Sleep state and vagal regulation of heart period patterns in the human newborn: 
An extension of the polyvagal theory

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Abstract
The influence of sleep state (i.e., active and quiet) on heart period, heart period variability, respiratory sinus arrhythmia (RSA), and the coupling between RSA and heart period was evaluated in 24 healthy full-term newborns. Electrocardiogram (ECG) data were collected, and sleep state was coded 1 hr after feeding until at least 10 min of data were collected in states of active and quiet sleep. ECG data were analyzed for the first five continuous minutes of each sleep state. Relative to active sleep, quiet sleep was associated with significantly higher amplitude RSA, lower heart period variability, and longer heart periods. Because RSA amplitude reflects the functional output of vagal pathways originating in the nucleus ambiguus, it was hypothesized that sleep state would influence how these vagal pathways regulate instantaneous changes in heart period. A new method, evaluating the instantaneous coupling of RSA and heart period, demonstrated that coupling was significantly greater during active sleep. The neurophysiological explanation extends the polyvagal theory to include potential cortical–brain stem connections.

Descriptors: Respiratory sinus arrhythmia, Polyvagal theory, Sleep state, Heart rate, Heart rate variability

In newborns, because of neural immaturity, the behaviors distinguishing active sleep from quiet sleep are more obvious than those observed in adults. Active sleep in adults is characterized by cortical activation, rapid eye movement (REM), and an absence of muscle tone and peripheral motor activity (Rechtschaffen & Kales, 1968). In adults, the neural pathways that regulate motor activity and motor tone to the limbs are depressed during active sleep. In newborns, in contrast to adults, the pathways regulating peripheral motor activity are not depressed during active sleep. Active sleep in newborns shares similarities with awake states (i.e., cortical activation and limb movements) but also includes eye closure and REM. This easily distinguishable behavioral difference between active and quiet sleep in the newborn provides an appealing natural experiment to study the influence of sleep state, and by inference cortical activation, on heart rate activity.

In the adult human, active or paradoxical sleep is a unique state during which cortical activation mimics alert states while there is an absence of peripheral motor tone and a presence of REM. This dissociation of upper and lower motor neuronal function during active sleep is dependent on neural maturation. Active sleep in the human newborn is different than that observed in the adult. In the newborn, during active sleep the upper motor neurons originating in the cortex communicate with lower motor neurons to produce sucking and mouthing behaviors and limb movements. In contrast, quiet sleep in the newborn is associated with a parallel depression of cortical activation and peripheral motor activity.

Myelinated pathways that populate portions of three cranial nerves (IX, X, XII) emerge from a medullary nucleus known as the nucleus ambiguus. Because most of the myelinated vagal fibers to

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the sinoatrial node originate in the nucleus ambiguus, the study of neural regulation of the nucleus ambiguous may be of great importance to psychophysiological. The nucleus ambiguous is anatomically organized into two subdivisions (Altschuler, Rinaman, & Miselis, 1992; Bieger & Hopkins, 1987). The dorsal subdivision is the source of the special visceral efferents that innervate the striated muscle of the upper gastrointestinal and respiratory tracts (i.e., pharynx, soft palate, larynx, and esophagus). These muscles control motor behaviors such as sucking, swallowing, and vocalizing. The ventral subdivision of the nucleus ambiguous is the source of the myelinated vagal fibers to the heart that produce respiratory sinus arrhythmia (RSA).

Pathways from frontal cortex terminate directly via corticobulbar pathways or indirectly via corticoreticular pathways on the dorsal subdivision of nucleus ambiguus. It is not clear from the neuroanatomy literature if there are direct corticobulbar pathways from cortex to the ventral subdivision. However, the observation that there is a respiratory rhythm in the visceromotor fibers that originate in the ventral subdivision and terminate in both the bronchi (e.g., Haselton Solomon, Motekaitis, & Kaufman, 1992) and the sinoatrial node (e.g., McAllen & Spyer, 1978), suggests an interneuronal communication between the two subdivisions and between the nucleus ambiguous and the source nucleus of the afferent vagus, the nucleus tractus solitarius (Richter & Spyer, 1990). Moreover, the neural communication between dorsal and ventral subdivisions is supported by empirical reports of sucking-related decreases in RSA amplitude (Porges & Lipsitt, 1993; Portales et al., 1997). These reports demonstrate concordant changes in processes determined by the dorsal subdivision (i.e., increased sucking behaviors) and the ventral subdivision (i.e., decreased RSA amplitude). Thus, the monitoring of RSA, a functional output from the ventral subdivision of nucleus ambiguous, may provide an indicator of the changing influence of upper motor neurons on the lower motor neurons in the brain stem, such as those originating in the nucleus ambiguous.

