

Effect of mother's voice on neonatal respiratory activity and EEG delta amplitude

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Abstract

While the influence of the mother's voice on neonatal heart-rate response and its relevant activity on cerebral cortex and the autonomic nervous system (ANS) are well known, few studies have assessed its influence on respiratory activity. We investigated the relationship among the respiration rate, the delta wave amplitudes through electroencephalography, and the basal state of ANS through the respiratory variability index while 22 full-term neonates hear their mother's voice and an unknown voice. It was found that when respiratory variability was large, a transient (<5 s) change in respiration rates was observed in response to an unknown voice, while a greater increase in the delta wave amplitude was observed in the frontal lobe than the parietal one in response to the mother's voice. Conversely, when respiratory variability was small, a sustained increase (>10 s) in respiration rates was observed in response to the mother's voice, while a greater increase in the delta wave amplitude was found in both the frontal and parietal lobes. These results suggest that the basal state of ANS influences the latency of increases in respiration rates. Furthermore, induced by the mother's voice, transient increases in respiration rates are reduced in association with frontal lobe activity, and sustained increases in respiration rates are promoted in association with frontal and parietal lobe activities.

KEYWORDS

attention, autonomic nervous system, electroencephalography delta rhythm, mother's voice, respiration

1 | INTRODUCTION

The infant is constantly exposed to the mother's voice, beginning at a time when these vocal sounds and vibrations are conducted through the intrauterine environment to the fetus' developing auditory mechanisms (Abrams et al., 2016). Therefore, the mother's voice is an important sound that is established as the most familiar source for the neonate and facilitates even various motor behaviors in the neonates. Previous

behavioral studies on the non-nutritive sucking of 1-month-old infants (Mehler, Bertoncini, Barrière, & Jassik-Gerschenfeld, 1978) and neonates (DeCasper & Fifer, 1980) indicated that infants generally sucked more while hearing the mother's voice, compared to while hearing the voice of an unknown female. Other studies on the effect of mother's voice on cardiac activities reported that the heart rates of infants and fetuses showed a significant acceleration (or deceleration) in response to the mother's voice for 3-month-old infants (Katagiri & Kamikokuryo, 1987),

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for fetuses at 38 weeks of gestation (Kisilevsky et al., 2003; Smith, Dmochowski, Muir, & Kisilevsky, 2007), and for fetuses at 32–34 weeks of gestation (Kisilevsky & Hains, 2011). Recent studies reported a decrease in the occurrence of critical events, such as apnea (i.e., suspension of breathing) and bradycardia (i.e., unduly slow heart rate), among pre-term infants in the neonatal intensive care unit in response to the mother's voice (Doheny, Hurwitz, Insoft, Ringer, & Lahav, 2012; Filippa, Devouche, Arioni, Imberty, & Gratier, 2013). Such findings suggest that the mother's voice influences motor behaviors including heart rates and respiratory rates (RR; the number of breaths taken per minute).

