Infants with univentricular heart have reduced heart rate and blood pressure responses to side motion and altered responses to head-up tilt

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Submitted 9 March 2004; accepted in final form 20 August 2004

Kirjavainen, Turkka, Suvi Viskari, Olli Pitkänen, and Eero Jokinen. Infants with univentricular heart have reduced heart rate and blood pressure responses to side motion and altered responses to head-up tilt. J Appl Physiol 98: 518–525, 2005; doi:10.1152/japplphysiol.00248.2004.—Cardiovascular control was studied in infants with univentricular heart (UVH). Side motion tests and 45–45° head-up tilt tests were performed in 11 control and 9 UVH infants at the age of 13 ± 3.2 wk. In addition, heart rate (HR) reactions to spontaneous arousals and HR variability during slow-wave sleep (SWS) were determined. All UVH infants had been hypoxic for several weeks, and during the sleep study the mean arterial oxyhemoglobin saturation was 82 ± 5%. Tests were done at night during SWS, confirmed by polysomnographic recording. Continuous beat-to-beat blood pressure (BP) was measured. In the side-motion tests, control infants consistently showed a transient increase in HR and BP. This response was markedly reduced in all of the UVH infants ($P < 0.0001$). In tilt tests, the UVH infants showed normal BP responses, but, although a sustained 2.0% decrease in HR was observed in the controls, the UVH infants presented with a sustained 2.6% mean HR increase ($P = 0.005$). The UVH infants also showed attenuated HR acceleration during spontaneous arousals ($P = 0.01$), but HR variability did not differ significantly from the controls. In conclusion, UVH infants with chronic hypoxia exhibit defective vestibulosympathetic pathways, as expressed by an absence of acute HR and BP reactivity to side motion. HR reactions to postural challenge and spontaneous arousal are also altered. Autonomic function abnormalities in these infants are suggested to be secondary to hypoxia.

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Systemic blood pressure (BP) control is a complex process, with a multitude of input signals improving the accuracy of the regulatory system. Long-term absence of one type of signal does not fundamentally alter BP control, but acute control becomes more inaccurate (24, 32, 37, 43). Cardiovascular reactions to postural challenge are known to be mediated by baroreflexes, peripheral venous reflexes, and vestibular sympathetic pathways, as expressed by an absence of acute HR and BP reactivity to side motion. HR reactions to postural challenge and spontaneous arousal are also altered. Autonomic function abnormalities in these infants are suggested to be secondary to hypoxia.

Clinical characteristics of the study population. Nine UVH infants and 11 age-matched control infants were included in the study. Demographic data from UVH infants are presented in Table 1. These infants were studied at the age of 12 ± 1.8 wk, the night before cardiac catheterization was performed as part of preparations for stage two surgery treatment of UVH. All but one of the UVH infants, pulmonary circulation was dependent on a Blalock-Taussig shunt. UVH infants were in a stable condition at the time of the study, with a normal (8 of 9) or mildly depressed (first studied infant, Table 1) contractility of the systemic pumping chamber in echocardiography and catheterization. One infant had weight below the normal limits, and two had mild general muscle hypotonia, but the others followed normal growth and were considered neurologically normal. All but one infant had aspirin and diuretic medications.

Control infants were recruited by asking all parents of newborn babies at the Helsinki University Hospital. If willing to participate, the parents contacted the researchers when the infant was 2 mo of age. The controls were healthy with an eventful neonatal history and were examined at the mean age of 14 ± 3.6 wk. The growth of control infants was within the normal limits (17). Both UVH and control infants were born full-term, and only one UVH infant was small-for-

