 34.53 46.20 | 0 117 2.33 5.35 14.93 32.75 46.40 | 0 143 4.03 7.92 18.92 35.88 46.87 |
| 6       | 205 5.70 10.38 22.69 39.30 48.78 | 6 95 4.41 8.93 20.77 37.13 46.97 | 6 110 7.38 11.95 24.16 40.83 50.28 |
| 12      | 198 7.78 13.81 28.45 45.46 53.70 | 12 86 6.21 12.26 26.77 43.32 51.23 | 12 112 9.33 15.33 29.91 46.83 55.01 |
| 18      | 187 9.11 16.81 34.56 53.09 61.03 | 18 82 7.73 15.37 32.99 51.41 59.21 | 18 105 9.89 18.04 36.12 53.85 61.04 |
| 24      | 182 9.67 19.35 40.94 62.11 70.67 | 24 80 8.98 18.23 39.37 61.29 70.84 | 24 102 9.07 20.11 42.83 61.92 68.38 |
| Total   | 1032 Total 460                      | Total 460                              | Total 572                            |

| Months n | Smoothed centiles for pcNN30 (%) (All) | Smoothed centiles for pcNN30 (%) (Girls) | Smoothed centiles for pcNN30 (%) (Boys) |
|---------|--------------------------------------|----------------------------------------|--------------------------------------|
|         | 3rd 10th 50th 90th 97th            | 3rd 10th 50th 90th 97th                | 3rd 10th 50th 90th 97th               |
| 0       | 260 1.27 2.90 8.88 23.45 37.84 | 0 117 1.32 2.38 7.12 22.57 41.97 | 0 143 1.57 3.60 10.29 24.25 36.40 |
| 6       | 205 1.91 4.25 11.64 25.95 37.79 | 6 95 1.54 3.54 10.12 24.43 38.16 | 6 110 2.62 5.08 12.79 27.17 38.40 |
| 12      | 198 2.36 5.78 15.45 30.73 41.11 | 12 86 1.81 4.95 14.03 29.00 39.68 | 12 112 3.11 6.64 16.57 32.01 42.33 |
| 18      | 187 2.63 7.49 20.34 37.84 47.85 | 18 82 2.12 6.64 18.90 36.33 46.53 | 18 105 3.04 8.27 21.59 38.72 48.15 |
| 24      | 182 2.70 9.38 26.27 47.19 57.94 | 24 80 2.47 8.58 24.66 46.34 58.65 | 24 102 2.42 9.98 27.87 47.33 55.89 |
| Total   | 1032 Total 460                      | Total 460                              | Total 572                            |

(continued on next page)
| Months | Smoothed centiles for pcNN50 (%) (All) | Smoothed centiles for pcNN50 (%) (Girls) | Smoothed centiles for pcNN50 (%) (Boys) |
|--------|--------------------------------------|-------------------------------------|-------------------------------------|
|        | 3rd | 10th | 50th | 90th | 97th | 3rd | 10th | 50th | 90th | 97th | 3rd | 10th | 50th | 90th | 97th |
| 0      | 260 | 0.56 | 1.11 | 3.62 | 13.08 | 27.49 | 0 | 117 | 0.51 | 0.92 | 2.92 | 11.53 | 26.57 | 0 | 143 | 0.64 | 1.37 | 4.37 | 13.75 | 25.98 |
| 6      | 205 | 0.52 | 1.12 | 3.80 | 13.46 | 27.53 | 6 | 95 | 0.47 | 0.92 | 3.09 | 12.12 | 26.75 | 6 | 110 | 0.63 | 1.37 | 4.44 | 14.33 | 27.54 |
| 12     | 198 | 0.50 | 1.42 | 5.12 | 16.48 | 31.07 | 12 | 86 | 0.47 | 1.20 | 4.36 | 15.32 | 30.77 | 12 | 112 | 0.59 | 1.66 | 5.76 | 17.40 | 31.58 |
| 18     | 187 | 0.49 | 2.01 | 7.61 | 22.17 | 38.16 | 18 | 82 | 0.51 | 1.77 | 6.73 | 21.16 | 38.67 | 18 | 105 | 0.52 | 2.24 | 8.33 | 22.95 | 38.05 |
| 24     | 182 | 0.50 | 2.88 | 11.24 | 30.47 | 48.72 | 24 | 80 | 0.59 | 2.63 | 10.19 | 29.59 | 50.37 | 24 | 102 | 0.41 | 3.12 | 12.15 | 30.96 | 46.97 |
| Total  | 1032 | Total | 460 | Total | 572 |                  |                  |                  |                  |                  |                  |                  |

| Smoothed centiles for rMSSD (ms) (All) | Smoothed centiles for rMSSD (ms) (Girls) | Smoothed centiles for rMSSD (ms) (Boys) |
|--------------------------------------|-------------------------------------|-------------------------------------|
| Months | n | 3rd | 10th | 50th | 90th | 97th | 3rd | 10th | 50th | 90th | 97th | 3rd | 10th | 50th | 90th | 97th |
| 0      | 260 | 13.5 | 16.6 | 26.8 | 47.5 | 65.1 | 0 | 117 | 13.2 | 15.8 | 24.6 | 43.2 | 59.7 | 0 | 143 | 14.1 | 17.6 | 28.8 | 50.4 | 68.3 |
| 6      | 205 | 13.0 | 15.9 | 25.8 | 48.2 | 69.6 | 6 | 95 | 12.4 | 15.0 | 24.0 | 44.1 | 62.9 | 6 | 110 | 14.0 | 16.9 | 27.2 | 51.4 | 75.4 |
| 12     | 198 | 13.1 | 16.3 | 27.9 | 55.0 | 81.5 | 12 | 86 | 12.3 | 15.4 | 26.2 | 50.7 | 74.3 | 12 | 112 | 14.0 | 17.3 | 29.2 | 58.3 | 88.2 |
| 18     | 187 | 13.6 | 18.0 | 33.1 | 67.7 | 100.8 | 18 | 82 | 13.1 | 17.1 | 31.2 | 63.3 | 94.0 | 18 | 105 | 14.3 | 18.8 | 34.6 | 71.2 | 106.4 |
| 24     | 182 | 14.6 | 20.7 | 41.4 | 86.4 | 127.3 | 24 | 80 | 14.5 | 20.0 | 38.9 | 81.5 | 121.8 | 24 | 102 | 14.7 | 21.4 | 43.5 | 89.9 | 130.3 |
| Total  | 1032 | Total | 460 | Total | 572 |                  |                  |                  |                  |                  |                  |                  |

(continued on next page)
| Months | n   | Smoothed centiles for SDANN (ms) (All) | Smoothed centiles for SDANN (ms) (Girls) | Smoothed centiles for SDANN (ms) (Boys) |
|--------|-----|--------------------------------------|------------------------------------------|----------------------------------------|
|        |     | 3rd  10th 50th 90th 97th             | 3rd 10th 50th 90th 97th                 | 3rd 10th 50th 90th 97th               |
| 0      | 260 | 25.5 31.8 47.5 66.4 75.9             | 0 117 24.0 30.3 46.2 65.7 75.7         | 0 143 26.3 33.1 49.1 66.4 74.1        |
| 6      | 205 | 32.1 39.5 57.6 79.5 90.4             | 6 95 32.6 38.9 55.5 77.1 88.9          | 6 110 32.1 40.2 59.6 80.7 90.3        |
| 12     | 198 | 35.5 44.1 65.3 90.1 102.2            | 12 86 36.6 43.9 62.7 86.6 99.3         | 12 112 35.2 44.8 67.5 92.3 103.5      |
| 18     | 187 | 35.7 45.9 70.6 98.5 111.6            | 18 82 36.0 45.3 67.8 94.2 107.2        | 18 105 35.6 46.8 73.0 101.0 113.5     |
| 24     | 182 | 32.7 44.8 73.4 104.5 118.5           | 24 80 30.9 43.1 70.9 99.8 112.4        | 24 102 33.5 46.3 76.0 107.0 120.4     |
| Total  | 1032|                                 | Total 460                            | Total 572                            |

| Months | n   | Smoothed centiles for SDNNIDX (ms) (All) | Smoothed centiles for SDNNIDX (ms) (Girls) | Smoothed centiles for SDNNIDX (ms) (Boys) |
|--------|-----|-----------------------------------------|--------------------------------------------|------------------------------------------|
|        |     | 3rd 10th 50th 90th 97th                | 3rd 10th 50th 90th 97th                   | 3rd 10th 50th 90th 97th                 |
| 0      | 260 | 24.5 29.2 42.0 60.7 72.1              | 0 117 27.9 39.1 57.6 70.4                | 0 143 25.8 30.9 44.4 62.8 73.4        |
| 6      | 205 | 23.3 27.1 37.8 54.9 66.4              | 6 95 22.8 26.1 35.8 51.9 63.2            | 6 110 24.5 28.3 39.3 56.8 68.7        |
| 12     | 198 | 22.9 26.6 37.6 56.5 70.1              | 12 86 22.5 25.9 36.1 53.5 66.3            | 12 112 23.7 27.4 38.8 58.5 72.8       |
| 18     | 187 | 23.2 27.8 41.5 65.6 83.3              | 18 82 23.3 27.4 40.0 62.6 79.6            | 18 105 23.4 28.2 42.8 67.7 85.6       |
| 24     | 182 | 24.3 30.6 49.6 82.2 105.7             | 24 80 25.1 30.5 47.6 79.0 103.2          | 24 102 23.6 30.7 51.3 84.5 107.0      |
| Total  | 1032|                                 | Total 460                               | Total 572                             |

HR (heart rate), SDNN (standard deviation of normal-to-normal intervals), SDNNIDX (mean of the standard deviation of all normal RR intervals for all 5-min segments). pNN (percent difference between adjacent normal RR intervals greater than 20 ms, 30 ms, 50 ms, greater than 50 ms). rMSSD (square root of the mean of the sum of the squared differences between adjacent normal RR intervals). SDANN (standard deviation of the mean of all normal RR intervals for 5-min segments), SDNNIDX (mean of the standard deviation of all normal RR intervals for all 5-min segments).
Table 2. HRV indices in the geometrical domain (all 5-min segments).

