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Heart rate asymmetry as a new marker for neonatal stress

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ABSTRACT

The autocorrelation of the heart rate variability is presented by various methods and models, but Poincaré plots remain valuable analytic tools. Heart rate asymmetry analysis (HRA) is used for the quantification of unevenly distributed points above and below the line of identity. The aim of this work is to implement HRA analysis in newborns, to use it as a marker for acute stress. Forty healthy term newborn infants were included in the study. The protocol included two baseline phases, and two stress phases (heel stimulation and heel stick blood sampling), during which the heart rate was measured. Additionally, to the standard HRA indices, a new index (SKG) related to the first differences of the RR interval time series is introduced. A ROC curve analysis was applied to test the diagnostic properties of the asymmetry indices. With AUC significantly different from 0.5, the results show that HRA indices may be used as clinical markers. With higher AUC values (0.906 and 0.785), accuracy (87.5% and 81.3%) and sensitivity (87.5% and 81.3%), the SKG index outperformed the traditional indices. This novel application of HRA shows potential benefit in stress assessment of newborns, and in nonverbal patients in general.

1. Introduction

The autocorrelation of the heart rate variability is presented by various methods and models, varying from linear to nonlinear, including spectral analysis, entropy measures, Poincaré plots and others [1–6]. As new methods arise, the Poincaré plot remains a valuable tool for heart rate variability analysis, which increasingly gets new indices. The Poincaré plot is a two-dimensional phase space scatter plot which contains the correlation between consecutive RR intervals, allowing to visualize hidden patterns in a time series. The successive RR_{j+1} intervals are plotted as a function of the previous RRj interval. This results with a cloud of points distributed along the line of identity (RR_{j+1}=RRj). The two standard descriptors are a result of ellipse fitting, where SD1 is determined by the standard deviations perpendicular to, and SD2 parallel to the line of identity [7]. It has been shown that SD1 represents short-term, and SD2 long-term variability [8].

Being a useful visual tool capable of summarizing the whole RR interval signal, it has been shown to be useful in autonomic nervous system research (ANS), arrhythmia detection and as a prognostic tool about mortality [9,10].

By careful inspection of a typical sinus rhythm Poincaré plot, concerning the line of identity, asymmetry can be observed. Heart rate asymmetry analysis is used for the quantification of unevenly distributed points above and below the line of identity in a Poincaré plot. Various indices have been discovered: [11–13].

Porta's index (PI) is based on the percentage of accelerations (ΔRR^-), with respect to the overall amount of RR points which do not lie on the main diagonal [12].

$$PI = \frac{N(\Delta RR^-)}{N(\Delta RR \neq 0)}$$

Ehler's index (EI) is calculated based on the skewness of the distribution of ΔRR. It does not have a predefined range, but if EI > 0,

Abbreviations: RR, RR interval; SD1, short axis of the Poincaré plot; SD2, long axis of the Poincaré plot; PI, Porta's index; EI, Ehlers index; SKG, the Sapina-Kramaric-Garcin index; ANS, the autonomic nervous system.

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the distribution is skewed to the right, and if EI < 0, the distribution is skewed to the left, respectively [13].

$$EI = \frac{\sum_{i=1}^{N(\Delta RR)} \Delta RR(i)^3}{\left(\sum_{i=1}^{N(\Delta RR)} \Delta RR(i)^2\right)^{3/2}}$$

Guzik's index (GI) represents the mean squared distance of the points from the y = x line above the identity-line divided by the mean squared distance of the points above plus below the identity-line [10,14].

$$GI = \frac{\sum_{i=1}^{N(\Delta RR^+)} \Delta (RR^+)^2(i)}{\sum_{i=1}^{N(\Delta RR)} \Delta RR^2(i)}$$

Although much effort is given to the understanding of neonatal pain, there is a significant lack of studies of Poincaré plot dynamics in newborn pain in contrast to spectral domain analyses [15,16]. Recently published studies discovered changes in the standard Poincaré plot descriptors, which gives new insight into the underlying occurrences, not usually monitored during painful procedures [5].