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Subject No. | Sex (M/F) | Diagnosis | Surgery Performed | Age at Surgery, days | Study Age, wk | Weight, g | Height, cm | Mean SpO₂, % | BP, mmHg | Medication
--- | --- | --- | --- | --- | --- | --- | --- | --- | --- | ---
1 | F | DILV, TGA, HAA, CoA, CoA banding | Norwood I | 10 | 10 | 4,880 (−0.7 SD) | 57 (−0.6 SD) | 85.7 | 79/33 (50) | ASA, diuretics
2 | M | HLHS, LSVC, HAA, CoA, dextrocardia | Norwood I | 6 | 11 | 4,750 (−1.9 SD) | 59 (−0.4 SD) | 78.0 | 78/43 (63) | ASA, diuretics, digoxin
3 | M | DILV, TGA, HAA, CoA, VSD | Norwood I | 14 | 16 | 5,780 (−1.4 SD) | 64.5 (+0.7 SD) | 78.5 | 95/54 (66) | ASA, diuretics
4 | F | TGA, RV hypoplasia, VSD, HAA, CoA, dextrocardia, LSVC | Pulmonary artery banding, CoA correction | 2 | 13 | 5,590 (−0.1 SD) | 57 (−1.3 SD) | 76.5 | 106/58 (80) | none
5 | F | HLHS | Norwood I | 7 | 11 | 5,150 (−0.3 SD) | 58.5 (+0.1 SD) | 77.2 | 74/48 (61) | ASA, diuretics, enalapril
6 | F | AVSD, PA, MA, common atrium, dextrocardia, right isomerism | BT-shunt | 2 | 11 | 4,750 (−1.3 SD) | 58.0 (0.0 SD) | 85.5 | 76/40 (63) | ASA, diuretics, sotalol
7 | M | HLHS | Norwood I | 7 | 11 | 4,960 (−1.5 SD) | 57.8 (−0.9 SD) | 82.9 | 90/41 (64) | ASA, diuretics
8 | M | HLHS | Norwood I | 14 | 12 | 4,910 (−1.8 SD) | 57.1 (−1.5 SD) | 81.3 | 89/43 (62) | ASA, diuretics
9 | F | DORV, LV-hypoplasia, AVSD, PS, TAPVD, PDA, right isomerism, common atrium, asplenia | BT-shunt, correction of TAPVD | 21 | 12 | 3,950 (−3.4 SD) | 55.8 (−1.8 SD) | 90.6 | 104/65 (84) | ASA, diuretics

Weight and height are presented in respect to normal values (17), and the deviation from the mean of the normal population is given in parentheses as standard deviation score. Blood pressure (BP) values are presented as systolic/diastolic (mean). ASA, aspirin 15–25 mg × 1; BT-shunt, Blalock-Taussig shunt; CoA, coarctation of the aorta; DILV, double inlet left ventricle; diuretics, furosemide with or without spironolactone; DORV, double outlet right ventricle; HAA, hypoplastic aortic arch; HLHS, hypoplastic left heart syndrome; LV, left ventricle; LSVC, left superior vena cava; MA, mitral atresia; PA, pulmonary atresia; RV, right ventricle; UVH, univentricular heart; F, female; M, male; TAPVD, total anomalous pulmonary venous drainage; TGA, transposition of the great arteries; VSD, ventricular septal defect; AVSD, atrioventricular septal defect; PS, pulmonary stenosis; PDA, patent ductus arteriosus.

The age difference between the UVH and control subjects was not significant ($P = 0.24$).

Written parental consent was obtained for all subjects. The study protocol was approved by the Ethics Review Committee of the Hospital for Children and Adolescents of the Helsinki University Hospital, Helsinki, Finland.

Study design. Resting BP levels (Table 1) were measured in UVH infants from the right forearm before the sleep study using a Criticon Dinamap 8100T. All tests were performed between 2200 and 0500. Three to nine side motion tests and head-up tilts were performed during polygraphically confirmed SWS, both in the supine and prone positions. Polygraphic sleep recordings consisted of continuous monitoring of two electroencephalograms (C3A2, O2A1), one or two electrooculograms, chin and diaphragm surface electromyograms, ECG, nasal airflow (RSS100-HR, Hans Rudolph), abdominal respiratory movements, arterial oxyhemoglobin saturation ($SpO₂$), end-tidal carbon dioxide (Capnomac Ultima ULT-SVI, Datex-Ohmeda), and BP (Finapres, Ohmeda). BP was measured with an enlarged extra-large-sized cuff, which was placed around the infant’s wrist (7, 14, 15). Regular hand rest periods were introduced during the BP measurements. Finapres servo adjustment was removed 1 min before each test and put on not earlier than 45 s after the test. Data were collected by use of the Amlab system (Amlab Technology), converted into European Data Format, and further analyzed by use of Somnologica sleep polygraph software (MedCare), together with special purpose software. ECG and electromyogram recordings were collected by using 16-bit amplitude resolution with 200-Hz data sampling, $SpO₂$ at 1 Hz, and the remaining signals at 100-Hz sampling rate.