In humans, the vagal efferent pathways to the heart function as a brake. The intrinsic rate of the heart in the healthy human, even without sympathetic excitation, is significantly faster than the resting heart rate. Thus under most conditions, the vagus, primarily via myelinated pathways originating in the nucleus ambiguous, actively inhibits heart rate. However, when there is a need to engage actively with select elements in the environment, cortical neurons inhibit homeostatic needs, and cardiac output is rapidly increased to match metabolic demands. Under these situations there is a transitory withdrawal of the vagal tone to the heart to increase heart rate, which defines the removal of the vagal brake (Porges, Doussard-Roosevelt, Portales, & Greenspan, 1996). When demands require a calm behavioral state, the reengagement of the vagal brake slows heart rate and provides the physiological support for self-soothing behaviors. When the vagal brake is efficient, to support the changing metabolic demands, the neural modulation of RSA is paralleled by a monotonic change in heart rate.

Within the context of the polyvagal theory (Porges, 1995; Porges et al., 1996), the vagal brake is conceptualized as an adaptive neural physiological mechanism to foster engagement and disengagement with the environment. The efficiency of the vagal brake might be evaluated along several dimensions, including changes in the amplitude of RSA or an index of heart rate change relative to RSA change in response to a defined challenge. The definition of a challenge is arbitrary and often defined within specific experimental paradigms (e.g., mental effort, attention, social interaction). Especially during alert or vigilant states, responses to challenges must be rapid and continuous. For example, environmental demands often dynamically change under real life conditions.

To evaluate whether the dynamic function of the vagal brake is state dependent, it was necessary to generate measures of RSA and heart rate for short sequential epochs. Most methods for quantifying RSA, such as spectral analysis (e.g., Oberlander, Berde, Lam, Rappaport, & Saul, 1994) and peak-to-trough analysis (e.g., Fouad, Tarazi, Ferrario, Fighaly, & Alicantro, 1984; Grossman & Wintjes, 1986; Schechtman, Kluge, & Harper, 1988), have assumed that the amplitude of RSA was a stationary characteristic of the heart rate time series. In general, these methods have been used to calculate an average amplitude of RSA over periods of several minutes. However, to evaluate the dynamic function of the vagal brake, the epoch-by-epoch shifts in RSA are not interpreted as measurement error distributed around a central tendency. Alternatively, the instability in RSA is interpreted as a measureable manifestation of dynamic changes in the vagal control of the heart. Therefore, it becomes necessary to quantify RSA over periods of a few seconds. Unlike other methods, the moving polynomial technology (i.e., Porges, 1985) provides a unique opportunity to study the dynamically changing amplitude of RSA independently of a potential nonstationary baseline representing dynamic changes in heart rate. A new procedure to evaluate this dynamic relationship was developed that calculates RSA and heart period for short duration epochs (i.e., 5 s) and includes regression analyses applied to the epoch-by-epoch measures of RSA and heart period.

The current study was conducted to investigate whether the levels of heart period and RSA and the coupling between instantaneous shifts in RSA and heart rate are sleep state dependent in the human newborn. From the literature on sleep and autonomic function in the human newborn, two hypotheses were tested. First, RSA amplitude would be higher and heart rate would be slower during quiet sleep because this is a period when homeostatic processes are maximized to foster growth and restoration through hypothalamic structures. Second, the instantaneous coupling of RSA and heart rate would be greater during active sleep, when cortical influences on the lower motor neurons located in the brain stem via corticobulbar tracts are increased relative to quiet sleep.

Method

Participants

Twenty-eight healthy full term newborn infants (10 male, 18 female) were tested. The infants were recruited through a university hospital in the Washington, DC, metropolitan area. Criteria for subject selection included (a) gestational age between 38 and 42 weeks, (b) average weight for gestational age, (c) minimum Apgar scores of 7 at 1 min and 8 at 5 min, (d) uncomplicated pregnancies, and (e) spontaneous or Cesarian deliveries that did not involve general anesthesia or high forcnpse. Subjects were primarily from educated middle-class families. On average, infants were tested 48 hr postpartum ($SD = 24$ hr), were 40 weeks ($SD = 1.4$ weeks) gestational age, and had a mean birth weight of 3.649 g.