The heart rates of infants and fetuses changed within 10 s after the onset or cessation of hearing the mother's voice (DeCasper, Lecanuet, Busnel, Granier-Deferre, & Maugeais, 1994; Katagiri & Kamikokuryo, 1987; Kisilevsky et al., 2009; Smith et al., 2007). Additional studies focused on stimulation-induced heart rate changes (with durations of 2–10 s) by applying various acoustic/visual stimuli, instead of exclusively using the mother's voice (Graham, Leavitt, & Strock, 1978; Ramírez, Sánchez, Fernández, Lipp, & Vila, 2005; Richards, 2003; Richards & Casey, 1991; Vila et al., 2007). Porges, Arnold, and Forbes, (1973) and Porges (1976, 1995) proposed a neural model to explain the differences in the latencies of heart rate changes due to stimulation. This model distinguished between two types of heart rate changes: a short latency of ≤ 6 s and a longer latency of > 6 s. The short latency responses (i.e., the transient responses) are considered as reflexive orienting responses to stimuli, mediated by the interaction between the sympathetic and vagal nerves of the autonomic nervous system (ANS) which regulates bodily function such as heart rate and respiration, while the long latency responses (i.e., the sustained responses) are considered as higher-level attentional responses to stimuli, mediated by the vagal nerves, and cortical functions. Smith et al. (2007) investigated that the relationship between the fetal heart rate and the state of vagal tone while hearing the mother's voice and an unknown voice. Here, the vagal tone means the activity of vagal nerve that decreases heart rates by inhibiting the natural pace maker tissue of the heart. According to Smith et al. (2007), a transient deceleration appeared in fetal heart rates in response to voice-stimulus onset under both high and low vagal tone states. After such deceleration, fetal heart rates sustainably increased under low vagal tones, whereas they did not increase under high vagal tones. This finding suggests that the state of the vagal nerve influences sustained changes in heart rates. Furthermore, Smith et al. (2007) reported a sustained decrease in fetal heart rates during high vagal tones (with a latency of approximately 10 s), in response to the offset of the mother's voice but not an unknown voice. This result suggests that sustained changes in heart rates are influenced not only by vagal tones but also by higher-level functions for auditory voice recognition, including attention. In fact, Richards (2003) reported that the components of electroencephalography (EEG), which reflect electrical brain activity associated with the attentional function, were amplified as the sustained heart rate responses to visual stimuli appeared in 4.5- to 7.5-month-old infants. More specifically, the negative central (Nc; with 450–550 ms latency after the stimulus onset) and positive slow wave (PSW; with 1,000–2,000 ms latency) components were amplified in the frontal and parietal lobes. Although no studies have ever investigated the relationship between EEG components and heart rates in infants

hearing their mother's voice, it can be stated that infants' cortical activities can influence the sustained heart rate responses.

While the influence of the mother's voice on infants' heart rate has been largely investigated, few studies have assessed its influence on RR. It seems natural that heart rates and RR improve at the same time while hearing the mother's voice, as both aspects are regulated by the same ganglionic nerves in the ANS. However, the ANS and cortical functions differentially regulate heart rates and RR in adults (Kreibig, 2010; Rainville, Bechara, Naqvi, & Damasio, 2006). Consequently, some changes in RR, due to voice stimuli (e.g., latency of changes in RR), may differ from the changes in heart rates. The investigation of the relationships among the latency of changes in RR, cortical activity, and the state of ANS using the mother's voice stimulus is important because it can confirm whether the cortical function and ANS regulate the RR in manner different from that of the heart rate regulation. Moreover, this investigation targeted at neonates will expand our understanding of the development of respiratory regulation by the reflexive orienting process or high-level processes such as attention and recognition. Therefore, the objective of this study was to investigate how neonatal RR are affected by the ANS and cortical functions in response to the mother's voice and an unknown voice.

For this objective, we needed some new measures which had not been used in previous studies introduced above. First, a new index for determining basal ANS states was needed. Smith et al. (2007) used the vagal tone index to determine the basal ANS states, and it was evaluated by the high frequency spectral component (HF, .2–.5 Hz) of the heart rate variability through the Fourier transform method (Äärimaa, Oja, Antila, & Välimäki, 1988; Akselrod et al., 1981; Fouad, Tarazi, Ferrario, Fighaly, & Alicandri, 1984). When attempting to understand how RR are affected by the basal ANS state in the present study, this state should be assessed according to the RR, rather than the heart rates because the ANS differentially regulates RR and heart rates. Instead of the cardiac vagal tone index, we evaluated the basal ANS state using respiratory variability (SDRR), which has been defined as one standard deviation (SD) of the RR in unit time (Etzel, Johnsen, Dickerson, Tranel, & Adolphs, 2006; Kreibig, 2010; Rainville et al., 2006). A larger SDRR indicates the influence of a "dynamic" basal ANS state on the RR, whereas a smaller SDRR indicates the influence of a "static" basal ANS state on the RR. Second, we needed another new measure to investigate the cortical functions related to the changes in RR. In the previous studies, slow latency components in several kinds of EEG such as Nc and PSW were measured as activities of the cortical attentional function (e.g., Richards, 2003; Siddappa et al., 2004; Therien, Worwa, Mattia, & deRegnier, 2004). These slow latency components correspond to the amplitude of EEG delta waves (.5–4 Hz). Therefore, this study examined the amplitude of EEG delta waves, which also reflect the cortical functions for attention (Del Giudice et al., 2016; Harmony, 2013; Harmony et al., 1996). Third, additional measures were needed to investigate how the SDRR was associated with the basal ANS state, which was determined on the basis of the heart rates. The length of the time series analyzed in the present study was too short to be applied to the Fourier transform method for the calculation of the cardiac vagal tone index used in Smith et al. (2007). Alternatively, the cardiac sympathetic index (CSI) and the cardiac vagal index (CVI) were

