Cardiovascular responses to three simple, provocative tests of autonomic activity in sleeping infants

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Harrington, C., T. Kirjavainen, A. Teng, and C. E. Sullivan. Cardiovascular responses to three simple, provocative tests of autonomic activity in sleeping infants. J Appl Physiol 91: 561–568, 2001.—Whereas defective cardiovascular autonomic control has been implicated in the sudden infant death syndrome, relatively little is known about the normal development of autonomic control, due to the inability to measure blood pressure in infants noninvasively. We studied 12 normal infants [age: 13 ± 2 (SD) wk] using a noninvasive method of continuous blood pressure recording and examined the cardiovascular responses to 45° head-up tilting, a modified cold face test, and a loud noise. In head-up tilting, in both slow-wave sleep and rapid eye movement sleep, all infants displayed a rapid biphasic heart rate response (mean increase of 16% and mean decrease of 21%) and blood pressure response (mean increase of 16% and mean decrease of 16%), with a return to pretest values within 20 s. Both ice and noise caused a less pronounced biphasic response. In conclusion, at 3 mo, infants show the adult pattern of response to postural challenge. The short latency of the response suggests that neural inputs, apart from baroreceptors, are involved in the initial phase of the response.

Autonomic function; arousal; blood pressure variability

In recent years, there has been growing interest in the role of autonomic function in the sudden infant death syndrome (SIDS) (10–12, 24). Numerous studies have examined the cardiovascular responses to various autonomic challenges in the sleeping infant, but these findings have been restricted mainly to heart rate (HR) and HR variability (HRV) measures (10, 34), and, consequently, there is a paucity of data concerning the infant’s autonomic control of blood pressure (BP). This is primarily due to the fact that, to date, there has not been a method that easily and noninvasively enables the accurate measurement of instantaneous BP responses to a chosen stimulus in infants. The development of Doppler flow and the oscillometric methods (Dynamapp, Critikon) have allowed a limited assessment of BP in the infant, but these methods are confined to single-point-in-time measures and do not provide a continuous beat-to-beat measure of BP and so have added little to our understanding of the precise mechanisms involved.

In adults, instantaneous, noninvasive BP measurement has been available for a number of years using the Finapres device (Ohmeda). It has been widely utilized in the investigation of autonomic function in adults (18, 19, 30) and has proven to be a reliable substitute for intra-arterial measurements (25, 29). The Finapres device measures continuous arterial BP with the use of the volume clamp (vascular unloading) method of Penaz (31, 32) rather than the traditional sphygmomanometry. Recently, Drouin and associates (7, 8) have described the applicability of this method to preterm and term neonates by wrapping the cuff around the neonate’s wrist instead of the finger to assess baroreflex sensitivity.

The purpose of the present study was, first, to establish whether BP could be adequately monitored in the infant noninvasively and, second, to determine the normal HR and BP responses in healthy 3-mo-old infants to several provocative tests of autonomic activity. Passive tilting, ice, and noise were chosen, as they have already been established as tests of autonomic function in the infant (10, 11, 21, 23).

METHODS

Subjects

We studied 12 full-term, healthy, 3-mo-old infants (Table 1). Parents of infants attending the local baby health center were asked to participate. All infants enrolled in the study had a normal clinical examination on the third day of life and before the study. Those with a family history of apparent life-threatening events or SIDS were excluded.

Written parental consent was obtained in all cases. The study protocol was approved by the Sydney Children’s Hospital Ethics Review Committee.

Study Protocol

Polysomnography. All infants were admitted for full overnight polygraphic sleep studies. Polysomnography was performed using the Compumedics S series system (Compumedics, Melbourne, NSW, Australia). The poly-
graphic recordings consisted of continuous monitoring of two electroencephalograms (EEGs; C3-A2 and O2-A1); two electrooculograms; chin, diaphragm, and abdominal muscle surface electromyograms; nasal airflow (transducer); thoracic and abdominal respiratory belts; arterial oxyhemoglobin saturation (Pulse Oximeter, Ohmeda); electrocardiogram (ECG); and BP (Portapres, TNO Biomedical Instrumentation).