Infants were laid on a mat placed on top of the usual crib mattress. The mat was made of canvas and had rigid sides. In the side motion test, the infant was first raised horizontally with the mat. After a steady period of over 30 s, a back-and-forth side motion with a radius of 0.5 m was performed within 3–5 s. In the tilt test, the infant was tilted manually from the horizontal position to a 45° head-up position in 2–3 s. The tilt position was then maintained for 45 s, after which the infant was returned to the horizontal position. The BP measuring cuff was held at the heart level throughout the test. After each test, the infant was kept still for at least 1 min before another test. Two researchers continuously observed the infant for any signs of arousal, such as facial, finger, or hand movements.

Data and statistical analysis. Sleep staging was performed by using the criteria defined by Guilleminault and Souquet (12). Data were analyzed with the accuracy of the original sampling rate with visual examination of ECG R-wave and BP values. Care was taken to exclude tests with any evidence of arousal, including movements of the face, body, or extremities, or a clear change in EEG frequency beyond the time of the movement artifact caused by the test.

For side motion and tilt tests, data were analyzed in 5-s time intervals. The statistical mean value analysis included four time intervals. The statistical mean value analysis included four time intervals.
20–35 s from tilt onset, and a posttilt control period 25–40 s after the infant was returned to the horizontal position. HRV and BP variability during test periods were estimated by using standard deviation as the measure. Statistical analysis was performed in the same way as with the mean value data but with simplified time intervals (side motion tests: pretest, 0–15 s, posttest; tilt tests: pretest, 0–10 s, 20–25 s, posttest).

To further characterize autonomic control of HR, HR reactions to spontaneous arousal and HRV were analyzed. One arousal from SWS both in the supine and prone condition with a clear increase in chin EMG activity and body movement lasting for more than 15 s was selected. The slope of change in HR (beats·min⁻¹·min⁻¹) during the first 10 s from onset of arousal was calculated. HRV analysis was made from 2-min segments of SWS without interruptions and regular breathing by use of Somnologica software. The HRV analyzer used oversampling techniques to enhance up to 10 times the original 200-Hz sampling rate. HRV spectra were integrated over three frequency bands: 0.04–0.15 (low-frequency variability, LFV), 0.15–1.0 Hz (high-frequency variability, HFV), and total power 0.003–1.0 Hz (total power, TP). The HRV indexes were logarithmically transformed (log₁₀) to normalize the distribution.

For statistical analysis of side motion and tilt tests, two-way, repeated-measures ANOVA (repeated-measures general linear model) was calculated by use of SPSS 11.0 software (SPSS). This was followed by Tukey’s (group effects) or Sidak’s (within-subject effects) pairwise multiple-comparison tests when the ANOVA showed a significant difference. For HR acceleration and HRV, Levene’s test and paired t-tests were used to compare group differences and differences between the supine and prone position, respectively. The results are presented as means ± SD.