calculated, as proposed by Toichi et al. (1997). These indices were determined on the basis of the variability in the inter-beat intervals (IBI) of the heart, and the constraint of the length of the time series for this method was not as severe as that for the Fourier transform method. According to Toichi et al. (1997), the CSI reflects cardiac sympathetic nerve activity, and it is not affected by vagal activity. In contrast, the CVI is a sensitive index of cardiac vagal function that is not affected by sympathetic activity. Hence, in the present study, we analyzed the relationship between the SDRR and the CSI (or the CVI) and clarified the difference between the basal ANS state estimated by the RR and that estimated by the heart rates. Based on these new measures, the more specific objective of this study was to investigate how neonatal RR are affected by EEG delta wave amplitudes and the basal state of ANS through SDRR in response to the mother's voice and an unknown voice.

2 | METHODS

2.1 | Participants

The participants in this study were 22 full-term neonates with normal hearing (9 girls and 13 boys; mean gestational age: 39.0 weeks [range: 37–40 weeks]; mean birth weight: 3,028 g [range: 2,476–3,533 g]; mean post-conceptual age: 39.63 weeks [range: 38–41 weeks]). Written informed consent was obtained from the parents of the neonates. This study was approved by the Ethics Committee of Keio University Hospital (No. 20090189).

2.2 | Stimuli and procedures

Two different auditory stimuli were applied in this study: the voice of each participant's mother and that of an unknown female. Both voices were recorded by using a digital voice recorder. The voices of the participants' mothers were used as the unknown voices for the other participants, and the different unknown voices were used across participants to ensure that the observed effects were not due to specific acoustic characteristics of the voices but rather unfamiliarity. The mean \pm SD values of the following acoustic parameters were not significantly different between the mothers' voices and the unknown voices (*t*-test, $p > .26$): the total utterance durations of 30.74 ± 2.92 s (mother) and 30.95 ± 2.95 s (unknown); the mean intensity values of 69.15 ± 2.72 dB (mother) and 68.49 ± 4.24 dB (unknown); and the mean fundamental frequency values of 240.93 ± 20.29 Hz (mother) and 245.94 ± 18.87 Hz (unknown). All of the speech stimuli consisted of reading aloud a series of short sentences (from a Japanese original script) with the rich intonations of infant-directed speech (Cooper & Aslin, 1990). In addition, the stimuli were presented to the participants at an intensity level corresponding to a slightly louder voice than ordinary speech (68 dB) via two speakers positioned 45 cm away from the head. The duration of each stimulus was 15 s, with a 10-s silent inter-stimulus interval. In the experimental sessions, the mother's voice and an unknown voice were presented to the neonates in random order. The experiment was considered complete when at

least five trials of each stimulus condition were successfully performed without neonatal body movement or crying.