The infant was prepared for the sleep study between 1500 and 1600, after which the normal nighttime procedure was adopted. When ready for sleep, the infant was placed supine in the cot, and recording of the study commenced when the infant fell asleep. Five to eight consecutive 45° head-up tilts, five modified cold face tests (mCFTs), and five auditory stimulation tests were performed, in this order, during slow-wave sleep (SWS) and REM sleep. There was at least a 1-min control period between tests.

Cardiovascular measurements. HR was assessed by continuous ECG recording. The ECG data were recorded with the use of a 500-Hz sampling rate. Continuous noninvasive arterial BP measurement was performed using the Portapres device, the portable equivalent of the Finapres device (TNO Biomedical Instrumentation). The technique employed by this device to measure BP is based on the concept that, if an externally applied pressure (via the bladder in the cuff) is equal to the arterial pressure at all times (instantaneously), the arterial walls will be unloaded (“zero transmural pressure”) and the arteries will not change in size. Because the arteries under the cuff are not changing in size, the blood volume, which is only contained in the arteries at these pressures, will not change; therefore, the photoplethysmogram will be constant at some value (31, 32).

The Finapres monitor technique provides an indirect measurement of BP in a finger by using the above concept in reverse. In adults, a plethysmographic cuff is placed around the finger and inflated automatically. The pressure in the cuff is driven to equal the arterial pressure throughout each pressure cycle. This cuff pressure is measured with an electronic pressure transducer, and the resulting signal is displayed as arterial pressure.

By wrapping the cuff around the infant’s wrist instead of the finger, it is possible to measure instantaneous BP in the radial artery. The cuff was placed comfortably around the right wrist once the infant was asleep and inflated for maximum periods of 10 min with rests of 5 min between inflations. Infants appeared to suffer no discomfort either from the placement of the cuff or from the inflation, as no arousal was detected in either circumstance. BP was recorded at the sampling rate of 125 Hz and monitored intermittently from 2200 to 0500 until testing was completed. Servo self-adjustment was disabled 30 s before all testing and during the test so that instantaneous BP readings could be obtained. After the test, the servo self-adjustment was enabled until the next test period. In all tests, a 30-s artifact-free period was analyzed just before the stimulus, and a 30-s period after the stimulus was also recorded. The beginning and ending of the tests were noted with an electrical event marker on the digital recording.

45° Head-up tilt test. Tilting was achieved by placing a mat on top of the usual cot mattress. The mat was made of canvas and had rigid sides and a pouch at its base. The infant was placed supine on the mat and allowed to fall asleep naturally. When the infant was in SWS (as evidenced by low-frequency, high-voltage EEG), the infant’s lower trunk was placed in the pouch. Before the tilt, the infant’s right arm was placed so that the wrist was at the same level as the heart. Throughout the tilt, the infant’s arm was maintained in this position so that at all times the position of the cuff did not vary in relation to the heart. When a steady baseline of both HR and BP was obtained, the mat, with the infant lying on top, was tilted manually from the horizontal position to a 45° angle within 2 s. This position was maintained for between 20 and 60 s. At the end of the tilting period, the mat was gradually lowered back to the cot mattress, and the infant was again horizontal. Head-up tilts were performed six to eight times in both REM and SWS. Both BP and HR were monitored continuously throughout the tilt. After the tilt, the infant was returned to the horizontal position. A minimum of 1 min elapsed before another tilt was performed and only after BP and HR had resumed to pretest values. To minimize the effect of other physiological events affecting the hemodynamic response to the head-up tilt, if the tilt resulted in a transient arousal, sigh, or apnea, these data were excluded from the hemodynamic analysis but were included in the assessment of arousal response. An arousal was defined as a full cortical arousal, as evidenced by the EEG polygraph, which was maintained for >3 s. Subcortical arousals were not noted.

mCFT. The mCFT was performed by placing an ice cube in a thin plastic bag on the infant’s forehead in the distribution of the ophthalmic division of the trigeminal nerve. The ice cube was kept on the forehead for 8 s or until the infant aroused. At the first indication of arousal, the ice cube was removed. Only those tests that did not elicit an arousal or apneic response were included in the hemodynamic analysis. Again, a minimum of 1 min elapsed before the next test was performed and only after BP and HR had resumed to pretest values. The ice cube was placed on the forehead five times in both SWS and REM sleep.