RESULTS

The mean polygraphic recording time was 3.8 ± 1.8 h for controls and 2.7 ± 1.8 h for the UVH infants. Sleep stage distribution in controls was 31.5% light non-rapid eye movement sleep, 41.5% SWS, and 27.0% rapid eye movement sleep. In UVH infants, the distribution was 23.9, 47.5, and 27.7%, respectively. The difference in sleep stage distribution was not significant (P = 0.29). One UVH child had mixed apneas during rapid eye movement sleep with an obstructive apnea/hypopnea index of 1.3/h, but the others had normal breathing during sleep. None of the infants presented with SpO₂ desaturation events in relation to apneas. UVH infants had all been clearly hypoxic for weeks before the study. During the study, their mean SpO₂ was 81.8 ± 4.8%, range 76.5–90.6%. In the control infants, the mean SpO₂ was 98.2 ± 1.2%, range 95.2–99.0% (P < 0.00001). There were no significant changes in SpO₂ during side motion and tilt tests. An example recording of a side motion test in a control and an UVH infant and side motion and tilt test numeric data are presented in the data supplement (http://jap.physiology.org/cgi/data/00248.2004/DC1/1).

Side motion test. In control infants, the side motion test was performed successfully for all infants in the supine and for 8 of 11 (73%) in the prone position. The number of arousals in side motion and tilt tests are presented in Table 2. The controls had a consistent biphasic response in the side motion test with an initial increase in HR, systolic BP (SBP) and diastolic BP (DBP) (P < 0.0005), immediately followed by a transient decrease in SBP (P = 0.03) below the baseline level (Fig. 1). The prone position did not have a significant effect on the responses.

In UVH infants, the side motion test without arousal was performed successfully for all infants in the supine position and for 6 of 9 (67%) in the prone position. There was no difference in arousal frequency compared with the controls (Table 2). The UVH infants had no significant HR, SBP, or DBP response to the side motion (Fig. 1). The differences during the first 5 s of side motion from the normal controls were substantial (P < 0.00005). Some responses to side motion occurred in the prone position (ANOVA P < 0.05) (Fig. 1). HR and BP reactions did not differ significantly in the prone or supine positions.

Control infants showed higher HRV (standard deviation) during the pretest period in the supine position than did UVH infants (P = 0.01), but this difference was not observed in SBP or DBP and was not present in the prone condition. In the supine position, control infants showed higher HRV (P < 0.05), SBP (P = 0.03), and DBP (P = 0.01) variability during side motion than did UVH infants.

Head-up tilting. In the control infants, successful 45° head-up tilt with no signs of arousal was obtained for all subjects in the supine and in 8 of 11 (73%) in the prone position. Control infants showed a biphasic response to head-up tilting in the supine position (Fig. 2). HR (P = 0.006) increased during the first 5 s without significant changes in SBP or in DBP. This initial phase was followed by a sustained decrease in SBP (P = 0.006), whereas HR and DBP did not differ from the pretilt period. After tilt, SBP (P = 0.0004) and DBP (P = 0.007) remained lower than pretilt levels, but BP gradually returned toward the pretilt levels. HR, SBP, and DBP responses were similar in the prone position (Fig. 2).

In UVH infants, tilting without arousal was obtained in all nine infants in the supine position but in only four of nine (44%) infants in the prone position. UVH infants were aroused more often in the prone than supine position (Table 2). In the supine position, tilting resulted in arousal at the same frequency as in the controls, but in the prone position the UVH infants were aroused more often than controls. At tilt onset, initial changes in HR, SBP, and DBP were not significant. The initial phase was followed by a sustained decrease in SBP (P = 0.006), whereas HR and DBP did not differ from the pretilt period. Compared with controls, BP responses were similar, but HR levels 20–35 s from tilt onset were significantly higher than in the controls (P = 0.005) (Fig. 2). HR and BP responses in UVH infants were similar in the supine and prone positions.

There were no significant differences in HRV or SBP and DBP variability (standard deviation) during pretilt periods between control and UVH infants, but during tilt UVH infants showed less HRV both in the supine and prone positions (P < 0.05).