Procedure

Informed consent was obtained from mothers of infants who met subject criteria. Infants were tested at least 1 hr after a feeding. ECG data and sleep behavior were recorded during individual sessions in which the infant was lying prone in a bassinet in a darkened, empty patient room on the maternity ward. Curtains were partially drawn to allow for low levels of natural light with which to record movements during sleep.
Sleep state was assessed by observing respiration pattern (i.e., regular or irregular) and the presence or absence of eye (REM), facial, limb, and gross body movements every 25 s. The absence of all of these movements, with the exception of startles, when respiration was regular, defined quiet sleep, and the presence of any one of these behaviors defined active sleep. In defining segments of active sleep, a minimum of 75 continuous seconds (three sequential behavioral recordings) within quiet sleep was used as the criterion for state change. Likewise, state change from quiet sleep required a minimum of 75 s of continuous active sleep.

To monitor ECG, three disposable Ag-AgCl electrodes were placed on the infant’s chest. After the electrodes were attached, the infant was swaddled and placed in the prone position on the bassinet mattress. Electrode leads were connected to an ECG pre-amplifier (Grass, Model P15) and output to a Vetter Model C-4 FM instrumentation tape recorder (A. R. Vetter, Rebersburg, PA). When the infant appeared to be in a drowsy state, the collection of ECG data was started. The ECG recording was continuous for 15–20 min, unless the infant awoke and began crying. If there was a disruption, data collection resumed when the infant returned to a sleep state. A minimum of 5 continuous minutes of ECG was recorded for each sleep state. The first 5 min in each sleep state were analyzed. Twenty-four (9 male, 15 female) of 28 infants had 5-min segments of both active and quiet sleep.

The data were quantified off line by replaying the tapes into a vagal tone monitor (Delta-Biometrics, Bethesda, MD). The vagal tone monitor detected the peak of the R-wave with a 1-ms accuracy and timed sequential heart periods to the nearest millisecond. The sequential heart periods were stored in a file on a personal computer. The data files of sequential heart periods were input to MXedit (version 2.21) software (Delta-Biometrics) to edit outliers, to quantify heart period, and to calculate the vagal tone index ($V_{NA}$) as a measure of the amplitude of RSA (Porges, 1985). This method for calculating the amplitude of RSA contains several sequential steps. First, when applied to newborn infants, heart period values are measured to the nearest millisecond and resampled into equal time intervals every 200 ms. Second, a detrending algorithm removes from the heart period times series the variance associated with complex aperiodic baseline shifts and oscillations slower than RSA. The detrending algorithm applies a moving polynomial filter (3rd order, 21 point) to remove aperiodic baselines and slow oscillations. Third, the residual output from the moving polynomial is bandpassed, and the heart period variance in the frequency band associated with spontaneous breathing in the newborn (i.e., 0.3–1.3 Hz) is quantified. Fourth, to reduce distribution distortions associated with variance estimates, the bandpassed variance is transformed with a natural logarithm and reported in units of ln(ms)$^2$.

To be consistent with other studies in which MXedit has been used to apply the moving polynomial–bandpass strategy to quantify RSA (Porges, 1985), an epoch duration of 30 s was used to quantify RSA, and the average of the sequential within sleep-state epoch values was used in the statistical analyses.

In addition, spectral analyses were performed on the detrended data (i.e., time sampled every 200 ms and detrended with a 3rd order, 21-point moving polynomial) to determine the frequency (i.e., frequency of peak of the spectrum) and amplitude (i.e., spectral density at peak frequency) of RSA. Average heart period and the natural logarithm of heart period variance over the 5-min sleep states were also quantified.

Regression analyses were used to evaluate the dynamic coupling between RSA and heart period within each sleep state. Repeated measures analyses of variance (ANOVAs), with state (active, quiet) as the repeated measure, were conducted to evaluate sleep state differences in the physiological variables (i.e., RSA amplitude, RSA frequency, heart period, heart period variability, and the coupling between RSA and heart period). Fisher’s r to Z transformation was used when correlations were evaluated in the ANOVAs. There were no differences in physiological measures as a function of gender, and all analyses reported are collapsed across gender.

Consistent with the reports that heart period exhibits a stronger linear relation with autonomic control than does heart rate (Bernston, Cacioppo, & Quigley, 1995; Quigley & Bernston, 1996), all cardiac variables evaluated in this study were quantified from the beat-to-beat heart period time series.

**Results**

**Sleep State Effects**

Table 1 summarizes the state effects for the physiological variables. Quiet sleep was associated with significantly longer heart period and higher amplitude RSA (i.e., quantified via either spectral analysis or MXedit). In addition, the peak of the spectrum indicated a slight but significant increase in frequency from 0.48 Hz (i.e., 28.8 cycles/min) during active sleep to 0.56 Hz (i.e., 33.6 cycles/min) during quiet sleep. All peak frequencies occurred within the bandwidth selected for MXedit of 0.3–1.3 Hz.