| Months n | Smoothed centiles for Tri ind (All) | Smoothed centiles for Tri ind (Girls) | Smoothed centiles for Tri ind (Boys) |
|----------|----------------------------------|--------------------------------------|--------------------------------------|
|          | 3rd | 10th | 50th | 90th | 97th | 3rd | 10th | 50th | 90th | 97th | 3rd | 10th | 50th | 90th | 97th |
| 0        | 260 | 11.7 | 14.1 | 20.5 | 28.5 | 32.9 | 0    | 117  | 13.4 | 19.8 | 28.3 | 33.1 | 0    | 143  | 12.0 | 14.8 | 21.2 | 28.2 | 31.4 |
| 6        | 205 | 12.4 | 14.9 | 21.1 | 28.5 | 32.1 | 6    | 95   | 12.6 | 14.7 | 20.3 | 27.7 | 31.8 | 6    | 110  | 12.4 | 15.2 | 21.7 | 28.8 | 32.0 |
| 12       | 198 | 12.8 | 15.5 | 22.2 | 29.6 | 33.1 | 12   | 86   | 13.3 | 15.6 | 21.3 | 28.5 | 32.3 | 12   | 112  | 12.8 | 15.7 | 22.7 | 30.4 | 33.9 |
| 18       | 187 | 12.9 | 16.1 | 23.6 | 32.1 | 35.9 | 18   | 82   | 13.1 | 16.0 | 22.9 | 30.8 | 34.6 | 18   | 105  | 12.9 | 16.3 | 24.2 | 32.9 | 36.9 |
| 24       | 182 | 12.7 | 16.5 | 25.5 | 35.7 | 40.5 | 24   | 80   | 12.0 | 16.0 | 25.0 | 34.4 | 38.6 | 24   | 102  | 13.0 | 16.9 | 26.2 | 36.4 | 41.1 |
| Total    | 1032|      |      |      |      |      | Total| 460  |      |      |      |      |      | Total| 572  |      |      |      |      |      |

| Smoothed centiles for TINN (ms) (All) | Smoothed centiles for TINN (ms) (Girls) | Smoothed centiles for TINN (ms) (Boys) |
|----------------------------------|--------------------------------------|--------------------------------------|
| Months n | 3rd | 10th | 50th | 90th | 97th | 3rd | 10th | 50th | 90th | 97th | 3rd | 10th | 50th | 90th | 97th |
| 0        | 260 | 183  | 221  | 320  | 446  | 513 | 0    | 117  | 170  | 209  | 310  | 443  | 516 | 0    | 143  | 189  | 231  | 331  | 442  | 493  |
| 6        | 205 | 193  | 233  | 330  | 445  | 502 | 6    | 95   | 196  | 230  | 318  | 433  | 497 | 6    | 110  | 195  | 238  | 339  | 451  | 501  |
| 12       | 198 | 199  | 242  | 346  | 463  | 518 | 12   | 86   | 208  | 243  | 333  | 446  | 505 | 12   | 112  | 199  | 245  | 355  | 475  | 529  |
| 18       | 187 | 201  | 251  | 369  | 501  | 562 | 18   | 82   | 206  | 250  | 357  | 481  | 541 | 18   | 105  | 202  | 254  | 378  | 515  | 577  |
| 24       | 182 | 199  | 258  | 399  | 558  | 633 | 24   | 80   | 189  | 250  | 390  | 538  | 604 | 24   | 102  | 204  | 265  | 409  | 569  | 643  |
| Total    | 1032|      |      |      |      |      | Total| 460  |      |      |      |      |      | Total| 572  |      |      |      |      |      |

(continued on next page)
Table 2. (Continued)

| Smoothed centiles for X (ms) (All) | Smoothed centiles for X (ms) (Girls) | Smoothed centiles for X (ms) (Boys) |
|-----------------------------------|--------------------------------------|------------------------------------|
| | Months n | | Months n | | Months n | |
| | 3rd 10th 50th 90th 97th | | 3rd 10th 50th 90th 97th | | 3rd 10th 50th 90th 97th |
| 0 | 260 396 418 472 539 575 | 0 117 | 392 415 471 537 571 | 0 143 | 398 420 474 540 574 |
| 6 | 205 375 405 476 551 585 | 6 95 | 373 403 472 545 578 | 6 110 | 376 408 480 555 588 |
| 12 | 198 371 407 490 575 610 | 12 86 | 370 405 483 564 599 | 12 112 | 371 409 496 582 616 |
| 18 | 187 382 422 515 610 650 | 18 82 | 384 421 506 596 635 | 18 105 | 381 425 523 620 659 |
| 24 | 182 409 451 551 657 704 | 24 80 | 414 451 539 639 686 | 24 102 | 406 453 560 669 715 |
| Total | 1032 | Total 460 | Total 572 |

| Smoothed centiles for Y (n) (All) | Smoothed centiles for Y (n) (Girls) | Smoothed centiles for Y (n) (Boys) |
|-----------------------------------|--------------------------------------|------------------------------------|
| | Months n | | Months n | | Months n | |
| | 3rd 10th 50th 90th 97th | | 3rd 10th 50th 90th 97th | | 3rd 10th 50th 90th 97th |
| 0 | 260 2517 3651 6457 9798 11433 | 0 117 | 2494 3764 6798 10188 11756 | 0 143 | 2560 3587 6189 9422 11071 |
| 6 | 205 2513 3483 5913 8911 10472 | 6 95 | 2517 3613 6279 9369 10859 | 6 110 | 2501 3415 5672 8398 9807 |
| 12 | 198 2414 3235 5360 8195 9830 | 12 86 | 2439 3370 5705 8587 10082 | 12 112 | 2367 3161 5151 7706 9178 |
| 18 | 187 2219 2903 4792 7643 9498 | 18 82 | 2260 3034 5071 7835 9419 | 18 105 | 2161 2825 4630 7349 9182 |
| 24 | 182 1929 2491 4215 7260 9481 | 24 80 | 1982 2607 4382 7121 8875 | 24 102 | 1881 2408 4104 7322 9814 |
| Total | 1032 | Total 460 | Total 572 |

(continued on next page)
| Months | n | Smoothed centiles for M (ms) (All) | Smoothed centiles for M (ms) (Girls) | Smoothed centiles for M (ms) (Boys) |
|-------|---|-----------------------------------|--------------------------------------|-----------------------------------|
|       |   | 3rd 10th 50th 90th 97th          | 3rd 10th 50th 90th 97th             | 3rd 10th 50th 90th 97th           |
| 0     | 260 | 521 549 624 722 776             | 0 117 518 641 711 774             | 0 143 524 557 636 728 772         |
| 6     | 205 | 534 566 646 750 805             | 6 95 532 634 738 797             | 6 110 539 573 656 758 808         |
| 12    | 198 | 549 586 678 789 845             | 12 86 549 667 777 836             | 12 112 553 592 687 797 850         |
| 18    | 187 | 565 611 720 840 896             | 18 82 569 690 710 830             | 18 105 564 614 728 846 897         |
| 24    | 182 | 583 640 771 902 957             | 24 80 593 642 761 896             | 24 102 574 639 779 904 950         |
| Total | 1032 | Total 460 Total 572       |                                      |                                    |

| Smoothed centiles for N (ms) (All) | Smoothed centiles for N (ms) (Girls) | Smoothed centiles for N (ms) (Boys) |
|-----------------------------------|--------------------------------------|-----------------------------------|
| Months | n | 3rd 10th 50th 90th 97th          | 3rd 10th 50th 90th 97th             | 3rd 10th 50th 90th 97th           |
| 0     | 260 | 226 251 305 354 371             | 0 117 222 249 304 350 365             | 0 143 228 253 307 355 373         |
| 6     | 205 | 243 266 318 371 393             | 6 95 245 267 317 368 389             | 6 110 242 266 320 373 395         |
| 12    | 198 | 256 279 332 392 419             | 12 86 262 282 332 390 418             | 12 112 252 276 333 392 419         |
| 18    | 187 | 264 289 347 416 449             | 18 82 273 295 349 417 452             | 18 105 259 284 346 414 446         |
| 24    | 182 | 268 296 363 444 483             | 24 80 279 304 369 449 491             | 24 102 262 290 359 438 475         |
| Total | 1032 | Total 460 Total 572       |                                      |                                    |

HRV triangular index (integral of the density distribution divided by the maximum of the density distribution (Y)).
TINN (Triangular interpolation of the RR interval histogram width of a triangle using the minimum square difference).
Table 3. HRV indices in the frequency domain (all 5-min segments).

| Smoothed centiles for Ptot (ms²/Hz) (All) | Smoothed centiles for Ptot (ms²/Hz) (Girls) | Smoothed centiles for Ptot (ms²/Hz) (Boys) |
|----------------------------------------|---------------------------------------------|---------------------------------------------|
| Months n                               | Months n                                    | Months n                                    |
|                                       | 3rd 10th 50th 90th 97th                    | 3rd 10th 50th 90th 97th                    | 3rd 10th 50th 90th 97th |
| 0                                     | 260 1266 1862 3712 7107 9723              | 0 117 1134 1662 3341 6449 8645             | 0 143 1399 2080 4081 7468 9957 |
| 6                                     | 205 1171 1714 3507 7243 10514             | 6 95 1171 1621 3172 6817 10598            | 6 110 1226 1835 3781 7585 10727 |
| 12                                    | 198 1106 1662 3607 8102 12435             | 12 86 1194 1628 3246 7669 12944           | 12 112 1105 1730 3865 8551 12824 |
| 18                                    | 187 1069 1705 4011 9693 15505             | 18 82 1201 1684 3564 9015 15709          | 18 105 1037 1763 4331 10353 16226 |
| 24                                    | 182 1061 1844 4716 11999 19692            | 24 80 1193 1788 4122 10838 18861         | 24 102 1022 1934 5178 12995 20939 |
| Total 1032                             | Total 460                                  | Total 572                                  |

| Smoothed centiles for ULF (ms²/Hz) (All) | Smoothed centiles for ULF (ms²/Hz) (Girls) | Smoothed centiles for ULF (ms²/Hz) (Boys) |
|----------------------------------------|---------------------------------------------|---------------------------------------------|
| Months n                               | Months n                                    | Months n                                    |
|                                       | 3rd 10th 50th 90th 97th                    | 3rd 10th 50th 90th 97th                    | 3rd 10th 50th 90th 97th |
| 0                                     | 260 473 806 1865 3895 5517                | 0 117 399 716 1729 3626 5017              | 0 143 549 895 1990 4080 5758 |
| 6                                     | 205 467 807 1956 4451 6741               | 6 95 511 793 1791 4250 6907              | 6 110 462 838 2077 4640 6869 |
| 12                                    | 198 451 801 2031 4908 7733              | 12 86 551 814 1815 4636 8047             | 12 112 407 813 2187 5174 7896 |
| 18                                    | 187 424 787 2091 5271 8502              | 18 82 520 780 1801 4788 8448            | 18 105 386 822 2320 5679 8832 |
| 24                                    | 182 387 765 2137 5537 9041              | 24 80 418 691 1750 4705 8106            | 24 102 398 863 2476 6159 9683 |
| Total 1032                             | Total 460                                  | Total 572                                  |

(continued on next page)
### Table 3. (Continued)

| Months | n     | 3rd  | 10th | 50th | 90th | 97th |
|--------|-------|------|------|------|------|------|
| 6      | 205   | 241  | 350  | 690  | 1322 | 1815 |
| 12     | 198   | 218  | 314  | 605  | 1113 | 1487 |
| 18     | 187   | 227  | 342  | 688  | 1286 | 1722 |
| 24     | 182   | 267  | 433  | 938  | 1840 | 2517 |
| Total  | 1032  |      |      |      |      |      |

| Months | n     | 3rd  | 10th | 50th | 90th | 97th |
|--------|-------|------|------|------|------|------|
| 6      | 205   | 241  | 350  | 690  | 1322 | 1815 |
| 12     | 198   | 218  | 314  | 605  | 1113 | 1487 |
| 18     | 187   | 227  | 342  | 688  | 1286 | 1722 |
| 24     | 182   | 267  | 433  | 938  | 1840 | 2517 |
| Total  | 1032  |      |      |      |      |      |

### Smoothed centiles for LF (ms²/Hz) (All)

| Months | n     | 3rd  | 10th | 50th | 90th | 97th |
|--------|-------|------|------|------|------|------|
| 6      | 205   | 137  | 203  | 435  | 980  | 1513 |
| 12     | 198   | 135  | 201  | 445  | 1058 | 1703 |
| 18     | 187   | 130  | 214  | 523  | 1298 | 2110 |
| 24     | 182   | 122  | 236  | 648  | 1669 | 2723 |
| Total  | 1032  |      |      |      |      |      |