One control infant once in supine, another twice in prone, and four UVH infants once each in supine positions presented with different responses to tilt (SBP and DBP, ANOVA P < 0.005) (Fig. 3). The different response was characterized by a

Table 2. Number of arousals in side motion and tilt tests

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<tr>
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<th>Supine</th>
<th>Prone</th>
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<tr>
<td></td>
<td>Control</td>
<td>UVH</td>
</tr>
<tr>
<td>Side motion</td>
<td>40 ± 28</td>
<td>39 ± 22</td>
</tr>
<tr>
<td>Tilt</td>
<td>57 ± 27</td>
<td>49 ± 21</td>
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Values are means ± SD, in %. *P < 0.01, supine vs. prone; †P < 0.05, control vs. UVH.
sustained increase in SBP and DBP, with a similar HR response to that observed during other tilt tests.

HR responses to arousal. HR responses to arousals from SWS were successfully analyzed in all 11 controls and in 8 of 9 (89%) UVH infants in the supine position and in 9 of 11 (82%) controls and 4 of 9 (44%) UVH infants in the prone position. The changes in HR are presented in Fig. 4. In the supine position, HR accelerated at 129 ± 45 beats·min⁻¹·min⁻¹ in the controls and at 73 ± 44 beats·min⁻¹·min⁻¹ (P = 0.01) in the UVH infants. In the prone position, the difference between the groups was not significant, with HR changes of 127 ± 39 beats·min⁻¹·min⁻¹ in the control and 100 ± 48 beats·min⁻¹·min⁻¹ in the UVH infants.

HRV. HRV in SWS was successfully determined in 9 of 11 (82%) controls in the supine and 8 of 11 (73%) in the prone position (Table 3). In the UVH infants, analysis was successfully performed in all nine infants in the supine and in six of nine (67%) in the prone position. There were no significant differences between the control and UVH infants in LFV, HFV, TP, or LFV-to-HFV ratio in the supine position. However, in the prone position, UVH infants had lower LFV (P = 0.004) and TP (P = 0.02) than the control infants. Control infants did not have significant differences in HRV between supine and prone positions, but UVH infants had reduced LF (P = 0.02) and TP (0.02) variability, increased HFV (P = 0.04), and reduced LFV-to-HFV ratio (P = 0.02) in the prone position.

DISCUSSION

Main result. We have shown that, compared with healthy controls, infants with UVH and chronic hypoxia have altered acute HR and BP responses to postural changes during sleep. UVH infants showed markedly reduced HR and BP responses to side motion. These findings indicate defective vestibulocardiovascular reflex pathways in the condition. During head-up tilting, UVH infants presented with a normal BP response but significantly higher sustained HR level than the controls. The observed defective autonomic functions in UVH infants are suggested to be central in origin and secondary to exposure to hypoxia.

Side motion. The control infants showed consistent reversible and biphasic HR and BP response to the side motion, whereas UVH infants showed no HR or BP response. These findings indicate specific impairments in vestibulocardiovascular reflex pathway function in these UVH infants.

The vestibular nucleus and cerebellum, especially the rostral portion of the fastigial nucleus, are important regulators of HR and BP responses in tilting, hypovolemia, and endotoxin shock (6, 28). Injury of either of these brain structures results in similar defects in HR and BP control (6). Although vestibulocardiovascular reflex pathways in the condition. During head-up tilting, UVH infants presented with a normal BP response but significantly higher sustained HR level than the controls. The observed defective autonomic functions in UVH infants are suggested to be central in origin and secondary to exposure to hypoxia.
be possible that the observed dysfunction of sympathoreflexes in UVH infants could result from defective neuronal circuitry involved in fastigial function.

The action of the vestibular nuclei on cardiovascular control is not exclusively due to labyrinthine signals (44), and circuits involving vestibular nuclei are likely to elicit compensatory cardiovascular responses during movements even after removal of labyrinthine signals (43). Removal of vestibular inputs also affects the basal BP level of test animals in an unpredictable way, whereas resting BP may be either increased or decreased (19). Hence, baseline BP control appears to become more inaccurate after vestibular injury. Interestingly, an essential cardiovascular adaptation in response to tilt occurs within 1 wk after vestibular damage in awake cats (19, 43). This adaptation is suggested to depend on alertness and visual information. However, changes in resting HR and BP levels do not show adaptation (19, 43). We studied infants 9 to 14 wk after palliative surgery, and, therefore, there should have been enough time for adaptive mechanisms to evolve. However, the infants were studied during sleep, and hence they did not have visual input.