The experiments were performed in a testing room at Keio University Hospital, and the participants were tested 2–7 days after birth. During this study, chest respiratory movements, electrocardiograms (ECGs), and EEG were simultaneously recorded, while the neonates in the supine position were exposed to the voice stimuli. Moreover, limb movements were recorded in order to identify the artifacts caused by body movements. ECGs, EEG, and chest respiratory and limb movements were recorded by using a digital polygraph system (Polymate AP1132; TEAC, Tokyo, Japan), a respiratory inductance plethysmography belt (Perfect Fit; Dymedix, MN), and piezoelectric sensors (PRO-TECH, WA). Two electrodes, placed at scalp sites Fz-A2 and Pz-A2 (according to the International 10–20 system of electrode placement), were used to monitor EEG in the frontal and parietal areas. Previous studies identified these cortical regions as sensitive to the mother's voice (Beauchemin et al., 2010; Dehaene-Lambertz et al., 2010; Siddappa et al., 2004; Therien et al., 2004). Furthermore, each EEG electrode was linked to an earlobe reference electrode at A2, and these signals were sampled at 1,000 Hz and filtered with a 50- or 60-Hz notch filter to suppress noise from alternating current power sources.

2.3 | Data analyses

The representative data for signal preprocessing are shown in Figure 1. According to Figure 1a (upper panel), the chest respiratory movement signal was band-pass-filtered between .2 and 2.0 Hz and transformed into phase data by using the Hilbert transform method. In addition, the respiration cycle (i.e., the time interval between each breath) was determined from the phase data (Witte, Rother, Griessbach, & Eisel, 1991). This time course of the RR, given by the reciprocal transformation of the respiration cycle, was interpolated at .1-s intervals (Figure 1a, lower panel) and held at a uniform temporal resolution for subsequent averaging of the participants' data. The IBI was measured by using the R-wave in the ECG signal (Figure 1b). The EEG signals, obtained from Fz and Pz, were transformed into the time course of the instantaneous amplitude of the delta rhythms (1–4 Hz), which was referred to as the "IA δ " (Figure 1c). The IA δ was generated with a .1-s temporal resolution by using an analysis program (CDM trend play, NoruPro Light Systems, Tokyo, Japan) based on the complex demodulation method (Fan et al., 2007; Schroeder & Barr, 2000).

In order to measure instantaneous respiratory and neural responses for each voice stimulus, as well as evaluate respiratory and cardiac autonomic functions during stimulus presentation, time courses of the RR, the IBI, and the IA δ were segmented into 25-s blocks. Each block consisted of a 3-s silent period before stimulus onset (the end of the preceding inter-stimulus interval), a 15-s stimulation period (voice presentation), and a 7-s silent period after stimulation offset (the beginning of the inter-stimulus interval). However, an unusually large EEG amplitude (exceeding 90 μ V) was observed when the head and body of the participant strongly moved during the experiment. Thus, data blocks with an IA δ exceeding 90 μ V were considered erroneous and excluded from subsequent analyses.