Auditory stimulus testing. Response to an auditory signal was measured by making a loud sudden noise (1-s duration) of 85 dB 1 m from the infant’s left ear. The noise was similar to that of an alarm and was calibrated by using a Bjoel and Koel sound-level meter. The noise was repeated five times in

### Table 1. Changes in heart rate and blood pressure according to sleep state

<table>
<thead>
<tr>
<th>Sleep State</th>
<th>n</th>
<th>HR, beats/min</th>
<th>DBP, mmHg</th>
<th>SBP, mmHg</th>
<th>MAP, mmHg</th>
<th>HRV (CV) %</th>
<th>BPV (CV) %</th>
</tr>
</thead>
<tbody>
<tr>
<td>SWS</td>
<td>12</td>
<td>117 ± 9</td>
<td>58 ± 5</td>
<td>80 ± 7</td>
<td>65 ± 5</td>
<td>3.6 ± 0.7</td>
<td>2.1 ± 0.5</td>
</tr>
<tr>
<td>REM</td>
<td>12</td>
<td>124 ± 12*</td>
<td>66 ± 6*</td>
<td>87 ± 8*</td>
<td>73 ± 6*</td>
<td>5.0 ± 1.6*</td>
<td>4.6 ± 1.5*</td>
</tr>
</tbody>
</table>

Values are means ± SD; n, no. of infants. SWS, slow-wave sleep; REM, rapid eye movement; HR, heart rate; DBP, diastolic blood pressure; SBP, systolic blood pressure; MAP, mean arterial pressure; HRV, heart rate variability; BPV, blood pressure variability; CV, coefficient of variation. Means for each sleep state were calculated by taking a 2-min artifact-free period in both SWS and REM sleep and calculating the mean for that period. The mean and SD were then calculated for the group. HRV was measured by taking a 2-min artifact-free period in both SWS and REM sleep and calculating the SD of the mean R-wave-to-R-wave (R-R) interval (ms). The CV was calculated (SD divided by the mean R-R interval) to minimize the effect of resting HR on SD. BPV was measured by taking a 2-min artifact-free period in both SWS and REM sleep and calculating the SD of the SBP during that period. The mean and SD were then calculated for the group. Significant difference vs. SWS, *p < 0.005.
each specified sleep state. As in the other testing procedures, if there was an apnea or an arousal, these data were excluded from the hemodynamic analysis but included in the arousal analysis.

To examine the accuracy of the Portapres device, we compared BP readings obtained via an indwelling catheter (umbilical artery) with readings obtained via the Portapres in seven critically ill neonates (gestation period: 37.5 ± 1.6 wk). BP was measured for a maximum of 5 min in each of the infants via the Portapres by using the cuff wrapped around the wrist. The signal from the Portapres was downloaded simultaneously with the readings from the intra-arterial lines (Spacelabs monitor, Spacelabs), and a direct comparison was made.

Data Analysis

Sleep staging was done according to the criteria of Guilleminault and Souquet (15). Apneas were recorded if there was a pause in breathing of greater than or equal to two respiratory cycles with or without oxygen desaturation. Apneas were divided into central, obstructive, and mixed apneas.

All autonomic test period data were analyzed visually to guard against artifact. Test periods were extracted and imported into Microsoft Excel. The data were analyzed by using software made for the purpose. Systolic BP (SBP) and diastolic BP (DBP) values and ECG R waves were detected under visual control with the accuracy of the original sampling frequency.