In identifying the spectral peak, the data were first detrended with the moving polynomial filter. The moving polynomial filter, like other filters, has a transfer function that may selectively amplify or attenuate specific frequencies. To deal with the possible influence of this transfer function on the spectral peak amplitude values, an analysis was conducted in which each spectral peak amplitude value was corrected. The correction consisted of multiplying the spectral density at the peak by the reciprocal of the

### Table 1. Means and Standard Deviations for Autonomic Measures as a Function of Sleep State

<table>
<thead>
<tr>
<th>Measure</th>
<th>Quiet sleep</th>
<th>Active sleep</th>
<th>$F(1,23)$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spectral peak (ln)</td>
<td>6.32 (1.87)</td>
<td>5.85 (1.49)</td>
<td>5.0</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Adjusted spectral peak (ln)</td>
<td>6.26 (1.86)</td>
<td>5.77 (1.46)</td>
<td>5.2</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Spectral frequency (Hz)</td>
<td>0.56 (0.15)</td>
<td>0.48 (0.08)</td>
<td>4.6</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Respiratory sinus arrhythmia (ln)</td>
<td>4.33 (1.59)</td>
<td>3.96 (1.33)</td>
<td>7.1</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Heart period variability (ln)</td>
<td>6.75 (1.33)</td>
<td>7.43 (0.83)</td>
<td>8.8</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Heart period (ms)</td>
<td>533 (41.6)</td>
<td>500 (34.8)</td>
<td>29.4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Standard deviation of RSA</td>
<td>0.83 (0.22)</td>
<td>1.05 (0.26)</td>
<td>22.4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Standard deviation of heart period</td>
<td>27.35 (16.6)</td>
<td>38.28 (15.7)</td>
<td>21.9</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>
transfer function for that specific frequency. For example, if the transfer function at a specific frequency was 0.98, the spectral density was corrected by 1/0.98 (1.02). Or, if the transfer function at another frequency was 1.02, the spectral density was corrected by 1/1.02 (0.98). Similar to the spectral peak amplitudes, the adjusted spectral peak amplitudes were transformed to their natural logarithms and then analyzed. The correlations between the adjusted and unadjusted peak amplitudes were .995 during active sleep and .997 during quiet sleep. Consistent with the analysis on the spectral peaks, significant differences between sleep states were also observed in the adjusted spectral peak amplitudes (Table 1).

To illustrate the state differences in RSA, a 60-s segment of heart period data from a typical subject is illustrated in Figure 1. The top panels illustrate the beat-to-beat heart period data for the two sleep states. The middle panels illustrate the heart period activity that characterizes RSA (data represent the beat-to-beat heart period data following detrending with the moving polynomial filter). The bottom panels illustrate the spectral density distributions of the detrended data illustrated in the middle panels. For this neonate, during quiet sleep the average heart period is longer, the overall heart period variability is less, the amplitude of RSA is higher, and the peak of the spectrum is at a higher frequency than during active sleep.

**Epoch Duration**

Short data epochs are necessary to evaluate the instantaneous shifts in the coupling between RSA and heart period, providing the opportunity to evaluate the influence of epoch duration on the amplitude of RSA. Although spectral analysis cannot be applied to short duration heart period epochs, the time domain method implemented in MXedit (Porges, 1985) can statistically extract extremely short epochs. MXedit accomplishes this by preprocessing the entire data file with two symmetrical cascading filters (i.e., moving polynomial and bandpass). The residual data from these filters contain only the heart period variability activity within the user defined frequency band. In the current study, a frequency band of 0.3–1.3 Hz was selected to extract heart period variability in the band of frequencies associated with spontaneous neonatal breathing. The residual times series can be quantified in user determined epoch durations. When the entire 5-min file is selected as the epoch, the MXedit method is a statistically equivalent time domain method in contrast to the more traditional frequency domain methods. To demonstrate this convergence, the MXedit method when applied to the entire 5-min file produced RSA values that were highly correlated with the peak of the spectrum during quiet sleep ($r = .969$) and during active sleep ($r = .979$). Correlations between the MXedit method and spectral analysis approach unity when the spectral densities are summed across an equivalent band (i.e., 0.3–1.3 Hz).

Individual differences for each epoch duration were defined as the average of RSA derived from sequential epochs within each 5-min sleep state. RSA estimates decreased monotonically with shorter epoch durations within each sleep state (see Table 2). However, as listed in Tables 3 and 4, the correlations among the epoch dependent values of RSA derived via the MXedit method are all at least .95 and at least .99 for the four shorter epochs. In addition, these estimates of RSA amplitude were correlated above .9 with the peak of the spectrum. The frequency component of RSA derived from the spectral analyses was not correlated with any of the RSA variables.