(continued on next page)
### Table 3. (Continued)

| Months | n   | Smoothed centiles for HF (ms²/Hz) (All) | Smoothed centiles for HF (ms²/Hz) (Girls) | Smoothed centiles for HF (ms²/Hz) (Boys) |
|--------|-----|----------------------------------------|--------------------------------------------|----------------------------------------|
|        |     | 3rd 10th 50th 90th 97th                | 3rd 10th 50th 90th 97th                    | 3rd 10th 50th 90th 97th                |
| 0      | 260 | 66.7 100.0 247.5 779.0 1554.4          | 0 117 63.5 88.6 202.5 625.8 1247.8       | 0 143 72.8 115.8 294.4 876.2 1676.1   |
| 6      | 205 | 67.5 102.0 263.0 902.1 1916.2          | 6 95 62.6 91.4 228.6 805.1 1783.7       | 6 110 74.3 114.4 295.5 968.7 1961.0   |
| 12     | 198 | 68.8 114.8 343.5 3192.8               | 12 86 64.6 106.7 315.6 1259.2 2963.8   | 12 112 74.1 123.2 367.8 1461.7 3385.3 |
| 18     | 187 | 70.6 138.5 489.7 2185.6 5398.1        | 18 82 69.7 134.9 464.4 1993.1 4801.1   | 18 105 72.3 142.1 510.2 2349.2 5931.7 |
| 24     | 182 | 73.0 172.9 700.1 3342.2 8508.2        | 24 80 77.7 175.6 673.3 2998.8 7275.5   | 24 102 68.8 171.0 723.0 3632.9 9605.0 |
| Total  | 1032|                                   |                                            | Total 460                                | Total 572                              |

| Months | n   | Smoothed centiles for LF/HF (All) | Smoothed centiles for LF/HF (Girls) | Smoothed centiles for LF/HF (Boys) |
|--------|-----|----------------------------------|-------------------------------------|-------------------------------------|
|        |     | 3rd 10th 50th 90th 97th          | 3rd 10th 50th 90th 97th             | 3rd 10th 50th 90th 97th             |
| 0      | 260 | 0.99 1.46 2.69 4.34 5.26         | 0 117 0.94 1.45 2.79 4.60 5.61      | 0 143 1.04 1.47 2.61 4.11 4.93     |
| 6      | 205 | 0.89 1.24 2.23 3.79 4.85         | 6 95 0.91 1.29 2.36 3.91 4.88       | 6 110 0.88 1.20 2.13 3.67 4.76     |
| 12     | 198 | 0.77 1.04 1.84 3.29 4.39         | 12 86 0.82 1.11 1.96 3.33 4.27      | 12 112 0.74 0.98 1.75 3.23 4.42    |
| 18     | 187 | 0.64 0.86 1.53 2.84 3.88         | 18 82 0.68 0.91 1.62 2.86 3.79      | 18 105 0.62 0.82 1.47 2.80 3.92    |
| 24     | 182 | 0.50 0.70 1.30 2.43 3.33         | 24 80 0.48 0.68 1.31 2.49 3.43      | 24 102 0.52 0.71 1.29 2.38 3.25    |
| Total  | 1032|                                   |                                    | Total 460                                | Total 572                              |

Ptot (total power), ULF (ultra-low frequencies), VLF (very low frequencies), LF (low frequencies), and HF (high frequencies).
Table 4. HRV indices by Poincaré plot (all 5-min segments).

| Months | n  | 3rd  | 10th | 50th | 90th | 97th | 3rd  | 10th | 50th | 90th | 97th | 3rd  | 10th | 50th | 90th | 97th |
|--------|----|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| 0      | 260| 420  | 433  | 467  | 515  | 544  | 0    | 117  | 420  | 430  | 460  | 508  | 539  | 0    | 143  | 421  |
| 6      | 205| 425  | 442  | 483  | 532  | 556  | 6    | 95   | 423  | 439  | 477  | 524  | 549  | 6    | 110  | 428  |
| 12     | 198| 435  | 455  | 504  | 558  | 583  | 12   | 86   | 432  | 452  | 499  | 551  | 575  | 12   | 112  | 436  |
| 18     | 187| 448  | 473  | 532  | 595  | 623  | 18   | 82   | 448  | 472  | 527  | 589  | 618  | 18   | 105  | 447  |
| 24     | 182| 464  | 494  | 565  | 642  | 677  | 24   | 80   | 470  | 496  | 560  | 638  | 677  | 24   | 102  | 461  |
| Total  | 1032|      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |
| 0      | 260| 7.41 | 9.14 | 14.64| 25.27| 33.89| 0    | 117  | 7.21 | 8.58 | 13.24| 23.64| 33.51| 0    | 143  | 7.95 |
| 6      | 205| 8.05 | 9.86 | 15.77| 27.65| 37.71| 6    | 95   | 7.62 | 9.24 | 14.59| 25.76| 35.65| 6    | 110  | 8.70 |
| 12     | 198| 8.52 | 10.76| 18.11| 33.22| 46.25| 12   | 86   | 8.05 | 10.14| 17.01| 31.19| 43.53| 12   | 112  | 9.12 |
| 18     | 187| 8.83 | 11.83| 21.71| 42.03| 59.59| 18   | 82   | 8.50 | 11.28| 20.53| 40.02| 57.24| 18   | 105  | 9.22 |
| 24     | 182| 8.98 | 13.07| 26.51| 54.00| 77.60| 24   | 80   | 8.97 | 12.65| 25.11| 52.13| 76.62| 24   | 102  | 8.98 |
| Total  | 1032|      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |
| Smoothed centiles for SD1 (ms) | Smoothed centiles for SD1 (ms) | Smoothed centiles for SD1 (ms) |
| (All) | (Girls) | (Boys) |
| 3rd  | 10th | 50th | 90th | 97th | 3rd  | 10th | 50th | 90th | 97th | 3rd  | 10th | 50th | 90th | 97th |
| 0    | 143  | 9.88 | 15.79| 26.43| 34.53| 6    | 105  | 9.22 | 12.37| 22.66| 43.46| 61.12| 24   | 102  | 8.98 |
| Total| 572  |      |      |      |      |      |      |      |      |      |      |      |      |      |      |

(continued on next page)
Table 4. (Continued)

| Months | n     | Smoothed centiles for SD2 (ms) (All) | Smoothed centiles for SD2 (ms) (Girls) | Smoothed centiles for SD2 (ms) (Boys) |
|--------|-------|------------------------------------|----------------------------------------|---------------------------------------|
|        |       | 3rd  | 10th | 50th | 90th | 97th | 3rd  | 10th | 50th | 90th | 97th | 3rd  | 10th | 50th | 90th | 97th |
| 0      | 260   | 52.08| 62.74| 89.66| 123.07| 140.36| 0    | 117  | 49.50| 59.68| 86.19| 121.23| 140.64| 0    | 143  | 52.27| 65.32| 94.21| 122.09| 133.11|
| 6      | 205   | 59.46| 70.42| 97.69| 130.71| 147.41| 6    | 95   | 59.66| 69.11| 93.80| 126.68| 145.05| 6    | 110  | 60.31| 72.27| 100.89| 133.07| 148.12|
| 12     | 198   | 63.53| 75.83| 106.03| 141.78| 159.44| 12   | 86   | 65.24| 75.32| 101.64| 136.58| 156.04| 12   | 112  | 64.29| 77.29| 108.98| 145.71| 163.35|
| 18     | 187   | 64.36| 79.02| 114.78| 156.40| 176.56| 18   | 82   | 66.29| 78.39| 109.81| 151.05| 173.72| 18   | 105  | 64.22| 80.38| 118.43| 159.92| 178.72|
| 24     | 182   | 61.92| 79.98| 123.84| 174.40| 198.60| 24   | 80   | 62.81| 78.27| 118.20| 169.92| 197.90| 24   | 102  | 60.13| 81.57| 129.28| 175.78| 194.32|
| Total  | 1032  |       |       |       |       |       | Total| 460  |       |       |       |       |       | Total| 572  |       |       |       |       |

| Months | n     | Smoothed centiles for SD1/SD2 ratio (All) | Smoothed centiles for SD1/SD2 ratio (Girls) | Smoothed centiles for SD1/SD2 ratio (Boys) |
|--------|-------|------------------------------------------|---------------------------------------------|---------------------------------------------|
|        |       | 3rd | 10th | 50th | 90th | 97th | 3rd | 10th | 50th | 90th | 97th | 3rd | 10th | 50th | 90th | 97th |
| 0      | 260   | 0.095 | 0.113 | 0.168 | 0.260 | 0.325 | 0    | 117  | 0.089| 0.107| 0.161| 0.253| 0.320| 0    | 143  | 0.102| 0.120| 0.173| 0.264| 0.330|
| 6      | 205   | 0.096 | 0.113 | 0.165 | 0.259 | 0.330 | 6    | 95   | 0.094| 0.110| 0.158| 0.247| 0.316| 6    | 110  | 0.098| 0.116| 0.171| 0.267| 0.338|
| 12     | 198   | 0.098 | 0.117 | 0.173 | 0.275 | 0.353 | 12   | 86   | 0.099| 0.115| 0.167| 0.263| 0.338| 12   | 112  | 0.098| 0.118| 0.179| 0.284| 0.361|
| 18     | 187   | 0.102 | 0.125 | 0.192 | 0.310 | 0.395 | 18   | 82   | 0.101| 0.123| 0.188| 0.301| 0.385| 18   | 105  | 0.102| 0.126| 0.197| 0.315| 0.400|
| 24     | 182   | 0.107 | 0.136 | 0.222 | 0.361 | 0.456 | 24   | 80   | 0.103| 0.133| 0.220| 0.362| 0.459| 24   | 102  | 0.110| 0.139| 0.223| 0.360| 0.453|
| Total  | 1032  |       |       |       |       |       | Total| 460  |       |       |       |       |       | Total| 572  |       |       |       |       |
| Months | SD1nu (All) | Months | SD1nu (Girls) | Months | SD1nu (Boys) |
|--------|-------------|--------|---------------|--------|--------------|
|        | 3rd  | 10th | 50th | 90th | 97th | 3rd  | 10th | 50th | 90th | 97th | 3rd  | 10th | 50th | 90th | 97th |
| 0      | 260  | 1.68 | 2.03 | 3.12 | 5.14 | 6.69 | 0    | 1.62 | 1.92 | 2.88 | 4.84 | 6.54 | 0    | 1.80 | 2.18 | 3.32 | 5.35 | 6.89 |
| 6      | 205  | 1.76 | 2.13 | 3.27 | 5.48 | 7.25 | 6    | 1.69 | 2.01 | 3.07 | 5.16 | 6.91 | 6    | 1.88 | 2.26 | 3.44 | 5.71 | 7.57 |
| 12     | 198  | 1.82 | 2.24 | 3.58 | 6.22 | 8.41 | 12   | 1.74 | 2.14 | 3.40 | 5.89 | 7.97 | 12   | 1.93 | 2.35 | 3.73 | 6.48 | 8.79 |
| 18     | 187  | 1.86 | 2.38 | 4.05 | 7.39 | 10.17| 18   | 1.79 | 2.28 | 3.87 | 7.06 | 9.74 | 18   | 1.94 | 2.47 | 4.19 | 7.64 | 10.53|
| 24     | 182  | 1.87 | 2.53 | 4.68 | 8.95 | 12.53| 24   | 1.83 | 2.45 | 4.48 | 8.64 | 12.20| 24   | 1.90 | 2.60 | 4.83 | 9.20 | 12.79|
| Total  | 1032 |     |     |     |     |     | Total | 460  |     |     |     |     | Total | 572  |     |     |     |     |