A reference period was calculated before each test by taking the mean rate of the 30 s directly preceding the test. Maximum values (and SDs) for DBP, SBP, and HR were then calculated for every 5-s epoch throughout the pretesting reference period and testing period. To standardize the HR and BP among subjects, the differences between the maximum values and the reference period were calculated as a percent change of the reference rate. A hemodynamic profile was obtained by plotting these mean maximum percent changes for each 5-s period against the time course of the test. The ratio of the R-wave-to-R-wave (R-R) interval changes was calculated by comparing the minimum R-R interval seen after the tilt with the maximum R-R interval within 25 beats of the postural change.

Intersleep-state comparisons of HR and BP were made by taking a 2-min artifact-free period in both SWS and REM and calculating the mean and SD of that period. HRV and BP variability (BPV) were measured by taking a 2-min artifact-free period in both SWS and REM and calculating the SD of the mean R-R interval and the SD of the mean SBP, respectively. The coefficient of variation was calculated (SD divided by the mean) to minimize the effect of baseline HR and SBP on SD.

Arousal responses were calculated as a percentage of the number of tilt tests to cause a sleep-state change as evidenced by the EEG.

Statistical Methods

Analysis of variance and Tukey’s multiple comparison test were used to determine the significance of the difference of the percent change at the −20-, 0-, 5-, and 20-s time epochs. Homogeneity of variance was calculated using Bartlett’s test. The Wilcoxon paired-sample test was used to determine significant differences among HRV, mean HR, mean BP, BPV, and arousal in REM and SWS.

RESULTS

Direct comparison of the indwelling catheter BP readings with the Portapres measurements showed good agreement. A typical example of the BP curves obtained from each method is shown in Fig. 1. The measurements ranged between 34 and 76 mmHg (intra-arterial line) and 40 and 77 mmHg (Portapres). The difference between the two methods was greater for DBP (3.8 ± 4.0 mmHg) than for SBP (−1.9 ± 4.0 mmHg). The limits of agreement between the two methods ranged from −9.5 to 6.5 mmHg for SBP and −4 to 9.75 mmHg for DBP; i.e., the Portapres may have underestimated SBP by up to 9.5 mmHg and DBP by up to 4 mmHg or overestimated SBP by up to 6.5 mmHg and DBP by up to 9.75 mmHg. However, within each patient, these differences tended to remain constant with changing BP values, with the correlation coefficient for the group being 0.68.

All infants had normal sleep breathing. Mean HR, HRV, BP, and BPV were higher in REM sleep than in SWS in all infants (Table 1). HR rose from a mean of 117 beats/min in SWS to a mean of 124 beats/min in REM sleep, and the mean arterial pressure increased by an average of 8 mmHg, from 65 mmHg in SWS to 73 mmHg in REM sleep. Both HRV and BPV increased in REM sleep (Table 1). All infants displayed a shift upwards in baseline for both HR and BP over and above this increased variability (Fig. 2).

45° Head-up Tilting

All infants displayed a characteristic response to the 45° head-up tilt. In SWS and REM, HR and BP began to increase immediately, rising rapidly to a peak within the first four to eight beats (Fig. 3). This peak was typically reached within 4 s, with the maximal rate being significantly increased from the other reference epochs (P < 0.005). There followed a similarly rapid fall in both HR and BP. Usually, HR fell to baseline levels within 10 s but then oscillated over the rest of the test. In contrast, BP fell smoothly back toward baseline within 10–15 s (Fig. 4, Table 2). When the infant was placed back to the horizontal position, there was again an increase in BP, with a return to baseline within 10–15 s. However, the HR responses during return to the horizontal position were more variable, with some infants exhibiting only a minor
increase in HR followed by a marked HR fall (see Figs. 3 and 4), suggestive of a predominant baroreceptor modulation.

**Arousals**

There were significantly more arousals during the tilt test in REM sleep compared with SWS, with the infant arousing to 72% of tests in REM sleep compared with 23% in SWS ($P < 0.001$). Because arousal was typically associated with arm movement (Fig. 2), it was not possible to compare cardiovascular responses to the postural challenge with and without arousal.