**Stability Across Sleep States**

Correlations were calculated between the values collected during active sleep and those collected during quiet sleep for each physiological variable. Although sleep state influenced the physiolog-

### Table 2. Decrease in Variance as a Function of Epoch Size

<table>
<thead>
<tr>
<th>Sleep state</th>
<th>5 min</th>
<th>30 s</th>
<th>10 s</th>
<th>5 s</th>
<th>2 s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quiet</td>
<td>4.47</td>
<td>4.33</td>
<td>4.22</td>
<td>4.13</td>
<td>4.01</td>
</tr>
<tr>
<td>Active</td>
<td>4.15</td>
<td>3.96</td>
<td>3.80</td>
<td>3.67</td>
<td>3.50</td>
</tr>
</tbody>
</table>

### Table 3. Correlation Matrix for Autonomic Measures within Quiet Sleep

<table>
<thead>
<tr>
<th></th>
<th>5 s</th>
<th>10 s</th>
<th>30 s</th>
<th>5 min</th>
<th>Peak</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 s</td>
<td>.999</td>
<td>.998</td>
<td>.991</td>
<td>.983</td>
<td>.954</td>
<td>.995</td>
</tr>
<tr>
<td>5 s</td>
<td>.994</td>
<td>.987</td>
<td>.952</td>
<td>.951</td>
<td>.951</td>
<td>.995</td>
</tr>
<tr>
<td>10 s</td>
<td>.996</td>
<td>.989</td>
<td>.951</td>
<td>.951</td>
<td>.951</td>
<td>.995</td>
</tr>
<tr>
<td>30 s</td>
<td>.992</td>
<td>.948</td>
<td>.915</td>
<td>.915</td>
<td>.915</td>
<td>.995</td>
</tr>
<tr>
<td>5 min</td>
<td>.969</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>.951</td>
</tr>
<tr>
<td>Peak</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>.969</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>.329</td>
</tr>
</tbody>
</table>
ical variables (see Table 1), individual differences in the variables were preserved across sleep states. As listed in Table 5, with the exception of the spectral frequency, all variables exhibited a strong stability across the sleep states.

**Covariation of Average Changes in Heart Period and RSA Between Sleep States**

A regression analysis was used to evaluate the covariation between individual differences in average changes in heart period and RSA from quiet to active sleep states. As illustrated in Figure 2, there is a significant linear relationship between these two variables \( r = .60 \), slope = 22.8). As RSA amplitude decreased from quiet to active sleep, there was a parallel decrease in the duration of heart period.

**The Instantaneous Coupling Between RSA and Heart Period**

Prior to applying regression analyses to evaluate state differences in the coupling between RSA and heart period, it was necessary to determine an appropriate epoch duration and whether there was a lag or delay between changes in RSA amplitude and heart period. Exploratory cross-correlational analyses were conducted with the infant heart period data to answer these questions. Sequential epoch durations of 2, 5, and 10 s derived from MXedit were used to generate synchronous times series of RSA and heart period. MXedit facilitates the generation of synchronous times series of RSA and heart period of short durations by performing the detrending and bandpass filtering of the entire data file prior to the calculation of epoch values.

If the temporal relationship between RSA and heart period is instantaneous, the magnitude of the cross-correlations and the slope of the regression lines will be maximized with short epochs and a lag of 0 between the two time series. However, if the maximum correlations reliably have negative or positive lags, it would indicate that the strongest association between RSA and heart period was not instantaneous but was characterized by one of the time series leading or lagging the other. Cross-correlations between the two variables at different lags indicated that regardless of epoch duration (2, 5, or 10 s), the distributions of maximum correlation centered on a lag of 0. The 5-s epoch was selected for subsequent analyses because it represents a duration in which at least one respiratory cycle would be completed and manifested in the heart period as RSA. In addition, Richards and Casey (1991) used 5-s epochs with a similar method of quantification.