| SD2nu (All) | SD2nu (Girls) | SD2nu (Boys) |
|-------------|---------------|--------------|
| Months | 3rd  | 10th | 50th | 90th | 97th | 3rd  | 10th | 50th | 90th | 97th | 3rd  | 10th | 50th | 90th | 97th |
| 0      | 260  | 11.96| 13.98| 19.04| 25.28| 28.48| 0    | 11.42| 13.43| 18.57| 25.11| 28.60| 0    | 14.06| 14.43| 19.72| 24.94| 27.06| 24 05-8440 C2019 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY license. |
| 6      | 205  | 13.11| 15.16| 20.16| 25.96| 28.77| 6    | 13.21| 15.02| 19.62| 25.37| 28.35| 6    | 13.12| 15.40| 20.65| 26.20| 28.62| 2049-8440 C2019 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY license. |
| 12     | 198  | 13.46| 15.71| 21.03| 26.86| 29.49| 12   | 13.80| 15.73| 20.46| 26.00| 28.69| 12   | 13.45| 15.85| 21.45| 27.44| 30.09| 24 05-8440 C2019 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY license. |
| 18     | 187  | 13.00| 15.63| 21.68| 27.97| 30.66| 18   | 13.22| 15.57| 21.07| 27.00| 29.65| 18   | 13.05| 15.79| 22.10| 28.66| 31.47| 24 05-8440 C2019 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY license. |
| 24     | 182  | 11.74| 14.91| 22.08| 29.28| 32.27| 24   | 11.45| 14.54| 21.47| 28.37| 31.20| 24   | 11.92| 15.23| 22.62| 29.86| 32.76| 24 05-8440 C2019 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY license. |
| Total  | 1032 |     |     |     |     |     | Total | 460  |     |     |     |     | Total | 572  |     |     |     |     | 2049-8440 C2019 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY license. |

SD1 and SD2 (standard deviation of the distances of the RR intervals from the y = x line and the y = −x + 2 mean (RR) line, respectively).
Table 5. HRV indices by an empirical mode decomposition (all 5-min segments).

| Months | n    | Smoothed centiles for pLF1 (All) | Smoothed centiles for pLF1 (Girls) | Smoothed centiles for pLF1 (Boys) |
|--------|------|---------------------------------|-----------------------------------|-----------------------------------|
|        |      | 3rd 10th 50th 90th 97th        | 3rd 10th 50th 90th 97th          | 3rd 10th 50th 90th 97th          |
| 0      | 260  | 76.2 112.5 237.6 518.3 781.7 | 0 117 68.8 200.7 457.4 726.8 | 0 143 91.0 270.8 555.0 803.5 |
| 6      | 205  | 83.4 119.1 245.2 541.9 833.6 | 6 95 81.2 219.0 495.9 795.6 | 6 110 93.3 266.3 572.0 866.1 |
| 12     | 198  | 86.3 128.5 277.8 631.1 980.6 | 12 86 88.6 255.3 582.0 930.6 | 12 112 90.5 295.3 666.7 1029.3 |
| 18     | 187  | 85.0 140.7 335.7 787.0 1224.5 | 18 82 91.2 310.0 716.9 1133.5 | 18 105 82.6 357.4 837.8 1291.3 |
| 24     | 182  | 79.5 155.8 418.4 1007.9 1562.5 | 24 80 89.0 382.4 898.9 1401.9 | 24 102 69.6 452.7 1085.7 1652.6 |
| Total  | 1032 | Total 460 | Total 572 |

| Months | n    | Smoothed centiles for pLF2 (All) | Smoothed centiles for pLF2 (Girls) | Smoothed centiles for pLF2 (Boys) |
|--------|------|---------------------------------|-----------------------------------|-----------------------------------|
|        |      | 3rd 10th 50th 90th 97th        | 3rd 10th 50th 90th 97th          | 3rd 10th 50th 90th 97th          |
| 0      | 260  | 85.8 128.3 263.4 525.1 738.4 | 0 117 78.5 234.1 493.6 736.6 | 0 143 93.0 293.5 532.4 694.4 |
| 6      | 205  | 89.4 129.1 255.5 499.0 695.8 | 6 95 88.8 231.6 465.7 673.9 | 6 110 94.4 276.3 518.6 699.9 |
| 12     | 198  | 92.4 137.7 279.8 545.7 754.5 | 12 86 95.5 250.9 502.0 700.5 | 12 112 94.6 296.4 579.4 799.5 |
| 18     | 187  | 94.6 154.0 336.6 665.8 915.2 | 18 82 98.8 316.6 602.8 816.7 | 18 105 93.6 353.1 713.9 992.0 |
| 24     | 182  | 96.0 178.0 425.3 857.8 1176.1 | 24 80 98.5 403.7 767.0 1021.2 | 24 102 91.4 446.6 922.2 1277.6 |
| Total  | 1032 | Total 460 | Total 572 |

(continued on next page)
Table 5. (Continued)

| Smoothed centiles for pHF1 (All) | Smoothed centiles for pHF1 (Girls) | Smoothed centiles for pHF1 (Boys) |
|----------------------------------|------------------------------------|----------------------------------|
| Months n                         | 3rd 10th 50th 90th 97th           | Months n                         | 3rd 10th 50th 90th 97th           | Months n                         | 3rd 10th 50th 90th 97th           |
| 0                                | 260 60.5 88.7 197.5 497.7 837.9   | 0                                | 117 60.3 79.8 161.0 427.1 785.2   | 0                                | 143 68.7 104.0 230.6 546.2 890.1 |
| 6                                | 205 54.7 78.0 172.3 460.5 824.3   | 6                                | 95 51.7 70.1 145.6 391.4 731.6   | 6                                | 110 64.1 89.9 193.8 516.9 940.6  |
| 12                               | 198 52.4 79.4 197.1 613.3 1214.7  | 12                               | 86 49.8 73.5 175.8 539.8 1085.6  | 12                               | 112 59.5 87.3 213.0 677.1 1363.4 |
| 18                               | 187 53.4 92.7 272.1 957.5 2013.2  | 18                               | 82 54.5 90.1 251.9 874.1 1851.0  | 18                               | 105 54.8 96.3 287.8 1024.4 2153.1 |
| 24                               | 182 57.8 117.9 396.4 1489.6 3211.2| 24                               | 80 65.8 119.7 373.2 1390.5 3019.5| 24                               | 102 50.0 116.6 418.0 1559.1 3311.0|
| Total                            | 1032 Total                        | 460 Total                        | 572 Total                        |

| Smoothed centiles for pHF2 (All) | Smoothed centiles for pHF2 (Girls) | Smoothed centiles for pHF2 (Boys) |
|----------------------------------|------------------------------------|----------------------------------|
| Months n                         | 3rd 10th 50th 90th 97th           | Months n                         | 3rd 10th 50th 90th 97th           | Months n                         | 3rd 10th 50th 90th 97th           |
| 0                                | 260 57.0 88.9 213.5 537.5 813.3   | 0                                | 117 57.2 82.0 178.4 405.4 509.2   | 0                                | 143 61.7 100.5 247.5 638.9 1065.1 |
| 6                                | 205 54.5 86.5 238.6 890.3 2045.0  | 6                                | 95 48.5 76.4 210.0 803.8 1907.7  | 6                                | 110 65.4 99.4 261.2 963.5 2221.3 |
| 12                               | 198 56.5 100.6 333.5 1510.0 3843.1| 12                               | 86 49.8 90.6 302.2 1365.8 3506.6 | 12                               | 112 67.4 112.3 357.3 1643.6 4235.1|
| 18                               | 187 63.1 131.5 499.2 2403.4 6227.1| 18                               | 82 61.2 124.8 456.0 2097.5 5323.5| 18                               | 105 67.8 139.0 534.5 2672.7 7088.4|
| 24                               | 182 74.3 178.9 734.1 3560.7 9171.2| 24                               | 80 82.4 178.8 669.7 2990.9 7338.4| 24                               | 102 66.4 179.6 793.2 4053.5 10790.1|
| Total                            | 1032 Total                        | 460 Total                        | 572 Total                        |

(continued on next page)
Table 5. (Continued)

| Months | n   | Smoothed centiles for IMAI1 (All) | Smoothed centiles for IMAI1 (Girls) | Smoothed centiles for IMAI1 (Boys) |
|--------|-----|----------------------------------|-------------------------------------|-----------------------------------|
|        |     | 3rd 10th 50th 90th 97th         | 3rd 10th 50th 90th 97th             | 3rd 10th 50th 90th 97th          |
| 0      | 260 | 0.383 0.501 0.819 1.262 1.522   | 0.389 0.517 0.857 1.328 1.604   | 0.384 0.493 0.787 1.202 1.449   |
| 6      | 205 | 0.382 0.487 0.774 1.192 1.451   | 0.402 0.513 0.807 1.220 1.468   | 0.370 0.469 0.747 1.163 1.426   |
| 12     | 198 | 0.349 0.442 0.702 1.100 1.359   | 0.372 0.469 0.729 1.106 1.342   | 0.333 0.423 0.681 1.089 1.362   |
| 18     | 187 | 0.284 0.367 0.604 0.986 1.246   | 0.298 0.383 0.621 0.985 1.224   | 0.275 0.355 0.591 0.983 1.258   |
| 24     | 182 | 0.189 0.262 0.479 0.849 1.113   | 0.179 0.257 0.485 0.858 1.115   | 0.196 0.265 0.475 0.843 1.114   |
| Total  | 1032| Total 460                       | Total 572                          |                                   |

| Months | n   | Smoothed centiles for IMAI2 (All) | Smoothed centiles for IMAI2 (Girls) | Smoothed centiles for IMAI2 (Boys) |
|--------|-----|----------------------------------|-------------------------------------|-----------------------------------|
|        |     | 3rd 10th 50th 90th 97th         | 3rd 10th 50th 90th 97th             | 3rd 10th 50th 90th 97th          |
| 0      | 260 | 0.356 0.513 0.962 1.682 2.167   | 0.372 0.548 1.054 1.859 2.402   | 0.346 0.492 0.899 1.513 1.902   |
| 6      | 205 | 0.352 0.482 0.851 1.435 1.824   | 0.377 0.516 0.909 1.518 1.919   | 0.337 0.460 0.809 1.354 1.712   |
| 12     | 198 | 0.320 0.430 0.746 1.256 1.605   | 0.344 0.458 0.780 1.281 1.613   | 0.306 0.410 0.718 1.228 1.586   |
| 18     | 187 | 0.260 0.357 0.645 1.142 1.505   | 0.274 0.375 0.667 1.145 1.479   | 0.252 0.345 0.628 1.137 1.524   |
| 24     | 182 | 0.172 0.263 0.551 1.095 1.526   | 0.165 0.265 0.570 1.112 1.520   | 0.176 0.262 0.538 1.080 1.526   |
| Total  | 1032| Total 460                       | Total 572                          |                                   |

Nonlinear and non-stationary time series are decomposed into a limited number of oscillatory components (modes), pLF1, pLF2, pHF1, and pHF2 (Low and high frequencies power associated to the selected mode). IMAI1 and IMAI2 (ratios between low and high frequency indices).
Table 6. HRV indices by a fractal analysis (all 5-min segments).