**mCFT**

Arousal was a common response to this stimulus, with the infant arousing 80% of the time in SWS and 65% of the time in REM sleep. In the circumstance when the infant did not arouse, an apnea was an uncommon response occurring only 10% of the time in SWS and 18% of the time in REM sleep. Hemodynamic responses to the mCFT were only analyzed in the absence of both arousal and apnea, and in these circumstances the hemodynamic response to the mCFT was much more pronounced in SWS compared with REM sleep (Fig. 5). In SWS, there was a pronounced rise in both DBP and SBP within the first 5 s of the ice application ($P < 0.01$), accompanied by only a slight rise in the HR ($P > 0.05$). This was followed by a decrease in both HR and BP, with minimal HR values ($P < 0.05$) being reached within 10–15 s of the ice application. The minimal BP values were reached within 15–20 s ($P > 0.05$). This reduction of HR was a maximally 16 ± 4% in SWS compared with 12 ± 5% in REM sleep. Both BP and HR stabilized at prestimulus levels within 30 s. In REM sleep, there were no significant changes in either BP or HR, although the hemodynamic profile followed that described for SWS.
Auditory Stimulation Test

The auditory stimulus produced a biphasic response with an initial acceleration in HR and increase in BP. The increase was followed by a deceleration of HR and a decrease in BP, with the HR returning to pretest HR levels within 10–15 s in both SWS and REM sleep. In contrast, the BP values had not returned to pretest values by the 25- to 30-s epoch and were, in fact, significantly lower at this time compared with pretest values (*P*, 0.05) (Fig. 6).

**DISCUSSION**

The accuracy of the Finapres device in measuring BP in infants has been examined by Drouin et al. (7) and found to be a reliable alternative to intra-arterial read-

### Table 2. HR, SBP, and DBP changes after 45° head-up tilt

<table>
<thead>
<tr>
<th>Sleep State</th>
<th>% Maximum Change</th>
<th>% Drop (max – min)</th>
<th>Drop (max – min)</th>
<th>% Change During Tilt</th>
<th>(max – min)</th>
<th>R-R Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>SWS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>16 ± 7*</td>
<td>21 ± 7</td>
<td>27 ± 8</td>
<td>+0.8 ± 2.4</td>
<td>1.3 ± 0.2</td>
<td></td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>16 ± 6*</td>
<td>16 ± 4</td>
<td>16 ± 5</td>
<td>−1.2 ± 3.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>22 ± 10*</td>
<td>19 ± 4</td>
<td>14 ± 5</td>
<td>+1.1 ± 2.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>REM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>15 ± 6*</td>
<td>19 ± 7</td>
<td>26 ± 9</td>
<td>+1.8 ± 2.7</td>
<td>1.3 ± 0.1</td>
<td></td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>20 ± 10*</td>
<td>16 ± 8</td>
<td>18 ± 8</td>
<td>+0.1 ± 2.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>21 ± 12*</td>
<td>15 ± 8</td>
<td>13 ± 8</td>
<td>−0.2 ± 2.4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are means ± SD. (max – min), Mean drop. Mean %maximum change for both HR and blood pressure was measured by taking the maximum rate after the initiation of the tilt (typically within the first 5 s) and expressing it as a percent change from the 30-s reference baseline. Mean %drop was calculated by taking the minimum rate (typically within 5–15 s from the initiation of the tilt) after the peak and expressing it as a percent change of the maximum rate. Mean drop (max – min) was calculated by a direct comparison of the raw maximum and minimum values after the tilt. Mean %change during tilt was calculated by subtracting the mean value of the last 10 s of the tilt from the pretest reference value and expressing it as a percentage of the pretest value. *P*, <0.005.