For each subject, the lag of maximum correlation for the cross-correlations between RSA and heart period was calculated. The distributions of these lags are illustrated in Figure 3 for the 2-s and 5-s epochs during active sleep and quiet sleep. Many subjects exhibited maximum correlations at 0 lag for both epochs. With the 5-s epoch, at least 50% of subjects had their maximal cross-correlation at 0 lag. In addition, if subjects had maximum correlations at lags other than 0, they had significantly lower maximum correlations than subjects with maximum correlations at lag 0. To support this observation, a correlation was calculated between the absolute lag of maximum correlation and the maximum correlation. The analysis demonstrated that as maximum correlation deviated from lag 0, the correlations became smaller during active sleep \( (r = -.60, p < .001) \) and during quiet sleep \( (r = -.52, p = .06) \). Subjects with maximum coupling at lag 0 \( (n = 14) \) had significantly higher coupling than the subjects with maximum coupling at other lags \( (n = 10) \), during both active sleep \( F(1, 23) = 13.2, p < .005 \), and quiet sleep, \( F(1, 23) = 9.0, p < .01 \).

**Sleep State Influences on the Coupling Between RSA and Heart Period**

Based on the cross-correlations, only lag 0 correlations for the sequential 5-s epoch values were used for these analyses. To conform to statistical assumptions for the ANOVA, the correlation coefficients were transformed by the Fisher r to Z formula. Statistical analyses demonstrated a significant state difference in the coupling between RSA and heart period, \( F(1, 23) = 5.79, p < .05 \); the instantaneous coupling between heart period and RSA would

### Table 4. Correlation Matrix for Autonomic Measures within Active Sleep

<table>
<thead>
<tr>
<th></th>
<th>5 s</th>
<th>10 s</th>
<th>30 s</th>
<th>5 min</th>
<th>Peak</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 s</td>
<td>.999</td>
<td>.996</td>
<td>.990</td>
<td>.956</td>
<td>.938</td>
<td>.361</td>
</tr>
<tr>
<td>5 s</td>
<td>.999</td>
<td>.994</td>
<td>.964</td>
<td>.946</td>
<td>.340</td>
<td></td>
</tr>
<tr>
<td>10 s</td>
<td>.997</td>
<td>.955</td>
<td>.955</td>
<td>.312</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 s</td>
<td></td>
<td>.965</td>
<td>.965</td>
<td>.303</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 min</td>
<td></td>
<td></td>
<td>.979</td>
<td>.249</td>
<td></td>
<td>.212</td>
</tr>
<tr>
<td>Peak</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 5. Correlations of Autonomic Measures Across Sleep State**

<table>
<thead>
<tr>
<th>Autonomic measure</th>
<th>Correlation</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory sinus arrhythmia</td>
<td>.91</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Heart period</td>
<td>.74</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Heart period variability</td>
<td>.85</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Spectral peak</td>
<td>.83</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Spectral frequency</td>
<td>.06</td>
<td>ns</td>
</tr>
<tr>
<td>Standard deviation of RSA</td>
<td>.42</td>
<td>&lt;.05</td>
</tr>
</tbody>
</table>

Figure 2. Scatterplot of changes in heart period and RSA from quiet sleep to active sleep.
greater during active sleep. However, because the data violated the assumption of homogeneity of variance, a Friedman nonparametric analysis of variance on ranks was calculated. The Friedman analysis confirmed the group difference reported in the parametric ANOVA ($\chi^2 = 7.35, p < .01$). The average correlation between RSA and heart period for the 24 subjects was .33 during quiet sleep and .57 during active sleep. Similar significant differences were observed with 10-s epochs (i.e., quiet sleep = .34, active sleep = .51), $F(1,23) = 7.16, p < .05$.

State differences in the within-subject variability of heart period and RSA (see Table 1) may have differentially extended or restricted the range of the variables and contributed to the observed state differences in correlations. Statistics confirm that the average range in RSA was significantly greater during active sleep, $F(1,23) = 20.22, p < .001$. A similar trend towards a greater range during active sleep was observed in heart period, $F(1,23) = 3.20, p < .1$. To deal with the possible confounding influence of range, state differences in the slopes of the regression lines were calculated. According to Cohen and Cohen (1983), distributions of regression line slopes are relatively immune to the influence of range. Analyses of the slopes indicated a state difference, with active sleep characterized by a significantly steeper slope (18.35) than quiet sleep (13.66), $F(1,23) = 7.23, p < .05$, confirming the stronger influence of RSA on heart period during active sleep.

**Discussion**

There were distinct state differences in the cardiovascular variables. Relative to active sleep, quiet sleep was characterized by increases in RSA amplitude, RSA frequency, and heart period and decreases in overall heart period variability and the instantaneous coupling between RSA amplitude and heart period. These findings are consistent with those of other studies of autonomic correlates of infant sleep state, that is, lower heart rate (Ashton & Connolly, 1971; Harper et al., 1977, 1983; Prechtl et al., 1969) and heart rate variability (Harper et al., 1976) during quiet sleep relative to active sleep. Similarly, in adults RSA amplitude has been observed to be greater during non-REM relative to REM states of sleep (Vanoli et al., 1995). Thus, there appears to be, as Vanoli et al. (1995) suggested, greater vagal activity during quiet sleep (i.e., non-REM) and a significant withdrawal of vagal activity during active sleep. These observations, however, do not provide insight into whether the regulation of vagal activity might be linked more to hypothalamic or cortical control mechanisms.