| Months | n | Smoothed centiles for alpha1 DFA (All) | Smoothed centiles for alpha1 DFA (Girls) | Smoothed centiles for alpha1 DFA (Boys) |
|--------|---|----------------------------------------|----------------------------------------|----------------------------------------|
|        |   | 3rd | 10th | 50th | 90th | 97th | 3rd | 10th | 50th | 90th | 97th | 3rd | 10th | 50th | 90th | 97th |
| -      |   |     |      |      |      |      |     |      |      |      |      |     |      |      |      |      |
| 0      | 260 | 0.96 | 1.04 | 1.20 | 1.35 | 1.40 | 0   | 117  | 0.95 | 1.04 | 1.22 | 1.36 | 1.41 | 0   | 143  | 0.96 | 1.04 | 1.19 | 1.33 | 1.38 |
| 6      | 205 | 0.92 | 0.99 | 1.15 | 1.31 | 1.37 | 6   | 95   | 0.92 | 1.00 | 1.17 | 1.32 | 1.37 | 6   | 110  | 0.92 | 0.99 | 1.14 | 1.30 | 1.36 |
| 12     | 198 | 0.87 | 0.94 | 1.10 | 1.27 | 1.34 | 12  | 86   | 0.88 | 0.95 | 1.11 | 1.28 | 1.34 | 12  | 112  | 0.87 | 0.93 | 1.09 | 1.26 | 1.34 |
| 18     | 187 | 0.81 | 0.88 | 1.05 | 1.23 | 1.32 | 18  | 82   | 0.81 | 0.89 | 1.06 | 1.24 | 1.32 | 18  | 105  | 0.82 | 0.88 | 1.04 | 1.23 | 1.31 |
| 24     | 182 | 0.75 | 0.82 | 1.00 | 1.20 | 1.29 | 24  | 80   | 0.73 | 0.81 | 1.01 | 1.21 | 1.31 | 24  | 102  | 0.76 | 0.83 | 1.00 | 1.19 | 1.28 |
| Total  | 1032|      |      |      |      |      | Total| 460  |      |      |      |      |      | Total| 572  |      |      |      |      |      |

| Months | n | Smoothed centiles for alpha2 DFA (All) | Smoothed centiles for alpha2 DFA (Girls) | Smoothed centiles for alpha2 DFA (Boys) |
|--------|---|----------------------------------------|----------------------------------------|----------------------------------------|
|        |   | 3rd | 10th | 50th | 90th | 97th | 3rd | 10th | 50th | 90th | 97th | 3rd | 10th | 50th | 90th | 97th |
| -      |   |     |      |      |      |      |     |      |      |      |      |     |      |      |      |      |
| 0      | 260 | 0.87 | 0.93 | 1.05 | 1.16 | 1.20 | 0   | 117  | 0.88 | 0.94 | 1.07 | 1.18 | 1.22 | 0   | 143  | 0.87 | 0.92 | 1.03 | 1.14 | 1.18 |
| 6      | 205 | 0.80 | 0.84 | 0.94 | 1.04 | 1.09 | 6   | 95   | 0.80 | 0.85 | 0.95 | 1.05 | 1.10 | 6   | 110  | 0.79 | 0.84 | 0.93 | 1.03 | 1.07 |
| 12     | 198 | 0.75 | 0.79 | 0.88 | 0.98 | 1.03 | 12  | 86   | 0.75 | 0.79 | 0.89 | 0.98 | 1.03 | 12  | 112  | 0.75 | 0.79 | 0.88 | 0.98 | 1.02 |
| 18     | 187 | 0.74 | 0.77 | 0.87 | 0.98 | 1.03 | 18  | 82   | 0.73 | 0.78 | 0.88 | 0.98 | 1.02 | 18  | 105  | 0.73 | 0.77 | 0.87 | 0.98 | 1.03 |
| 24     | 182 | 0.75 | 0.80 | 0.91 | 1.03 | 1.09 | 24  | 80   | 0.75 | 0.80 | 0.92 | 1.02 | 1.06 | 24  | 102  | 0.75 | 0.79 | 0.90 | 1.03 | 1.10 |
| Total  | 1032|      |      |      |      |      | Total| 460  |      |      |      |      |      | Total| 572  |      |      |      |      |      |

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Table 6. (Continued)

| Months | n     | 3rd       | 10th      | 50th      | 90th      | 97th      | 3rd       | 10th      | 50th      | 90th      | 97th      | 3rd       | 10th      | 50th      | 90th      | 97th      |
|--------|-------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| 0      | 260   | 0.94      | 0.97      | 1.04      | 1.11      | 1.14      | 0         | 117       | 0.95      | 0.98      | 1.04      | 1.12      | 1.15      | 0         | 143       | 0.94      | 0.97      | 1.03      | 1.10      | 1.14      |
| 6      | 205   | 0.93      | 0.95      | 1.01      | 1.07      | 1.10      | 6         | 95        | 0.92      | 0.95      | 1.01      | 1.07      | 1.09      | 6         | 110       | 0.93      | 0.95      | 1.00      | 1.07      | 1.10      |
| 12     | 198   | 0.91      | 0.93      | 0.98      | 1.04      | 1.07      | 12        | 86        | 0.90      | 0.93      | 0.98      | 1.04      | 1.06      | 12        | 112       | 0.91      | 0.93      | 0.98      | 1.05      | 1.08      |
| 18     | 187   | 0.89      | 0.91      | 0.97      | 1.03      | 1.06      | 18        | 82        | 0.89      | 0.91      | 0.97      | 1.02      | 1.05      | 18        | 105       | 0.90      | 0.92      | 0.97      | 1.03      | 1.07      |
| 24     | 182   | 0.88      | 0.90      | 0.96      | 1.03      | 1.07      | 24        | 80        | 0.89      | 0.91      | 0.96      | 1.03      | 1.06      | 24        | 102       | 0.88      | 0.90      | 0.96      | 1.03      | 1.07      |
| Total  | 1032  | Total 460 | Total 572 |

| Months | n     | 3rd       | 10th      | 50th      | 90th      | 97th      | 3rd       | 10th      | 50th      | 90th      | 97th      | 3rd       | 10th      | 50th      | 90th      | 97th      |
|--------|-------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| 0      | 260   | 1.45      | 1.49      | 1.61      | 1.75      | 1.82      | 0         | 117       | 1.45      | 1.50      | 1.61      | 1.75      | 1.81      | 0         | 143       | 1.45      | 1.49      | 1.60      | 1.75      | 1.82      |
| 6      | 205   | 1.52      | 1.57      | 1.70      | 1.83      | 1.89      | 6         | 95        | 1.52      | 1.57      | 1.69      | 1.83      | 1.89      | 6         | 110       | 1.51      | 1.57      | 1.70      | 1.84      | 1.89      |
| 12     | 198   | 1.57      | 1.63      | 1.76      | 1.90      | 1.95      | 12        | 86        | 1.57      | 1.62      | 1.75      | 1.89      | 1.95      | 12        | 112       | 1.57      | 1.63      | 1.77      | 1.90      | 1.95      |
| 18     | 187   | 1.61      | 1.67      | 1.80      | 1.94      | 2.00      | 18        | 82        | 1.60      | 1.66      | 1.79      | 1.93      | 1.99      | 18        | 105       | 1.62      | 1.68      | 1.81      | 1.94      | 2.00      |
| 24     | 182   | 1.64      | 1.69      | 1.81      | 1.96      | 2.03      | 24        | 80        | 1.63      | 1.68      | 1.80      | 1.95      | 2.03      | 24        | 102       | 1.65      | 1.70      | 1.82      | 1.96      | 2.02      |
| Total  | 1032  | Total 460 | Total 572 |
Table 6. (Continued)

| Months | n | 3rd | 10th | 50th | 90th | 97th | Months | n | 3rd | 10th | 50th | 90th | 97th | Months | n | 3rd | 10th | 50th | 90th | 97th |
|--------|---|-----|------|------|------|------|--------|---|-----|------|------|------|------|--------|---|-----|------|------|------|------|
| 0      | 260 | 1.26 | 1.30 | 1.41 | 1.56 | 1.65 | 0      | 117 | 1.26 | 1.29 | 1.39 | 1.54 | 1.63 | 0      | 143 | 1.27 | 1.31 | 1.42 | 1.57 | 1.65 |
| 6      | 205 | 1.30 | 1.34 | 1.44 | 1.61 | 1.72 | 6      | 95  | 1.29 | 1.32 | 1.43 | 1.58 | 1.68 | 6      | 110 | 1.31 | 1.35 | 1.45 | 1.62 | 1.74 |
| 12     | 198 | 1.32 | 1.36 | 1.48 | 1.68 | 1.81 | 12     | 86  | 1.31 | 1.35 | 1.47 | 1.65 | 1.75 | 12     | 112 | 1.33 | 1.37 | 1.50 | 1.70 | 1.83 |
| 18     | 187 | 1.33 | 1.38 | 1.54 | 1.77 | 1.91 | 18     | 82  | 1.32 | 1.37 | 1.52 | 1.73 | 1.86 | 18     | 105 | 1.34 | 1.39 | 1.55 | 1.79 | 1.95 |
| 24     | 182 | 1.32 | 1.40 | 1.59 | 1.87 | 2.04 | 24     | 80  | 1.32 | 1.39 | 1.57 | 1.83 | 1.98 | 24     | 102 | 1.32 | 1.40 | 1.61 | 1.90 | 2.07 |
| Total  | 1032| 0.198| 0.253| 0.370| 0.476| 0.515 | 0      | 117 | 0.202| 0.256| 0.372| 0.478| 0.518 | 0      | 143 | 0.196| 0.251| 0.368| 0.474| 0.514 |
| 0      | 260 | 0.198| 0.253| 0.370| 0.476| 0.515 | 0      | 117 | 0.202| 0.256| 0.372| 0.478| 0.518 | 0      | 143 | 0.196| 0.251| 0.368| 0.474| 0.514 |
| 6      | 205 | 0.142| 0.191| 0.304| 0.421| 0.471 | 6      | 95  | 0.146| 0.198| 0.313| 0.424| 0.468 | 6      | 110 | 0.139| 0.186| 0.297| 0.416| 0.470 |
| 12     | 198 | 0.097| 0.144| 0.254| 0.376| 0.433 | 12     | 86  | 0.102| 0.152| 0.267| 0.381| 0.429 | 12     | 112 | 0.093| 0.137| 0.244| 0.370| 0.430 |
| 18     | 187 | 0.063| 0.109| 0.220| 0.343| 0.400 | 18     | 82  | 0.070| 0.119| 0.233| 0.351| 0.401 | 18     | 105 | 0.057| 0.102| 0.210| 0.335| 0.394 |
| 24     | 182 | 0.039| 0.088| 0.202| 0.321| 0.372 | 24     | 80  | 0.050| 0.099| 0.213| 0.332| 0.384 | 24     | 102 | 0.032| 0.081| 0.194| 0.311| 0.362 |
| Total  | 1032| 0.198| 0.253| 0.370| 0.476| 0.515 | 0      | 117 | 0.202| 0.256| 0.372| 0.478| 0.518 | 0      | 143 | 0.196| 0.251| 0.368| 0.474| 0.514 |

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Table 6. (Continued)

| Months | n   | Smoothed centiles for Beta 1/f Slope (All) | Months | n   | Smoothed centiles for Beta 1/f Slope (Girls) | Months | n   | Smoothed centiles for Beta 1/f Slope (Boys) |
|--------|-----|------------------------------------------|--------|-----|------------------------------------------|--------|-----|------------------------------------------|
|        |     | 3rd 10th 50th 90th 97th                | 3rd 10th 50th 90th 97th                | 3rd 10th 50th 90th 97th                |
| -      | 0   | 260 -1.63 -1.49 -1.15 -0.73 -0.51     | 117   | -1.65 -1.49 -1.14 -0.78 -0.62     | 143   | -1.62 -1.49 -1.15 -0.71 -0.48     |
|        | 6   | 205 -1.80 -1.62 -1.21 -0.76 -0.55     | 95    | -1.78 -1.61 -1.20 -0.76 -0.56     | 110   | -1.80 -1.62 -1.21 -0.78 -0.58     |
|        | 12  | 198 -1.91 -1.71 -1.23 -0.74 -0.52     | 86    | -1.89 -1.69 -1.23 -0.71 -0.47     | 112   | -1.93 -1.71 -1.24 -0.78 -0.59     |
|        | 18  | 187 -1.98 -1.75 -1.22 -0.67 -0.43     | 82    | -1.96 -1.74 -1.22 -0.64 -0.36     | 105   | -1.99 -1.75 -1.22 -0.71 -0.50     |
|        | 24  | 182 -2.00 -1.75 -1.17 -0.55 -0.27     | 80    | -2.00 -1.75 -1.17 -0.53 -0.23     | 102   | -2.01 -1.75 -1.16 -0.57 -0.32     |
| Total  | 1032| Total 460                               |       | Total 572                          |

DFA (detrended fluctuation analysis to quantify the degree of self-similarity (fractuality) of the RR signal.