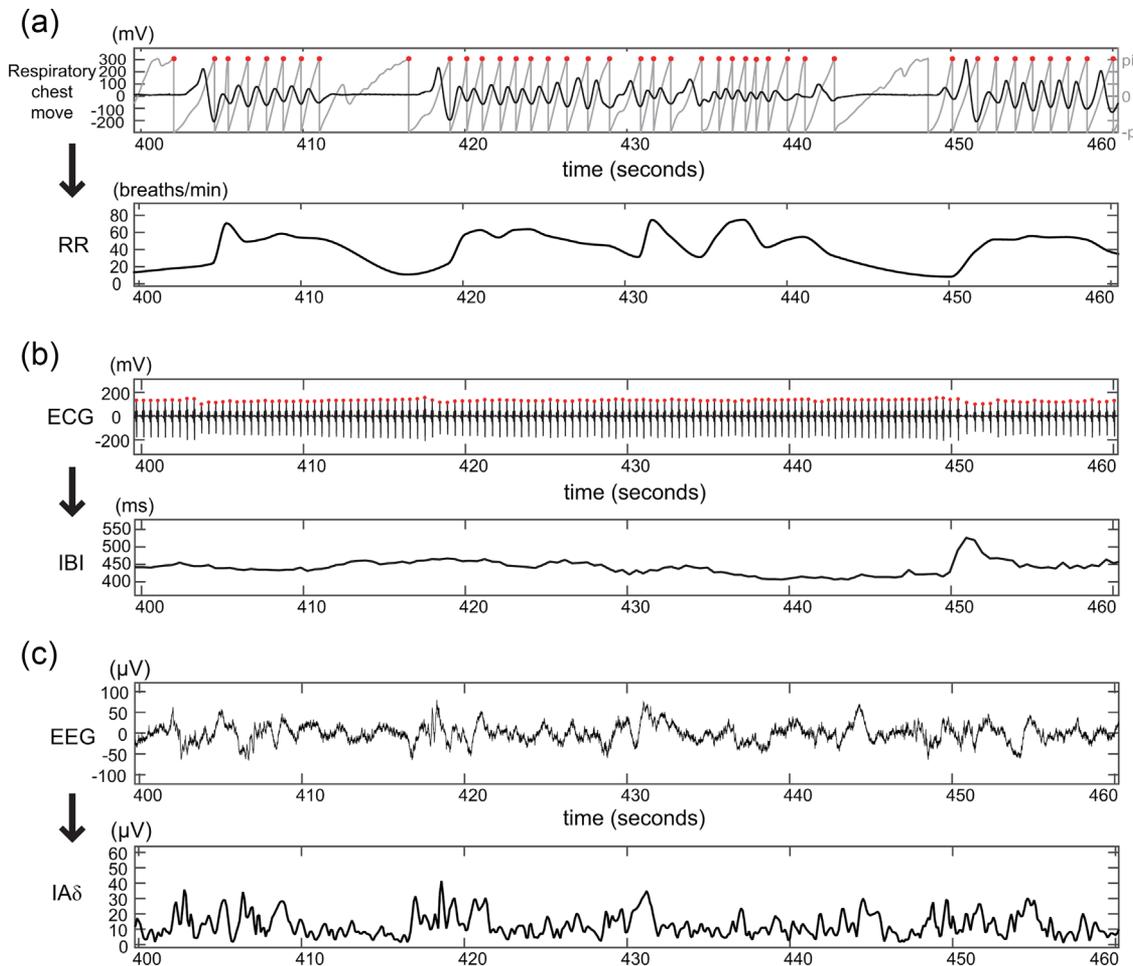


FIGURE 1 Examples of simultaneously recorded respiration, electrocardiogram (ECG), and electroencephalography (EEG) data. (a) Chest respiratory movements (black line) were transformed into phase data (gray line) and used in the Hilbert transform method to determine the respiration cycle (interval between neighboring red dots). The instantaneous respiration rates (RR), shown in the lower panel, were calculated from the respiration cycle. (b) The peaks (red dots in the upper panel) were detected by using the R-wave of ECGs, and the inter-beat interval (IBI) was calculated (lower panel). (c) The upper panel includes the raw EEG data collected at Pz. The data were filtered according to the frequency range for delta rhythms and transformed into the instantaneous amplitude (IA δ) shown in the lower panel

The respiratory and neural response patterns to the vocal stimuli varied, depending on the sleep-wake state and the basal ANS state. Thus, it was necessary to determine these states during the measurement and examine the respiratory and neural response patterns for each state. The sleep state was determined by the EEG patterns and the motor activity of the eyeballs and limbs by using the criteria of Anders, Emde, and Parmelle (1971) and Scholle and Schäfer (1999). All of the participants were asleep during the measurements. The sleep state of the participants was determined as “active sleep” because the EEG patterns were mainly composed of low-voltage irregular and mixed patterns, with occasional limb and eye movements. The basal ANS state was determined by using the SDRR as an index for evaluating respiratory autonomic functions (Etzel et al., 2006; Kreibig, 2010; Rainville et al., 2006). This index was defined as one SD of the RR in each block period, which reflects the variation in RR. Examples of the waveforms of the RR, with small and large SDRR, are shown in Figure 2. In the blocks with smaller SDRR (Figure 2a), the flat waveforms of the RR reflect a steady and sustained ANS state throughout the block period. Conversely, the