The initial construct of the vagal brake focused on shifts between RSA and heart period in response to metabolic demands. According to this initial definition of the vagal brake, the increased metabolic demands associated with active sleep should have been associated with decreases in RSA amplitude and heart period. In support of this definition, there was a significant correlation between the changes in the two variables ($r = .60$). As illustrated in Figure 2, increases in RSA were associated with increases in heart period. Thus, newborn neonates functionally withdraw the vagal brake to decrease heart period (i.e., increase heart rate) when shifting from a state of lower metabolic demand (i.e., quiet sleep) to a state of higher metabolic demand (i.e., active sleep). These findings are consistent with previously reported data with older children, demonstrating a covariation between RSA depression and heart period decreases in response to an attention demanding task (Porges et al., 1996). In addition, there was a significant relationship between RSA amplitude during quiet sleep and the magnitude of both RSA ($r = .54$) and heart period ($r = .43$) decreases from quiet sleep to active sleep. These findings were also consistent with those of the Porges et al. (1996) study, which demonstrated that baseline RSA levels were significantly correlated with the magnitude of RSA and heart period changes during an attention-demanding task.

Studies investigating thermoregulation during sleep provide important insights into sleep state differences in central regulation of autonomic function. Parmeggiani and colleagues have studied the neural control of thermoregulatory changes during quiet sleep (i.e., synchronized) and active sleep (i.e., desynchronized). They and others (for review, see Parmeggiani, 1982) have demonstrated that thermoregulatory mechanisms are active during quiet sleep and inactive during active sleep. Parmeggiani (1985) concluded that the somatic and autonomic phenomena associated with quiet sleep were characteristic of a closed-loop operation (i.e., negative feedback system) consistent with the maintenance of homeostasis at a low level of energy expenditure. In contrast, the phenomena associated with active sleep and wakeful periods were characteristic of an open-loop operation not consistent with neural control of homeostasis. Parmeggiani argued that because hypothalamic structures play an important role in thermoregulation, autonomic function is reliant on hypothalamic mechanisms during quiet sleep and that higher brain structures depress hypothalamic regulation of autonomic state during active sleep. Thus, the evidence suggests that quiet sleep is a period during which the hypothalamus is in control of the brain stem, and neural traffic from the cortex to the brain stem is depressed.

During active sleep, brain stem reflex and integrative mechanisms are released from the hypothalamic regulatory influences that are active during quiet sleep (Parmeggiani, 1985). As a result, many biological variables are less precisely regulated during active sleep. This phenomenon has been observed in newborns as state differences in autonomic function. Quiet sleep, in contrast to active...
sleep, has respiratory activity that is more regular, reflecting tighter control by brain stem mechanisms. In addition, inspection of our data (see Table 1) indicates similar differences in regularity of physiological activity. For example, heart period variability and the variance of the 5-s epoch-by-epoch values of RSA and heart period were significantly greater during active sleep.

When states of alertness and self-control wane, often they are replaced with disorganized, poorly planned behavior or drowsiness and sleep. The decrease in alertness is paralleled by a decrease in cortical regulation of the brain stem that is replaced by homeostatic regulation via subcortical structures such as the hypothalamus. The coupling between RSA and heart period may provide a noninvasive view of shifts in the cortical regulation of the brain stem. If the coupling between RSA and heart period is a reliable indicator of cortical regulation of brain stem structures, then noninvasive monitoring of heart period patterns may provide an accurate mechanism to monitor state and state regulation.

Consistent with the shift from cortical to hypothalamic control of visceral function during periods of decreased cortical activation, behavioral states associated with a loss of voluntary behavioral control may reflect a similar decoupling between cardiac vagal tone and heart period. Preliminary data from our laboratory support this contention (Rinio, Doussard-Roosevelt, & Porges, 1994). Ambulatory monitoring of heart period in adults over a 24-hr period demonstrated stronger correlations and steeper slopes between RSA and heart period during alert states. Correlations during drowsy and sleep periods were low, and during the early phases of sleep these correlations approached zero in some subjects. Additional research is needed to evaluate whether specific manipulations known to increase (e.g., stimulants) and decrease (e.g., depressants) cortical activation are manifested in the covariation between RSA and heart period. Similarly, EEG activity should be monitored to further link the coupling between RSA and heart period as an index of cortical activation.

