Differences of Heart Rate Variability during Sevoflurane Anesthesia in Children by Age

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ABSTRACT

Background: The child’s central nervous system develops with aging, and heart rate variability (HRV), which is controlled by the brain, differs from that of adults. We investigated changes in HRV during sevoflurane anesthesia in children.

Methods: One 138 children aged from 2 - 12 years without major underlying problems were enrolled. During maintenance with 2 - 2.5 vol% sevoflurane anesthesia, electrocardiographic data were obtained and power spectral analysis, approximate entropy (ApEn) or Hurst exponent were analyzed and compared in three groups (age 2 - 5 years, 6 - 9 and 10 - 12 years of age).

Results: The RR interval increased with aging, but low-frequency powers did not. High-frequency power was greater in the oldest children \( P < 0.05 \), while ApEn and Hurst exponents were lower \( P < 0.05 \).

Conclusion: Change in HRV is one of the characteristics of development in children.

Keywords: Children; Heart Rate Variability; Sevoflurane

1. Introduction

Heart rate variability (HRV) is a physiologic change of heart rate or electrocardiographic R-R interval regulated by the autonomic nervous system [1], and is therefore under direct or indirect control of the brain [2,3]. HRV changes with aging, [4] anesthesia [5-7] and exercise [8, 9]. Indices of various nonlinear dynamic analyses such as approximate entropy (ApEn) or Hurst exponent (H) for HRV are useful for diagnosis or predictors of prognosis in some clinical situations [10-13]. The human brain develops continuously from birth to adolescence, and thus HRV should also change with aging. HRV becomes less random with increasing age in normal subjects in normal condition [14]. Special condition such as under general anesthesia, it may reflect the brainstem component [15]. Sevoflurane is commonly used in children and, during induction of anesthesia may depress parasympathetic activity more than halothane [6]. We hypothesized that in children, HRV might vary with age during sevoflurane anesthesia.

2. Methods

This prospective observational study of children requiring orthopedic surgery was done after institutional review board approval. Informed consent was obtained from parents or guardians. We recruited 138 children aged from 2 to 12 years (group T: 2 - 5, group P: 6 - 8, group S: 9 - 12). They were classified as American Society of Anesthesiologists physical status I. Exclusion criteria were neurologic abnormalities, history of epilepsy, concurrent antiepileptic drug, developmental delay, or heart problems (Table 1).

<table>
<thead>
<tr>
<th>Table 1. Demographic characteristics.</th>
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<tbody>
<tr>
<td>Group T (N = 45, 2 - 5 years old)</td>
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<tr>
<td>Gender (M/F)</td>
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<tr>
<td>Age (years)</td>
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<tr>
<td>Body Weight (kg)</td>
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<tr>
<td>Height (cm)</td>
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<tr>
<td>Duration of Surgery (min)</td>
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<tr>
<td>Duration of Anesthesia (min)</td>
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Patients were fasted according to guidelines (at least 8 hours for solid food, 2 hours for clear fluid) and were appropriately hydrated. They arrived in the operating room without any premedication. Blood pressure was measured and the electrocardiogram (ECG), SpO₂ (Solar 8000, GE, Milwaukee, WI) was attached. Another lead II ECG (MP100A-CE, Biopac Systems, Santa Barbara) was monitored for data collection. After preoxygenation, anesthesia was induced with pentothal 6 mg/kg and atropine 0.02 mg/kg (maximum dose: 0.5 mg) intravenously. Patients were ventilated with 8 vol% of sevoflurane in 100% of oxygen via mask after loss of consciousness. After full anesthesia and paralysis with 0.6 mg/kg of rocuronium, a laryngeal mask airway (LMA) of appropriate size was inserted or intubation was performed. Anesthesia was maintained with 2.5% sevoflurane in 35% oxygen in air with total flow of 3 l/min. Mechanical ventilation was at a tidal volume of 7 - 10 ml/kg and respiratory rate was adjusted by age (group T: 18/min, group P: 15/min, group S: 12/min) to give an end-tidal carbon dioxide tension of 35 - 40 mmHg. Lactated Ringer’s solution was administered at 8 ml/kg/h. When the inspiratory and end-tidal sevoflurane concentration had been maintained at 2.5 vol% for more than 10 minutes before surgery, we collected the ECG data for 15 minutes and stored it on a personal computer. At the same time, blood pressure and heart rate were checked and recorded at 5 minute intervals. The LMA or endotracheal tube was removed after surgery and the patients were transferred to the postanesthetic care unit (PACU) when fully awake and opening their eyes on verbal command.

2.1. Data Processing

All ECG data were reviewed by visual inspection. Segments with signal loss, significant noise or with atrial or ventricular extrasystoles were discarded. R peak was determined by the algorithm of Pan and Tompkins [16]. RR intervals (RRI) were measured and tested for the presence of outliers (HR < 30 or >200 beats/min), which were removed. All RRI data were linearly interpolated at 1000 Hz to construct a real-time series of RRIs, and then re-sampled at 2 Hz. The 1800 points (15 min of data) were used for calculating HRV indices. All data processing, including visual inspection, spectral analysis, and Hurst analysis, was conducted using Matlab 7.0.1 (Mathwork Inc., MA, USA).

2.2. Power Spectral Analysis

The RR interval data were divided into 512 data point sections (4.26 min of data). After being detrended, these sections were fast Fourier transformed [17] and averaged to form a power spectral density function. Power spectral analysis of HRV is regarded as the index of autonomic nervous systemic regulation for sinus rhythm. [18,19] We calculated low-frequency (LFP) and high-frequency power (HFP) by integrating the power spectral density curve in the 0.04 - 0.15 and 0.15 - 0.4 Hz ranges. LFP is regarded as representative of activity of sympathetic and parasympathetic activity and HFP of the parasympathetic.