\( \alpha_1 \) and \( \alpha_2 \) (the slope of short-and long-term fluctuations, respectively).

Higuchi and Katz algorithms and \( H \) (Hurst exponent) measure the self-similarity of the RR signal.

\( \beta \) 1/f slope index (calculated on the PSD plotted on a log-log scale from \( 10^{-4} \) to \( 10^{-2} \) Hz).
Table 7. HRV indices by a Chaos and DC or AC analysis (all 5-min segments).

| Months | n   | Smoothed centiles for Skewness (All) | Smoothed centiles for Skewness (Girls) | Smoothed centiles for Skewness (Boys) |
|--------|-----|-------------------------------------|----------------------------------------|---------------------------------------|
|        |     | 3rd | 10th | 50th | 90th | 97th | 3rd | 10th | 50th | 90th | 97th | 3rd | 10th | 50th | 90th | 97th |
| 0      | 260 | -0.292 | -0.116 | 0.389 | 1.194 | 1.732 | 0   | 117 | -0.280 | -0.106 | 0.396 | 1.202 | 1.748 | 0   | 143 | -0.300 | -0.123 | 0.383 | 1.187 | 1.726 |
| 6      | 205 | -0.179 | -0.015 | 0.472 | 1.289 | 1.862 | 6   | 95  | -0.181 | -0.020 | 0.449 | 1.204 | 1.712 | 6   | 110 | -0.174 | -0.008 | 0.493 | 1.354 | 1.974 |
| 12     | 198 | -0.151 | 0.025 | 0.530 | 1.339 | 1.890 | 12  | 86  | -0.144 | 0.024 | 0.498 | 1.228 | 1.700 | 12  | 112 | -0.151 | 0.030 | 0.557 | 1.422 | 2.025 |
| 18     | 187 | -0.209 | 0.002 | 0.562 | 1.344 | 1.814 | 18  | 82  | -0.167 | 0.026 | 0.545 | 1.276 | 1.712 | 18  | 105 | -0.233 | -0.010 | 0.577 | 1.389 | 1.881 |
| 24     | 182 | -0.351 | -0.082 | 0.569 | 1.303 | 1.636 | 24  | 80  | -0.250 | -0.014 | 0.588 | 1.348 | 1.747 | 24  | 102 | -0.419 | -0.127 | 0.552 | 1.258 | 1.543 |
| Total  | 1032 |       |       |       |       |       | Total | 460 |       |       |       |       |       | Total | 572 |       |       |       |       |       |

| Months | n   | Smoothed centiles for Kurtosis (All) | Smoothed centiles for Kurtosis (Girls) | Smoothed centiles for Kurtosis (Boys) |
|--------|-----|-------------------------------------|----------------------------------------|---------------------------------------|
|        |     | 3rd | 10th | 50th | 90th | 97th | 3rd | 10th | 50th | 90th | 97th | 3rd | 10th | 50th | 90th | 97th |
| 0      | 260 | 2.84 | 3.41 | 5.82 | 13.97 | 25.19 | 0   | 117 | 2.66  | 3.27  | 5.94  | 15.63 | 30.27 | 0   | 143 | 3.07  | 3.56  | 5.66  | 13.00 | 23.37 |
| 6      | 205 | 3.31 | 3.97 | 6.45 | 13.20 | 20.95 | 6   | 95  | 3.19  | 3.91  | 6.43  | 12.81 | 20.09 | 6   | 110 | 3.44  | 4.05  | 6.46  | 13.56 | 22.26 |
| 12     | 198 | 3.50 | 4.19 | 6.62 | 12.23 | 17.59 | 12  | 86  | 3.42  | 4.17  | 6.58  | 11.07 | 14.28 | 12  | 112 | 3.58  | 4.24  | 6.68  | 13.06 | 19.97 |
| 18     | 187 | 3.42 | 4.09 | 6.34 | 11.07 | 15.07 | 18  | 82  | 3.34  | 4.08  | 6.39  | 10.39 | 12.77 | 18  | 105 | 3.49  | 4.11  | 6.33  | 11.52 | 16.53 |
| 24     | 182 | 3.06 | 3.65 | 6.23 | 9.72  | 13.42 | 24  | 80  | 2.97  | 3.63  | 5.86  | 10.78 | 15.58 | 24  | 102 | 3.16  | 3.69  | 5.42  | 8.93  | 11.92 |
| Total  | 1032 |       |       |       |       |       | Total | 460 |       |       |       |       |       | Total | 572 |       |       |       |       |       |

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Table 7. (Continued)

| Months | n   | 3rd | 10th | 50th | 90th | 97th |         | 3rd | 10th | 50th | 90th | 97th |         | 3rd | 10th | 50th | 90th | 97th |
|--------|-----|-----|-----|-----|-----|-----|--------|-----|-----|-----|-----|-----|--------|-----|-----|-----|-----|-----|
| Smoothed centiles for Lyapunov exponent (All) | | | | | | | Smoothed centiles for Lyapunov exponent (Girls) | | | | | | | Smoothed centiles for Lyapunov exponent (Boys) | | | | | | |
| 0      | 260 | 0.136 | 0.161 | 0.233 | 0.347 | 0.422 |         | 0   | 0.135 | 0.155 | 0.215 | 0.322 | 0.404 |         | 0   | 0.143 | 0.171 | 0.248 | 0.363 | 0.437 |
| 6      | 205 | 0.130 | 0.152 | 0.217 | 0.323 | 0.395 |         | 6   | 0.125 | 0.147 | 0.207 | 0.302 | 0.365 |         | 6   | 0.110 | 0.137 | 0.199 | 0.225 | 0.336 | 0.417 |
| 12     | 198 | 0.129 | 0.153 | 0.222 | 0.328 | 0.397 |         | 12  | 0.124 | 0.149 | 0.216 | 0.310 | 0.365 |         | 12  | 0.112 | 0.134 | 0.158 | 0.227 | 0.341 | 0.420 |
| 18     | 187 | 0.132 | 0.164 | 0.249 | 0.364 | 0.429 |         | 18  | 0.130 | 0.161 | 0.242 | 0.346 | 0.403 |         | 18  | 0.105 | 0.134 | 0.168 | 0.256 | 0.375 | 0.446 |
| 24     | 182 | 0.139 | 0.185 | 0.298 | 0.428 | 0.490 |         | 24  | 0.143 | 0.183 | 0.284 | 0.412 | 0.479 |         | 24  | 0.102 | 0.136 | 0.188 | 0.310 | 0.440 | 0.496 |
| Total  | 1032|     |     |     |     |     |         | Total|     |     |     |     |     |         | Total|     |     |     |     |     |     |
| Smoothed centiles for Acceleration Capacity (AC) (All) | | | | | | | Smoothed centiles for Acceleration Capacity (AC) (Girls) | | | | | | | Smoothed centiles for Acceleration Capacity (AC) (Boys) | | | | | | |
| 0      | 260 | -5.93 | -5.10 | -3.38 | -1.94 | -1.45 |         | 0   | -5.89 | -4.98 | -3.18 | -1.79 | -1.36 |         | 0   | -5.90 | -5.16 | -3.57 | -2.10 | -1.56 |
| 6      | 205 | -7.18 | -6.28 | -4.35 | -2.55 | -1.86 |         | 6   | -7.17 | -6.22 | -4.22 | -2.44 | -1.79 |         | 6   | -7.13 | -6.30 | -4.47 | -2.65 | -1.91 |
| 12     | 198 | -8.43 | -7.42 | -5.19 | -3.03 | -2.17 |         | 12  | -8.43 | -7.39 | -5.11 | -2.97 | -2.16 |         | 12  | -8.38 | -7.43 | -5.28 | -3.08 | -2.15 |
| 18     | 187 | -9.69 | -8.52 | -5.92 | -3.39 | -2.39 |         | 18  | -9.70 | -8.50 | -5.87 | -3.41 | -2.47 |         | 18  | -9.65 | -8.53 | -5.99 | -3.39 | -2.29 |
| 24     | 182 | -10.97 | -9.58 | -6.54 | -3.64 | -2.50 |         | 24  | -10.96 | -9.53 | -6.48 | -3.73 | -2.72 |         | 24  | -10.94 | -9.61 | -6.61 | -3.58 | -2.32 |
| Total  | 1032|     |     |     |     |     |         | Total|     |     |     |     |     |         | Total|     |     |     |     |     |     |

(continued on next page)
Table 7. Continued

| Smoothed centiles for Deceleration Capacity (DC) (All) | Smoothed centiles for Deceleration Capacity (DC) (Girls) | Smoothed centiles for Deceleration Capacity (DC) (Boys) |
|-----------------------------------------------------|--------------------------------------------------------|--------------------------------------------------------|
| Months | n | 3rd | 10th | 50th | 90th | 97th | Months | n | 3rd | 10th | 50th | 90th | 97th | Months | n | 3rd | 10th | 50th | 90th | 97th |
|--------|---|-----|-----|-----|-----|-----|--------|---|-----|-----|-----|-----|-----|--------|---|-----|-----|-----|-----|-----|
| 0      | 260 | 1.70 | 2.30 | 3.73 | 5.31 | 6.04 | 0      | 117 | 1.49 | 2.09 | 3.50 | 5.08 | 5.82 | 0      | 143 | 1.49 | 2.01 | 3.50 | 5.06 | 5.79 |
| 6      | 205 | 2.13 | 2.83 | 4.52 | 6.41 | 7.29 | 6      | 95  | 2.33 | 2.89 | 4.33 | 6.17 | 7.18 | 6      | 110 | 2.05 | 2.86 | 4.68 | 6.47 | 7.20 |
| 12     | 198 | 2.45 | 3.04 | 4.73 | 6.62 | 7.52 | 12     | 86  | 2.77 | 3.34 | 5.01 | 7.01 | 8.01 | 12     | 112 | 2.53 | 3.31 | 5.18 | 6.95 | 7.85 |
| 18     | 187 | 2.95 | 3.54 | 5.23 | 7.12 | 8.12 | 18     | 82  | 3.27 | 3.84 | 5.51 | 7.51 | 8.51 | 18     | 105 | 3.84 | 4.61 | 6.58 | 7.58 | 8.58 |
| 24     | 182 | 3.56 | 4.15 | 5.85 | 7.74 | 8.74 | 24     | 80  | 3.96 | 4.63 | 6.60 | 8.60 | 9.60 | 24     | 102 | 4.53 | 5.30 | 7.27 | 8.27 | 9.27 |
| Total  | 102  | 102  | 102  | 102  | 102  | 102  | Total  | 460 | 460 | 460 | 460 | 460 | 460 | Total  | 572 | 572 | 572 | 572 | 572 | 572 |