Auditory Stimulation Test

The auditory stimulus produced a biphasic response with an initial acceleration in HR and increase in BP. The increase was followed by a deceleration of HR and a decrease in BP, with the HR returning to pretest HR levels within 10–15 s in both SWS and REM sleep. In contrast, the BP values had not returned to pretest values by the 25- to 30-s epoch and were, in fact, significantly lower at this time compared with pretest values (P < 0.05) (Fig. 6).
ings. They examined eight critically ill neonates who had in place umbilical catheters and found the limits of agreements between the two methods to be reasonably small (−5.26–8.74 mmHg for SBP and −5.17–5.50 mmHg for DBP). Similarly, in the present study, we found the limits of agreement to be of the same order (−9.5–6.5 mmHg for SBP and −4–9.75 mmHg for DBP). These differences remained constant with the changing BP values for each patient, and the BP measurements obtained from the Portapres device appear to be a reliable and alternative measurement of BP in the infant. Indeed, although the number of studies examining BP in infants is limited, the SBP in SWS of 80 ± 7 mmHg obtained in this study compares well with the value of 82.3 ± 8.8 mmHg obtained by Chong et al. (5) using intermittent BP readings (at 5-min intervals) in a group of 44 infants (mean age, 7.9 wk) when they were quietly asleep.

To our knowledge, these are the first studies of autonomic function during sleep in the human infant using a noninvasive method that provides a continual measure of instantaneous systemic arterial BP. Our first new finding is that, in infants, BP is elevated in REM sleep compared with SWS. This compares well with what has been observed in adult human studies in which BP is significantly reduced in SWS compared with awake values, with BP in REM sleep close to the awake values (36). We did not attempt to report awake values in this study because of the large variations due to activity and movement artifact.

We have confirmed previous studies (17, 33) that have shown that HRV and HR are increased in REM sleep compared with SWS and have further shown, as may have been expected, that there is an increase in variability in BP in REM sleep.

As in other studies, the tilt test revealed a sharp distinction between the arousal threshold in REM sleep compared with SWS (12, 28). Full cortical arousals were determined according to EEG criteria and in REM sleep: three out of four tilts resulted in an arousal, compared with SWS, where only one in four tilts caused arousal. Subcortical arousals were not noted. The cause of the arousal during these tests is uncertain. Although changes in HR and BP may have contributed to the arousal through stimulation of cardiovascular receptors, it is much more likely that other afferent inputs were responsible for triggering the arousal. Our method minimizes any tactile stimulus, although such stimuli could have contributed through, for example, a change in pressure distribution of the infant’s body with the tilting. However, the most likely source of afferent stimulus causing arousal was that of vestibular nerve stimulation. Rapid postural change is the primary source of stimulus to the vestibular apparatus. In the present context, our data provide indirect evidence that arousal response to vestibular inputs is differentially influenced by sleep state, with the REM state being more sensitive than SWS.

There was clear habituation to the tilting in SWS that was not as evident in REM. All infants in SWS habituated to the tilt within the first two to three tilts. However, 8 of the 12 infants did not habituate to the stimulus at all in REM sleep, with arousals occurring intermittently and throughout the testing period. The four infants who did habituate took longer in REM sleep than in SWS, and habituation did not usually occur until the fourth or fifth tilt.

The second major result of this study is the characterization of the normal infant cardiovascular response to three tests of autonomic function and the assessment of the effect of sleep state on these responses.

**Tilting**

The cardiovascular response to a head-up tilt in normal control infants follows the same general pattern found in healthy adult men (4, 13, 37). Because of the ease of the measurement, this response has been widely described in adults, but, to date, the BP profile in infants could only be examined via indwelling catheters (14), and so the response to the head-up tilt has usually been confined to characterization of the HR response alone (10) or the HR response with intermittent BP measurements (5, 11).

The typical change in healthy adult men is an increase in both HR and BP followed by a decrease, with stabilization usually being reached within 1 min at around pretilt values. This pattern of response was seen in all of the infants studied, but with stabilization being achieved within ~30 s. During tilting in SWS, there was a mean 1.2% drop in SBP, which is of the same order as that observed in previous studies (2, 5). However, this drop was not observed in REM sleep, in which BP values returned to within ±0.2% of the pretilt reference value. This increase, followed by a sharp decrease and rapid return to baseline, has also been observed in a group of newborn infants with indwelling arterial lines during a 70° head-up tilt (27).