As for the newborn infant, during the first 72 h, it will experience at least one painful procedure. Usually, a heel prick blood sampling, due to screening purposes. The more immature the newborn is, the more frequent and invasive the procedures become [17,18]. Only in the last few decades, the capability of feeling pain and its potentially harmful long-term effects on the human infants have been given the right amount of attention [19].

There is a universal lack of a satisfying scale or marker for pain assessment and evaluating of stress in nonverbal patients. Due to its noninvasiveness and easiness to obtain, the heart rate asymmetry may be used as a novel marker for pain and stress.

As a response to pain, hunger or any distress, neonates react (in the physiological sense) by increasing the heart and respiration rate. We hypothesize that heart rate asymmetry indices can be useful in the evaluation of stressed newborns.

2. Subjects and methods

By using simple random sampling, a total of 40 (21 females and 19 males, birth weight 3542.05 ± 339.09 g, with an estimated gestational age of 39.1 ± 1.17 weeks) subjects were obtained. Only healthy full-term infants, without prenatal and perinatal risk factors, 72 h of chronological age, ready for discharge from the maternity ward, were included in this study.

A high-resolution (1024 Hz) heart rate monitor (Firstbeat Bodyguard 2 (Firstbeat Technologies Ltd, Jyvaskyla, Finland) was used to obtain RR interval data. The raw data were visually inspected, corrected for artifacts, and further used for analysis. Before conducting the data analysis, third-degree polynomial detrending was used to eliminate existing trends in the obtained signal.

2.1. Study protocol

To eliminate external artifacts due to irritability, excessive movement and crying, infants were fed before the procedure and placed in supine position. The environment was insured to be without excessive noise pollution.

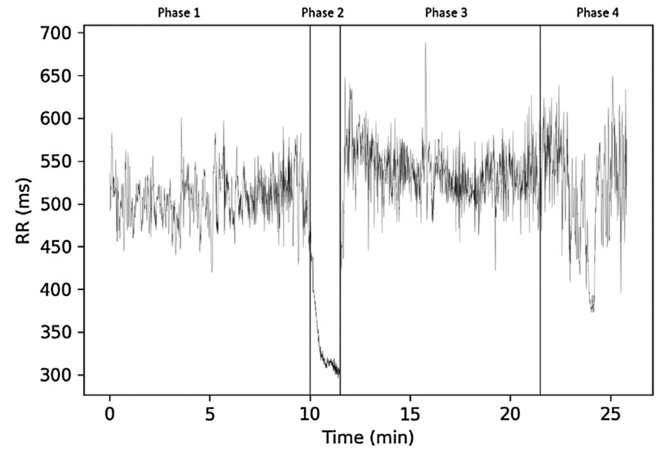

Fig. 1. A sample recording across the phases.

The protocol included three parts: a) dummy stimulation phase, b) the heel stick intervention phase, c) the intervention phase.

Only parts a) and b) were used in this work, and consisted of two subphases. Phase a) starts with the first baseline phase lasting 10 min (phase 1), followed by simulating the heel stick procedure (phase 2), by intermittently pressing the heel to improve the local circulation, in a way the standard heel stick blood drawing is performed. A fixed duration was chosen to be 90 s, which is the average time to perform the actual procedure. Phase b) starts at the ending of the second subphase, and lasts for 10 min, as the second baseline (phase 3), followed by the actual heel stick blood sampling (phase 4), which ends at the beginning of phase c) (Fig. 1).

2.2. Ethical statement

All procedures performed in this research were in accordance with the ethical standards of the institutional and research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consents were obtained from all research participant's parents or guardians.

2.3. Asymmetry assessment

After the data cleaning process, indices of asymmetry have been calculated as stated before. A surrogate analysis was conducted to check the validity of the method. To distinguish HRA from randomness using the physiological data, all calculations were repeated after random shuffling, and further statistically compared with the original dataset.

2.4. The SKG index

The SKG index is calculated taking into account the sum of differences of consecutive RR intervals.

We first create a new phase space with $x = RR_i$, and $y = \Delta RR = RR_{i+1} - RR_i$.

The y = 0 line is the new reference line, an equivalent to the line of identity in a standard Poincaré plot.

C_{up} – decelerations, the sum of every $\Delta RR > 0$

$$C_{up} = \sum_{i=1}^{N(\Delta RR^+)} \Delta RR_i^+ \qquad (1)$$