Skewness, Kurtosis and Lyapunov exponent used in nonlinear analysis of physiological signals for detecting chaos. DC (deceleration capacity calculated by the difference between the mean of the 2 beats following deceleration and the mean of the 2 beats before deceleration). AC (acceleration capacity calculated by detecting all sequences that decrease).
Table 8. Entropy analysis (all 5-min segments).

| Months | n   | 3rd  | 10th | 50th | 90th | 97th |
|--------|-----|------|------|------|------|------|
| 0      | 260 | 0.72 | 0.78 | 0.94 | 1.13 | 1.23 |
| 6      | 205 | 0.90 | 0.95 | 1.09 | 1.23 | 1.30 |
| 12     | 198 | 1.00 | 1.06 | 1.17 | 1.29 | 1.34 |
| 18     | 187 | 1.04 | 1.09 | 1.21 | 1.32 | 1.36 |
| 24     | 182 | 1.00 | 1.05 | 1.18 | 1.31 | 1.36 |
| Total  | 1032|      |      |      |      |      |

| Smoothed centiles for AppEn (approximate entropy) (Girls) |
|---------------|-----|------|------|------|------|------|
| 0             | 117 | 0.70 | 0.77 | 0.94 | 1.11 | 1.18 |
| 6             | 95  | 0.89 | 0.95 | 1.08 | 1.21 | 1.27 |
| 12            | 86  | 1.00 | 1.05 | 1.16 | 1.28 | 1.33 |
| 18            | 82  | 1.04 | 1.09 | 1.19 | 1.31 | 1.36 |
| 24            | 80  | 1.01 | 1.05 | 1.16 | 1.30 | 1.36 |
| Total         | 460 |      |      |      |      |      |

| Smoothed centiles for AppEn (approximate entropy) (Boys) |
|---------------|-----|------|------|------|------|------|
| 0             | 143 | 0.73 | 0.79 | 0.95 | 1.14 | 1.25 |
| 6             | 110 | 0.91 | 0.96 | 1.10 | 1.24 | 1.31 |
| 12            | 112 | 1.01 | 1.06 | 1.19 | 1.30 | 1.35 |
| 18            | 105 | 1.04 | 1.09 | 1.22 | 1.33 | 1.37 |
| 24            | 102 | 0.99 | 1.06 | 1.19 | 1.31 | 1.36 |
| Total         | 572 |      |      |      |      |      |

| Smoothed centiles for SampEn (Sample entropy) (All) |
|---------------|-----|------|------|------|------|------|
| 0             | 117 | 0.51 | 0.56 | 0.71 | 0.89 | 0.99 |
| 6             | 95  | 0.75 | 0.81 | 0.96 | 1.15 | 1.25 |
| 12            | 86  | 0.89 | 0.95 | 1.10 | 1.30 | 1.41 |
| 18            | 82  | 0.95 | 1.00 | 1.14 | 1.35 | 1.48 |
| 24            | 80  | 0.92 | 0.96 | 1.08 | 1.30 | 1.46 |
| Total         | 460 |      |      |      |      |      |

| Smoothed centiles for SampEn (Sample entropy) (Girls) |
|---------------|-----|------|------|------|------|------|
| 0             | 143 | 0.56 | 0.56 | 0.73 | 0.96 | 1.09 |
| 6             | 110 | 0.74 | 0.81 | 0.98 | 1.19 | 1.30 |
| 12            | 112 | 0.88 | 0.95 | 1.12 | 1.33 | 1.43 |
| 18            | 105 | 0.93 | 1.00 | 1.17 | 1.38 | 1.48 |
| 24            | 102 | 0.88 | 0.95 | 1.12 | 1.33 | 1.45 |
| Total         | 572 |      |      |      |      |      |

| Smoothed centiles for SampEn (Sample entropy) (Boys) |
|---------------|-----|------|------|------|------|------|
| 0             | 143 | 0.73 | 0.79 | 0.96 | 1.14 | 1.25 |
| 6             | 110 | 0.91 | 0.96 | 1.10 | 1.24 | 1.31 |
| 12            | 112 | 1.01 | 1.06 | 1.19 | 1.30 | 1.35 |
| 18            | 105 | 1.04 | 1.09 | 1.22 | 1.33 | 1.37 |
| 24            | 102 | 0.99 | 1.06 | 1.19 | 1.31 | 1.36 |
| Total         | 572 |      |      |      |      |      |

(continued on next page)
| Months | n   | 3rd  | 10th | 50th  | 90th | 97th | 3rd  | 10th | 50th  | 90th | 97th | 3rd  | 10th | 50th  | 90th | 97th |
|--------|-----|------|------|-------|------|------|------|------|-------|------|------|------|------|-------|------|------|
| 0      | 260 | 2.32 | 2.45 | 2.76  | 3.07 | 3.20 | 0.53 | 0.57 | 0.66  | 0.77 | 0.83 | 0.52 | 0.56 | 0.66  | 0.76 | 0.80 |
| 6      | 205 | 2.49 | 2.61 | 2.89  | 3.17 | 3.28 | 0.61 | 0.65 | 0.73  | 0.83 | 0.87 | 0.61 | 0.64 | 0.73  | 0.82 | 0.86 |
| 12     | 198 | 2.59 | 2.71 | 2.97  | 3.24 | 3.36 | 0.66 | 0.70 | 0.78  | 0.87 | 0.91 | 0.66 | 0.69 | 0.77  | 0.86 | 0.90 |
| 18     | 187 | 2.62 | 2.74 | 3.01  | 3.30 | 3.42 | 0.67 | 0.71 | 0.80  | 0.89 | 0.93 | 0.67 | 0.71 | 0.79  | 0.88 | 0.92 |
| 24     | 182 | 2.57 | 2.70 | 3.00  | 3.32 | 3.47 | 0.65 | 0.69 | 0.79  | 0.89 | 0.93 | 0.65 | 0.70 | 0.78  | 0.88 | 0.93 |
| Total  | 1032|      |      |       |      |      |      |      |       |      |      |      |      |       |      |      |

**Smoothed centiles for SE (Shanon entropy) (All)**

**Smoothed centiles for SE (Shanon entropy) (Girls)**

**Smoothed centiles for SE (Shanon entropy) (Boys)**

*(continued on next page)*
Table 8. (Continued)

| Months | n   | Smoothed centiles for CCE (Corrected conditional entropy) (All) | Smoothed centiles for CCE (Corrected conditional entropy) (Girls) | Smoothed centiles for CCE (Corrected conditional entropy) (Boys) |
|--------|-----|----------------------------------------------------------------|------------------------------------------------------------------|-----------------------------------------------------------------|
|        | 3rd | 10th | 50th | 90th | 97th | 3rd | 10th | 50th | 90th | 97th | 3rd | 10th | 50th | 90th | 97th |
| 0      | 260 | 0.56 | 0.60 | 0.71 | 0.84 | 0.90 | 0    | 117  | 0.55 | 0.60 | 0.71 | 0.82 | 0.88 | 0    | 143  | 0.57 |
| 6      | 205 | 0.64 | 0.68 | 0.78 | 0.89 | 0.94 | 6    | 95   | 0.64 | 0.68 | 0.77 | 0.88 | 0.93 | 6    | 110  | 0.65 |
| 12     | 198 | 0.69 | 0.73 | 0.82 | 0.92 | 0.98 | 12   | 86   | 0.69 | 0.72 | 0.81 | 0.92 | 0.97 | 12   | 112  | 0.69 |
| 18     | 187 | 0.70 | 0.74 | 0.84 | 0.94 | 0.99 | 18   | 82   | 0.70 | 0.74 | 0.83 | 0.94 | 0.99 | 18   | 105  | 0.70 |
| 24     | 182 | 0.67 | 0.72 | 0.83 | 0.95 | 1.00 | 24   | 80   | 0.68 | 0.72 | 0.82 | 0.94 | 1.00 | 24   | 102  | 0.66 |
| Total  | 1032|      |      |      |      |      | Total | 460  |      |      |      |      |      | Total | 572  |      |

| Months | n   | Smoothed centiles for NCCE (Normalized CCE) (All) | Smoothed centiles for NCCE (Normalized CCE) (Girls) | Smoothed centiles for NCCE (Normalized CCE) (Boys) |
|--------|-----|-------------------------------------------------|--------------------------------------------------|--------------------------------------------------|
|        | 3rd | 10th | 50th | 90th | 97th | 3rd | 10th | 50th | 90th | 97th | 3rd | 10th | 50th | 90th | 97th |
| 0      | 260 | 0.43 | 0.46 | 0.53 | 0.62 | 0.67 | 0    | 117  | 0.42 | 0.45 | 0.52 | 0.61 | 0.64 | 0    | 143  | 0.44 |
| 6      | 205 | 0.50 | 0.52 | 0.59 | 0.67 | 0.70 | 6    | 95   | 0.49 | 0.52 | 0.58 | 0.65 | 0.69 | 6    | 110  | 0.50 |
| 12     | 198 | 0.53 | 0.56 | 0.63 | 0.70 | 0.72 | 12   | 86   | 0.53 | 0.56 | 0.62 | 0.69 | 0.71 | 12   | 112  | 0.53 |
| 18     | 187 | 0.54 | 0.58 | 0.64 | 0.71 | 0.73 | 18   | 82   | 0.55 | 0.57 | 0.63 | 0.70 | 0.73 | 18   | 105  | 0.54 |
| 24     | 182 | 0.53 | 0.56 | 0.63 | 0.70 | 0.73 | 24   | 80   | 0.54 | 0.56 | 0.63 | 0.70 | 0.73 | 24   | 102  | 0.53 |
| Total  | 1032|      |      |      |      |      | Total | 460  |      |      |      |      |      | Total | 572  |      |