**Tilt tests.** Control infants had a biphasic response to head-up tilting with an initial increase in HR followed by a sustained decrease in SBP. This is somewhat different from what has been previously described (14, 15). However, in this study, tilt tests with signs of an arousal, including subcortical arousals, were excluded.

The initial HR and BP responses within the first 5 s in the UVH infants were similar to the controls. However, UVH infants had higher HR levels thereafter throughout the tilt. A suggested explanation for the observed sustained HR increase is the impaired ability to increase systemic vascular resistance.

Acute hypoxia induces HR and BP responses (27, 38), but hypoxia alone is unlikely to affect the baroreflex, unless it disrupts baroreflex pathways (3, 5). During orthostatic challenge, the decrease in BP may lead to stimulation of carotid chemoreceptors. However, this effect should not be important for longer than the first 5–10 s (2, 25). Despite the chronic hypoxia in the UVH infants, HR and BP responses are not likely to be modified by hypoxia alone because 1) one of the UVH infants was not clearly hypoxic during testing but had similar HR and BP responses to other UVH infants during both side motion and tilt tests, 2) UVH infants did not become more hypoxic during tilting, and 3) HR and BP responses at tilt onsets were normal. Hence, altered cardiovascular control in the UVH infants observed during head-up tilting indicates either defective baroreflex or vestibular sympathoreflex pathways.

It seems evident that several compensatory circuitries may be involved in HR and BP regulation during head-up tilting. Hence, unambiguous interpretation of the tilt results is difficult. Given the clearly defective vestibulosympathetic reflex observed in the UVH infants in the side motion tests, we suggest that the change in the tilt response may be due to altered function of the vestibular sympathoreflex circuitry. The study was not designed to examine baroreflex activity alone, but we made an effort to determine the baroreflex activity noninvasively using the method described by Drouin and associates (8). Unfortunately, no such episodes that would fulfill the analysis criteria with simultaneous increase in SBP and de-
crease in HR or vice versa were detected in any of the infants during SWS.

Four UVH infants in supine, one control infant in supine, and one control infant in prone presented once or twice with an increase rather than decrease in BP (Fig. 3). A similar response has been observed in some ALTE infants (10, 15) and in the minority of awake, conscious cats after bilateral vestibular lesions (19). In light of the animal studies, it is suggested that the variability of BP responses in UVH infants is due to inaccuracy in BP control secondary to vestibular dysfunction.

HR response to arousal and HRV. The assessment of HR responses to arousal and determination of HRV were not the original target of this study. They were determined to estimate whether the UVH infants had intact peripheral heart innervation. HR increased more slowly in the UVH infants than in control infants in response to spontaneous arousals from SWS. However, the difference from controls was only about twofold, with significant overlap. In subjects with denervated hearts, a 10-fold decrease in the rapidity of HR acceleration has been described, together with increased resting HR level (1). The resting HR levels in the UVH infants were normal when measured before all of the test episodes. The UVH infants also had similar HFV as the control infants, both in supine and prone positions, suggesting normal modulation of heart vagal activity (29). On the basis of their resting HR, HR acceleration during arousal, and HRV, we assume that the UVH infants did not have significant damage to heart innervation, but the observed differences suggest an altered central cardiovascular control.

Limitations of the study. The original objective was to investigate the effects of hypoxia on cardiovascular control in infants. We included UVH infants with heart malformations that caused chronic systemic hypoxia. All but one of these children had a Blalock-Taussig shunt-dependent pulmonary circulation. We cannot be sure what had caused the altered HR and BP responses in the UVH infants. The diversity of cardiac anomalies in the infants argues against the idea that the anomaly alone with abnormal circulation would be the cause. On the other hand, aortic baroreceptors may have been severed by the surgical Norwood type I operation and by correction of aortic coarctation. However, we were unable to link HR and BP responses to the extent of surgery (Table 1). Finally, major hypoxia during the surgery could have caused brain damage. All UVH infants, however, had similar responses to both side motion and tilt tests, and these responses were independent of the need for perfusion during anesthesia. It seems that the most obvious common factor in these children remains chronic hypoxia.