The present explanation for the changes in HR and BP induced by a postural challenge (35) is that there is an immediate fall in venous return, followed by a delay of about six heartbeats of left ventricular stroke volume with a subsequent reduction in carotid sinus and aortic arch arterial pressure and a reduction in baroreceptor stimulation. This withdrawal of baroreceptor input in turn induces a reflex increase in HR and peripheral vasoconstriction, stabilizing the arterial pressure. Other mechanisms also enhance venous return.

However, given the very rapid and immediate rise in BP and HR observed in all infants (maximum values for HR and BP being achieved within four to eight beats of the initiation of the tilt), there may well be other physiological mechanisms that play an important role in this early part of the response. The change may, in part, be due to the increased vasoconstriction caused by the tilt itself. However, the effect that vasoconstriction had on the BP readings was kept to a minimum as BP was measured via the radial artery and not cutaneously at the fingers. Alternatively, Harper (16) has suggested that vestibular regulation plays a major role in BP control in infants. Certainly, it is well
known that vestibular stimulation can influence cardiovascular autonomic control (6, 38), and deficiencies in vestibular regulation are often observed clinically to affect circulatory changes when there is a sudden change from horizontal to upright.

Thus it may be that the stereotypical rise and fall of BP and HR seen in the head-up tilt in infants is the result of both a vestibular and baroreceptor input. The immediate response seen in infants may well be the result of the initial action of the rapidly acting vestibular system, with baroreceptor regulation having a secondary and more gradual effect. Supporting this explanation is the very short latency period for the HR and BP rises that is again observed when the infant is placed back in the horizontal position.

mCFT

Previous research has shown that the ophthalmic division of the trigeminal nerve is the most sensitive trigeminal pathway involved in the dive reflex in humans, and that the response elicited from ice applied to this region correlates well with that produced by full facial immersion in cold water (22). This test assesses both the trigeminal sympathetic and parasympathetic efferent pathways and does not directly involve the baroreflex or its primary central connections (9). In adults, the ice is maintained on the forehead for 1 min for maximal effect, and in previous infant studies the ice was left on the forehead for 20 s. Our preliminary studies had shown that even this reduced amount of time was a very effective arousal stimulus, and thus the ice was kept on the forehead for only 8 s.

The infant response to the mCFT was similar to that described in adults, with a rise in BP and bradycardia. The extent of the bradycardia seen in this study (16%) was similar to that seen in other infant studies (23). Notably, significant changes in HR and BP were only observed in SWS and not in REM, suggesting different gain settings for this reflex in the two major sleep states (26).

Auditory Stimulus

The sudden noise caused an immediate increase in HR followed by a decrease in all but one infant in both SWS and REM sleep, with a return to baseline values within 15 s of the noise. This is in contrast to the adult, who almost always has a sustained tachycardic response to a sudden noise (3). Our results confirm previous findings of the infant HR response to a sudden noise where the biphasic response is usual (1, 23). It has been suggested that this is part of the fear reflex, which is widespread in birds and mammals and which is characterized by bradycardia and apnea as seen in the diving response (1). Whereas this may be so, in our study, in the absence of an arousal or a startle, apnea was not a common response, occurring only 8% of the time. Of interest, one of the infants had, on repeated tests, only a bradycardic response to the auditory stimulus.

The BP response to the auditory stimulus was also biphasic. However, there was a sustained decrease in both SBP and DBP that was still present 30 s after the noise. This sustained decrease in BP, not previously described, may well play a vital role in the fear reflex, which has been suggested to be responsible for sudden death in pigs and also for SIDS in human infants (20).

This study has provided the first normative data for the influence of sleep state on systemic arterial pressure in the normal infant. It demonstrates that, in the infant, BP and BPV are higher in REM sleep than in SWS, as has been shown in the adult. It has also demonstrated that the infant cardiovascular response to a postural challenge is similar to that found in adults but, not surprisingly, occurs over a shorter time interval. The very short latency of both HR and BP to a tilt greatly suggests that vestibular stimulation plays a dominant role in the early phase of the response.

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REFERENCES