waveforms of the RR (especially in the blocks with larger SDRR) varied rapidly and transiently, suggesting a transient change in ANS activity (Figure 2b). In addition, the blocks were specifically classified into two types: blocks with an SDRR smaller than approximately 40% (2.5–42.5%), and blocks with an SDRR larger than 60% (57.5–97.5%).

We also compared the SDRR with the CSI and the CVI as cardiac autonomic functions. The CSI and CVI in each block period were calculated by using the method proposed by Toichi et al. (1997). More specifically, the sequence of IBI (l_1, l_2, \dots, l_n) in each block was transformed into a two-dimensional plane by plotting l_{k+1} against l_k (Figure 3), after which two components of the IBI fluctuation were calculated: the lengths of the transverse axis (T) and the longitudinal axis (L). The T and L were then calculated to four times the SDs of the plotted points along their axes, while the CSI and CVI were calculated in which $\text{CSI} = L/T$ and $\text{CVI} = \log_{10}(T \times L)$.

After sorting the block data, based on the SDRR, the respiratory and neural responses to the mother's voice and an unknown voice were examined. First, we investigated the average time-course

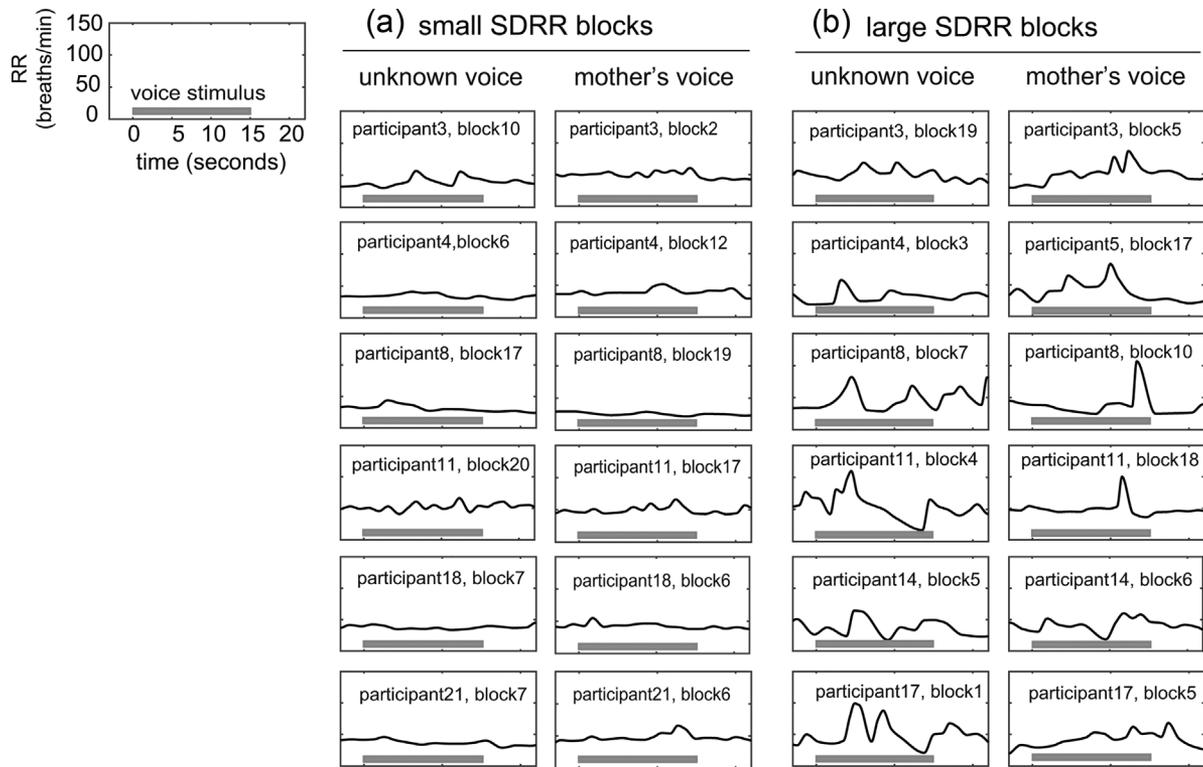


FIGURE 2 Block waveforms of the RR. One standard deviation (SD) of the RR was defined for each block, as respiratory variability (SDRR). (a) Samples from the small SDRR blocks. (b) Samples from the large SDRR blocks. The gray horizontal thick line between 0 s and 15 s at the bottom of each sample indicates the voice stimulus duration. Within (a) and (b), both an unknown voice (left column) and the mother's voice (right column) are presented

patterns of the RR for each SDRR type as well as each stimulus condition. The latency (t_{peakRR}) of the maximum peak was determined after the stimulus onset in the RR averaged the time course across all of the participants. Moreover, the changes in the RR, from the baseline to the peak (t_{peakRR}), were calculated for each block. In this regard, the "baseline" was the median rate during the 3-s period before stimulus