2.3. Approximate Entropy (ApEn) [20,21]

The methodologic details for computing approximate entropy, ApEn (m, r, N), have been published elsewhere [20,21] and will be described briefly. ApEn (m, r, N) is approximately equal to the negative average natural logarithm of the conditional probability that 2 sequences are similar for m points remain similar, that is, within a tolerance, r, at the next point. Thus, a low value of ApEn reflects a high degree of regularity.

2.4. Hurst Analysis Using Structure Function [22,23]

The rth RRI was denoted as RRI(t) and we calculated the fluctuations in the difference as the structure function of RRI

$$\Delta y(t) = RRI(t + \tau) - RRI(t)$$

for different time increments, τ s. Δy(t) is the magnitude of the change in RRI after t s. In order to perform Hurst analysis, we estimated the average of these local variations, which depended on the scaled time increments as shown in the following equation:

$$\langle \Delta y(t) \rangle - \tau^{H}$$

where $\langle \rangle$ indicates the time average and − indicates the presence of the power law behavior of $\langle \Delta y(t) \rangle$ against $\tau$

$$H = \lim_{\tau \to 0} \frac{\langle \Delta y(t) \rangle}{\tau}$$

In order to quantify the scaling behavior of $\langle \Delta y(t) \rangle$, this value was plotted for $\log_{2}(\tau) = 2, \cdots, 10$. The scaling region was then obtained and the slopes of $\langle \Delta y(t) \rangle$ were calculated against $\tau$ at the scaling region, thus yielding the Hurst exponent, H. Since H is the slope of $\langle \Delta y(t) \rangle$ against $\tau$ in the log-log scale and $H > 0$, this value measures the rate of increase in the mean RRI difference over time $\tau$. In other words, the exponent measures how the mean RRI changes as time advances.

2.5. Statistics

Repeated-measures ANOVA was performed to compare the differences in HRV indices between groups; P-values < 0.05 were considered significant. All values shown are means (SD). All statistical analyses were conducted us-
3. Results

Three patients (two in group T, one in group P) were excluded from analysis because of loss of data. RR intervals during sevoflurane anesthesia increased by 100 msec per year of age. These changes corresponded with decreases in heart rate (Figure 1) \( (P < 0.001) \). There were no significant changes in LFP. HFP in group S increased more than in the other groups (Table 2, \( P < 0.05 \)).

ApEn and the Hurst exponent in group T and P were similar each other and those in group S decreased (Table 2, \( P < 0.05 \)).

4. Discussion

HFP was greater in children over ten years of age than in younger ones during sevoflurane anesthesia, while ApEn and the Hurst exponent were less. The decrease in heart rate with aging has been frequently observed, and in this study RR intervals increased about 100 msec with aging (Table 2).

Signal linearity implies linear changes with time, and therefore it should be possible to predict the results of changes if we know the variation of signal changes by time.

On the other hand, it is hard to predict when the signal is nonlinear. The decrease in complexity of HRV in adults is well known [4].

In a previous study [24], power spectral analysis was performed on electrocardiographic data gathered from children and young adults aged 5 - 24 years in the supine and erect positions. LFP and HFP decreased in both positions with aging; in children of 10 - 12 years it decreased profoundly more than in those of 5 - 7 years.

In our study, HFP was maintained or increased in children of 10 - 12 years, which may imply maintenance of parasympathetic activity during sevoflurane anesthesia.

In the other study, girls (aged (9 ± 0.25) years) showed higher resting heart rate but HRV were not different between genders [25]. Our study also showed no difference between genders.

As the respiratory rate was fixed during collection of

![Figure 1](image.jpg)

**Figure 1.** This shows RR intervals during sevoflurane anesthesia from 3 patients in each group.

<table>
<thead>
<tr>
<th></th>
<th>Group T (N = 45, 2 - 5 years old)</th>
<th>Group P (N = 48, 6 - 9 years old)</th>
<th>Group S (N = 45, 10 - 12 years old)</th>
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<tbody>
<tr>
<td>RRI (msec)</td>
<td>498.7 ± 67.4</td>
<td>588.2 ± 98.9*</td>
<td>682.6 ± 69.6*</td>
</tr>
<tr>
<td>LFP (msec²)</td>
<td>35.9 ± 19.6</td>
<td>22.0 ± 23.2</td>
<td>36.1 ± 25.3</td>
</tr>
<tr>
<td>HFP (msec²)</td>
<td>21.8 ± 13.5</td>
<td>29.8 ± 15.9</td>
<td>111.2 ± 34.5*</td>
</tr>
<tr>
<td>LF/HF ratio</td>
<td>0.8 ± 0.95</td>
<td>1.84 ± 1.98</td>
<td>0.62 ± 0.96*</td>
</tr>
<tr>
<td>ApEn</td>
<td>4.1 ± 1.6</td>
<td>4.2 ± 1.7</td>
<td>3.4 ± 1.3*</td>
</tr>
<tr>
<td>Hurst exponent</td>
<td>0.48 ± 0.17</td>
<td>0.46 ± 0.21</td>
<td>0.34 ± 0.15*</td>
</tr>
</tbody>
</table>

RRI: R-R interval in ECG, LFP: low-frequency power (0.04 - 0.15 Hz), HFP: high-frequency power (0.15 - 0.4 Hz), ApEn: approximate entropy. *P < 0.05 compared with group T. **P < 0.05 compared with group P.
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5. Acknowledgements

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REFERENCES


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