(continued on next page)
| Months | n   | Smoothed centiles for rho (Entropy) (All) | Smoothed centiles for rho (Entropy) (Girls) | Smoothed centiles for rho (Entropy) (Boys) |
|--------|-----|-----------------------------------------|-------------------------------------------|------------------------------------------|
|        |     | 3 rd  | 10 th | 50 th | 90 th | 97 th | 3 rd | 10 th | 50 th | 90 th | 97 th | 3 rd | 10 th | 50 th | 90 th | 97 th |
| 0      | 260 | 0.34  | 0.38  | 0.47  | 0.54  | 0.57  | 0    | 117  | 0.35  | 0.39  | 0.48  | 0.55  | 0.58  | 0    | 143  | 0.33  | 0.38  | 0.47  |
| 6      | 205 | 0.30  | 0.33  | 0.41  | 0.48  | 0.51  | 6    | 95   | 0.31  | 0.34  | 0.42  | 0.48  | 0.51  | 6    | 110  | 0.29  | 0.33  | 0.40  |
| 12     | 198 | 0.28  | 0.30  | 0.37  | 0.44  | 0.47  | 12   | 86   | 0.28  | 0.31  | 0.38  | 0.44  | 0.47  | 12   | 112  | 0.27  | 0.30  | 0.36  |
| 18     | 187 | 0.27  | 0.29  | 0.35  | 0.43  | 0.46  | 18   | 82   | 0.27  | 0.30  | 0.37  | 0.43  | 0.45  | 18   | 105  | 0.26  | 0.29  | 0.35  |
| 24     | 182 | 0.27  | 0.30  | 0.36  | 0.44  | 0.47  | 24   | 80   | 0.28  | 0.31  | 0.37  | 0.44  | 0.47  | 24   | 102  | 0.27  | 0.30  | 0.36  |
| Total  | 1032| 0.95  | 0.97  | 1.00  | 1.03  | 1.03  | 0    | 117  | 0.95  | 0.97  | 1.00  | 1.02  | 1.03  | 0    | 143  | 0.95  | 0.97  | 1.01  |

| Months | n   | Smoothed centiles for LZC (Lempel-Ziv Complexity) (All) | Smoothed centiles for LZC (Lempel-Ziv Complexity) (Girls) | Smoothed centiles for LZC (Lempel-Ziv Complexity) (Boys) |
|--------|-----|--------------------------------------------------------|----------------------------------------------------------|--------------------------------------------------------|
|        |     | 3 rd  | 10 th | 50 th | 90 th | 97 th | 3 rd | 10 th | 50 th | 90 th | 97 th | 3 rd | 10 th | 50 th | 90 th | 97 th |
| 0      | 260 | 0.95  | 0.97  | 1.00  | 1.03  | 1.03  | 0    | 117  | 0.95  | 0.97  | 1.00  | 1.02  | 1.03  | 0    | 143  | 0.95  | 0.97  | 1.01  |
| 6      | 205 | 0.90  | 0.92  | 0.96  | 1.00  | 1.01  | 6    | 95   | 0.89  | 0.91  | 0.96  | 1.00  | 1.01  | 6    | 110  | 0.90  | 0.92  | 0.96  |
| 12     | 198 | 0.84  | 0.87  | 0.93  | 0.97  | 0.99  | 12   | 86   | 0.84  | 0.87  | 0.93  | 0.97  | 0.99  | 12   | 112  | 0.85  | 0.88  | 0.93  |
| 18     | 187 | 0.80  | 0.84  | 0.91  | 0.96  | 0.97  | 18   | 82   | 0.78  | 0.83  | 0.91  | 0.96  | 0.97  | 18   | 105  | 0.81  | 0.85  | 0.91  |
| 24     | 182 | 0.76  | 0.81  | 0.89  | 0.96  | 0.97  | 24   | 80   | 0.74  | 0.79  | 0.89  | 0.95  | 0.96  | 24   | 102  | 0.78  | 0.82  | 0.90  |
| Total  | 1032| 0.76  | 0.81  | 0.89  | 0.96  | 0.97  | 0    | 117  | 0.74  | 0.79  | 0.89  | 0.95  | 0.96  | 0    | 143  | 0.78  | 0.82  | 0.90  |

Entropy is a measure of the regularity and complexity of pattern of different length.
Fig. 1. Fitted 3rd, 10th, 90th, and 97th smoothed centil curves (full lines) for mean heart rate according to age, for all children (upper panel) and separately for girls (middle panel) and boys (lower panel).
Chaos and DC/AC (Table 7), and entropy analysis (Table 8). Each index is presented for 5 different periods of time, 0, 6, 12, 18 and 24 months and with smoothed values in the 3rd, 10th, 50th, 90th and 97th percentiles. Data are also presented for the full cohort (left) and individualized by sex to account for gender variability (center and right).

More frequently used data are illustrated for HR, SDNN, LF and HF (Figs. 1, 2, 3, and 4).

3.1. HRV temporal and frequential approaches

In the temporal-domain (Table 1), the resting heart rate decreases regularly by 5 bpm on average every 6 months of age and is moderately lower, although not significantly, for boys than for girls, regardless of age.

In parallel, pNN20 increases regularly by 5% on average every 6 months of age, whereas pNN50 only increases by 1–2% over these same periods. These values are physiologically higher, although not significantly, for boys than for girls, regardless of age.

For the geometrical indices (Table 2), both the HRV triangular index and the TINN grow regularly from birth to age 2 regardless of gender.

In the frequency domain (Table 3), Ptot increases moderately in the first year while progressed exponentially afterwards, with a very large inter-individual variability. From birth, boys have a higher Ptot, which also progresses faster than girls (4081–5178 ms²/Hz vs 3341–4122 ms²/Hz). VLF values are very stable whatever the period considered and the gender. LF, which represents 12–13% of the entire frequency spectrum at this age, presents with a slow and steady increase of these values (435–648 ms²/Hz) between 0 and 2 years, with no noticeable peak and no major influence of gender, even if basal values are moderately higher for boys. The kinetics of maturation of the HF values is remarkable and very different from the LF values as, while it begins at low values, only 6–7% of the total spectrum, their progression is much faster and the values exceed the LF values at 2 years (14–15%), regardless of the genre. As a result, the LF/HF ratio decreases between birth and 2 years for both boys and girls (see Fig. 5).

3.2. HRV complexity by nonlinear approach

Poincaré plot SD1 increases regularly between 0 and 24 months (Table 4), being slightly higher in boys regardless the period. While SD1/SD2 ratio seems to increase with age, SD2 representing long-term variability has always values 4 to 6 times larger than SD1, as evidenced by the clear predominance of SD2nu and increases regularly with age.
Fig. 2. Fitted 3rd, 10th, 90th, and 97th smoothed centil curves for SDNN according to age, for all children (upper panel) and separately for girls (middle panel) and boys (lower panel).
Fig. 3. Fitted 3rd, 10th, 90th, and 97th smoothed centile curves for LF according to age, for all children (upper panel) and separately for girls (middle panel) and boys (lower panel).
Fig. 4. Fitted 3rd, 10th, 90th, and 97th smoothed centil curves for HF according to age, for all children (upper panel) and separately for girls (middle panel) and boys (lower panel).
Fig. 5. Fitted 3rd, 10th, 90th, and 97th smoothed centil curves for LF/HF ratio according to age, for all children (upper panel) and separately for girls (middle panel) and boys (lower panel).
Considering the Empirical Mode Decomposition (Table 5), we can observe that both low (pLF1, pLF2) and high (pHF1, and pHF2) frequencies increase from birth to age 2, as the ratio between low and high frequency indices (IMAI1 and IMAI2) decrease.

Indices of fractality (Table 6) decrease regularly with age, whatever the gender: the 2 exponents $\alpha_1$ and $\alpha_2$ of the detrended fluctuation analysis (DFA) used to quantify the degree of self-similarity of RR fluctuation [$\alpha_1$ for short-term fluctuation decreasing from 1.20 to 1, and $\alpha_2$ for long-term fluctuations decreasing from 1.05 to 0.9], H DFA decreasing 1.04 to 0.96 and Hurst exponent from 0.37 to 0.20.

Conversely, Higuchi and Katz algorithms proposed to determine the fractal dimension of heart rate variability signal increases respectively from 1.6 to 1.8 and from 1.4 to 1.6 over the same period.

The power-law slope ($\beta$) influenced mainly by autonomic input to the heart quantifies the complexity of the RR interval. While the smaller the slope, the greater the loss of complexity, this index is however difficult to interpret in that population.

The “chaotic” exponent (Skewness, kurtosis and largest Lyapunov exponent) in our population increase respectively (0.39–0.57–5.82 to 6.23–0.23 to 0.3) meaning higher variations of the RR with age (Table 7).

If we consider the heart Deceleration and Acceleration Capacities indices used to estimate the vagal and sympathetic capacities, it is interesting to note that these two indices also progress with age in the same proportion, with a usual aspect in mirror.

What is remarkable in our population is the fact that all these entropy markers regularly increase by 20% on average between birth and 2 years (Table 8).

Another way to measure the rate of patterns recurrences in RR series is the Lempel-Ziv complexity. This last index decreases by 10% with age in our population.

4. Discussion

The main objective of the Autonomic Baby Evaluation cohort (AuBE) was to determine the physiological autonomic maturation profile from birth to 2 years in a healthy population of term neonates. This the first time such longitudinal survey was conducted in a large newborns healthy population.

In summary, during these two years of maturation, there is a large gain in global autonomic maturation giving progressively a new equilibrium privileging the parasympathetic activity over the sympathetic activity. This underlines a gain in fine-tuning autonomic modulations.
Thus the balance of the autonomic nervous system (ANS), essential for homeostasis and cardiorespiratory control, depends closely not only on states of wakefulness (awakening, quiet sleep, active sleep) [40, 41, 42, 43, 44] but also on postnatal age.

This study has provided a comprehensive analysis of HRV indices which may serve as reference data, are of interest in assessing global autonomic maturation. These markers have also gain some interest in pathological conditions as growth restricted and prematurity status [45], sepsis [23], inflammation [25], as well as in particular physiological settings as skin-to-skin [46], and stress or pain [47, 48].

The difference in values we measured from birth according to gender is notable. All HRV values in any field of analysis are slightly higher in boys. We do not have a rational explanation. This does not explain the higher risk of SIDS in premature male infants [49]. Conversely, it has been shown that girls presented significantly higher values than boys for SDNN and absolute high frequency (HF; p < 0.05) in the supine position, the most significant indices of the vagal activity [50]. We do not know when this occurs during childhood. For adults, females showed significantly lower mean RR interval and SDNN power spectral density but a significantly greater vagal activity [51].

There may be some limitations to our study. The first is related to the technical design of the study forcing us to analyze the data over 24 hours thus mixing waking and sleeping periods and day and night periods, which could change the basal values of HRV. In fact, we have dissociated sleep-wake data from polysomnography at birth and at 6 months of life, but it was no longer possible to obtain them on such a cohort, on an ambulatory basis and at an age when child is not compliant for physiological explorations. Nevertheless, the accumulation of 24-hour global data has the advantage of allowing measurements on a much larger number of RRs (more than 150,000 per day per child) and thus of attenuating the impact of brain activity stages on the results.

Mothers’ sleep and mood could interfere with the child’s sleep quality [52], while this was not taken into account in this results which thus includes such variations. There could be also unmeasured confounding factors as the impact of nicotine exposure during pregnancy which may target different organs of the fetus, particularly the lung and the central nervous system [53, 54], including learning disorders, hyperactivity and attentional deficits or moderate intellectual disabilities [55, 56, 57, 58, 59, 60]. Another limitation lies in the large standard deviations of normal values. For some indices, the data can vary from 1 to 20. It is therefore necessary to integrate this when used for a personalized follow-up. Each individual probably has his own autonomic resources predefined by his gender, and genetics as well as environmental factors. A human being his thus also its own witness able to improve his autonomic balance.
Using these tools may allow a complete non-invasive neurophysiological approach of the cardiorespiratory self-regulation. The innovative the longitudinal follow-up of healthy child allowed establishing normative data useful for the evaluation of an autonomic risk at a critical age of faintness and unexpected sudden death occurrence. Persistent dysautonomia in the neonatal period, as a biomarker of neuronal dysfunction, may warrant early and prolonged neurodevelopmental follow-up and perhaps corrective actions.

5. Conclusion

The physiological autonomic maturation profile from birth to 2 years in a healthy population of term neonates results in a fine autonomic maturation underlying increasingly a new equilibrium and benefitting the parasympathetic activity over the sympathetic activity.

Declarations

Author contribution statement

Hugues Patural: Conceived and designed the experiments; Wrote the paper.

Vincent Pichot: Analyzed and interpreted the data.

Sophie Flori, Antoine Giraud: Performed the experiments.

Patricia Franco, Patrick Pladys, Alain Beuchée: Contributed reagents, materials, analysis tools or data.

Jean-Claude Barthelemy, Frédéric Roche: Conceived and designed the experiments.

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Competing interest statement

The authors declare no conflict of interest.

Additional information

The clinical trial described in this paper was registered at ClinicalTrials.gov under the registration number NCT01583335.
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