This study extends the metaphor of the vagal brake from a tonic link between RSA and metabolic output (i.e., heart period or heart rate) in response to environmental challenge to a state-dependent index of the dynamic regulation of brain stem function by cortical neurons. Specifically, during active sleep, a state assumed to represent cortical regulation of brain stem structures, instantaneous changes in heart period were more coupled with changes in RSA. In contrast, during quiet sleep, when cortical activation is reduced and hypothalamic structures have been assumed to regulate brain stem structures, the coupling between RSA and heart period is significantly reduced. Thus, this study is the first demonstration that the dynamic relation between instantaneous changes in RSA and heart period is state dependent.

The findings that there are state differences in these cardiopulmonary variables may indicate that the assumed relations between RSA and heart period and between RSA and breathing frequency may be mediated by higher brain structures. For example, it has been assumed that when an individual is not under great metabolic demands, RSA (as an indicator of vagal tone) should be highly correlated with heart period. Inherent in this assumption is the complementary position that under metabolically conservative states such as quiet sleep the sympathetic contribution to the neural regulation of the heart should be minimal and relatively constant, so that under these neural constraints heart period should be a sensitive index of parasympathetic tone. Thus, based on this metabolic argument, higher correlations between instantaneous measures of RSA (as an indicator of vagal tone) and heart period would be hypothesized to occur during quiet sleep.

However, there is an alternative and plausible hypothesis based on the polyvagal theory and referenced to current knowledge of the neural regulation of the heart. The polyvagal theory, as extended here, places an emphasis on neural pathways (i.e., corticobulbar) that originate in the motor areas of cortex and regulate brain stem nuclei, including the nucleus ambiguus. Therefore, cortical activation would influence the regulation of vagal tone to the heart because the primary vagal fibers that regulate heart period originate in the nucleus ambiguus. In this model, the cortex would monitor visceral state and provide an immediate neural command to make instantaneous adjustments via dynamic shifts in the vagal control of the heart. Thus, the relation between RSA and heart period would be dependent upon cortical activation. Increased cortical activation during active sleep would be expected to be associated with a tighter coupling between RSA and heart period. This explanation is plausible only if it is assumed that the corticobulbar pathways, which regulate the dorsal subdivision of the nucleus ambiguus, have a reliable regulatory control over the visceromotor fibers originating in the ventral subdivision. The testing of this assumption is dependent upon future research in neuroanatomy demonstrating that specific corticobulbar pathways terminate in the ventral subdivision of the nucleus ambiguus and/or interneuronal pathways communicating between the dorsal and ventral subdivisions.

This study demonstrated that the covariation of the short epoch-by-epoch changes in RSA and heart period were maximized at a lag of 0, even with epochs as short as 2 s. Thus, it was established that the changes in RSA were associated with instantaneous changes in heart period. These findings may have a practical implication for future research evaluating the coupling between RSA and heart period. Because it is often difficult to obtain long segments of quiet sleep, these findings justify the calculation of this covariation within state, even when the periods monitored are not contiguous.

In summary, we tested a neurophysiological model that proposed that the dynamic coupling between RSA and heart period was influenced by the cortical activation associated with different sleep states. The model provides a plausible explanation that the state influences on the temporal relationship between RSA and heart period are mediated by cortical regulation of the nucleus ambiguus via corticobulbar pathways. The findings support the model. During active sleep, a state associated with cortical activation, the coupling was greater than that during quiet sleep, a state associated with decreased cortical activation and hypothalamic regulation. These findings emphasize the importance of conceptualizing the central mechanisms that mediate heart period patterns and demonstrate the unique sensitivity of RSA and the coupling between RSA and heart period as psychophysiological variables.

Future research applying the coupling variable as an index of cortical regulation of the heart should be conducted with concurrent EEG recordings to confirm this model. Application of this technology may provide important insights into clinical conditions that have been assumed to reflect a deficit in the central regulation of autonomic function, such as sleep disorders including risk for sudden infant death syndrome and those associated with behavioral or autonomic dysfunctions. For example, study of the coupling variable may provide a neurophysiological explanation of why episodes of apnea and bradycardia in high-risk preterm neonates are frequently observed in quiet sleep (Guilleminault & Souquet, 1979) and how theophylline (e.g., Uauy, Shapiro, Smith, & Warshaw, 1975) might reduce these episodes by enhancing cortical regulation of brain stem lower motor neurons, such as the nucleus ambiguus.
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