Table 3. Heart rate variability (log₁₀ values, arbitrary units) in slow-wave sleep

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<th>Supine</th>
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<tr>
<td></td>
<td>Control</td>
<td>UVH</td>
</tr>
<tr>
<td>LFV</td>
<td>2.9±0.2</td>
<td>2.6±0.5</td>
</tr>
<tr>
<td>HFV</td>
<td>2.7±0.3</td>
<td>2.4±0.6</td>
</tr>
<tr>
<td>TP</td>
<td>3.3±0.2</td>
<td>3.1±0.4</td>
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<tr>
<td>LFV/HFV</td>
<td>1.1±0.1</td>
<td>1.1±0.2</td>
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Values are means ± SD. LFV, low-frequency heart rate variability; HFV, high-frequency heart rate variability; TP, total power of heart rate variability; *P < 0.05 supine vs. prone; ‡P < 0.05, †P < 0.01, control vs. UVH.
One of the novelties of this study was inclusion of continuous measurement of BP using Finapres with a modified finger cuff wrapped around the infant’s wrist. Finapres is known to be unreliable in the measurement of absolute BP values but is ideal for continuous monitoring of BP to detect deviations from the basal level (8, 14, 26). This was evident also in this study, in which marked differences in the baseline BP values were observed. Accordingly, we measured percent changes in BP compared with pretest values. Any movement of the measuring cuff markedly affects signal detection. For this reason, BP detection analysis was performed under visual control, and all suspicious BP waves and values were excluded from the analysis. Because of these considerations, we feel that the results should reflect true physiological changes that occurred during the tests.

Tilt and side motion tests were performed manually. Manual motion control is likely to add some variability to the testing. Tilt rise time was ~3 s. In adults, with tilt times between 2 and 5 s, the speed of the maneuver has little or no influence on the orthostatic response (35). More prominent differences in the responses may have been achieved by using a more vertical end-tilt position. In animal studies, a defective vestibulosym pathetic reflex causes a much more prominent difference in cardiovascular reactions after 60° than 30° tilts (6, 19). However, we used a 45° angle, because a more vertical end-tilt position would have resulted in more difficulty in performing tilts without arousing the infant. For vestibular stimulation, we selected a linear side motion, which was easy to perform. The direction of vestibular stimulation has little effect on the HR and BP responses in adults (42).

It became evident during the early stages of the study that even a modest subcortical arousal, indicated, for example, only by a small finger movement, significantly affected HR and BP responses during the tests. Thus care was taken to exclude tests with any observable signs of arousal. Test maneuvers caused artifacts to polysomnographic signals, hampering the detection of short arousals. Hence, a special effort was made of close visual observation of the infants.

Clinical implications. The results of this study suggest that the vestibular sympathorheal pathway may be injured by chronic hypoxia. Impairment of this reflex may predispose infants to life-threatening events (6, 28) in situations such as during prolonged mixed apneas (21, 23) or prone positions with unfavorable face-straight-down positions (40). Sudden unexplained interim deaths are not uncommon in hypoxic UVH infants with a Blalock-Taussig shunt. Such deaths, for which the reason remains unexplained, occur in about 3% of infants with a Blalock-Taussig shunt, and they account for one-third of all interim deaths in shunt infants (9).

In conclusion, we have shown that infants with congenital heart disease and chronic hypoxia have defective vestibular sympathoreflex, as expressed by a marked reduction of HR and BP responses to a linear side motion. HR responses to head-up tilt and to spontaneous arousals from SWS were also altered in these infants. We suggest that cardiovascular control is altered in UVH infants secondary to hypoxia.

REFERENCES


GRANTS

This study has been supported by grant no. TYH3230 from the Helsinki University Hospital.