onset. In order to determine whether the amount of change from the baseline to the peak (t_{peakRR}) was significantly different from 0, the two-sided Wilcoxon signed-rank test ($\alpha = .05$) was conducted as a nonparametric test, especially as the data did not satisfy the normality.

Next, we investigated the significant differences in the $\text{IA}\delta$, as a function of the stimulus type (i.e., the mother's voice and an unknown voice) and the electrode locations (Fz and Pz) for each SDRR type. In each block, the maximum $\text{IA}\delta$ from the stimulus onset to t_{peakRR} ($\text{max-IA}\delta$) was measured. As the measured $\text{max-IA}\delta$ data did not satisfy the normality, the rank-based robust ANOVA test (Hettmansperger & McKean, 2011; Hocking, 1985) was conducted as a nonparametric test to determine the main effects and interactions in two-way factorial designs. Finally, effect size was calculated by using the equation: $r_{\text{es}} = Z/\sqrt{N}$, where Z and N represent the z-score and sample size, respectively (Field, 2005).

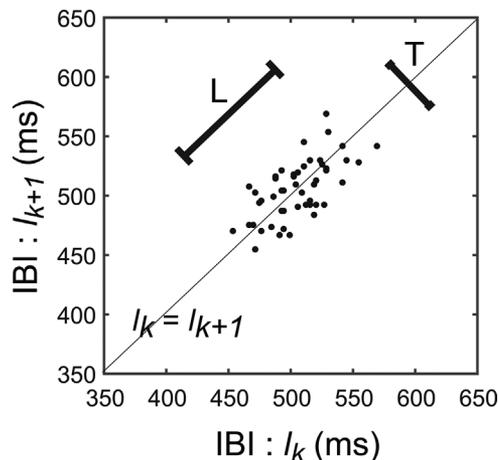


FIGURE 3 Lorenz plot of the IBI used to calculate the cardiac sympathetic index (CSI) and the cardiac vagal index (CVI). In this plot, the fluctuation of the IBI data was represented as lengths T and L . T reflects the beat-to-beat variations, while L reflects the variations in overall IBI amplitude

3 | RESULTS

Using SDRR index for evaluating respiratory autonomic functions, the blocks were separated into two groups: blocks with a SDRR smaller than 40% ($1.66 < \text{SDRR} < 6.57$) and blocks with a SDRR larger than 60% ($8.55 < \text{SDRR} < 19.62$). We compared the waveforms of the RR between the vocal stimuli for each SDRR type. In the small SDRR group, the average RR marginally increased, while the maximum peak (at a latency of 12.4 s) was significantly higher than the baseline average (Wilcoxon

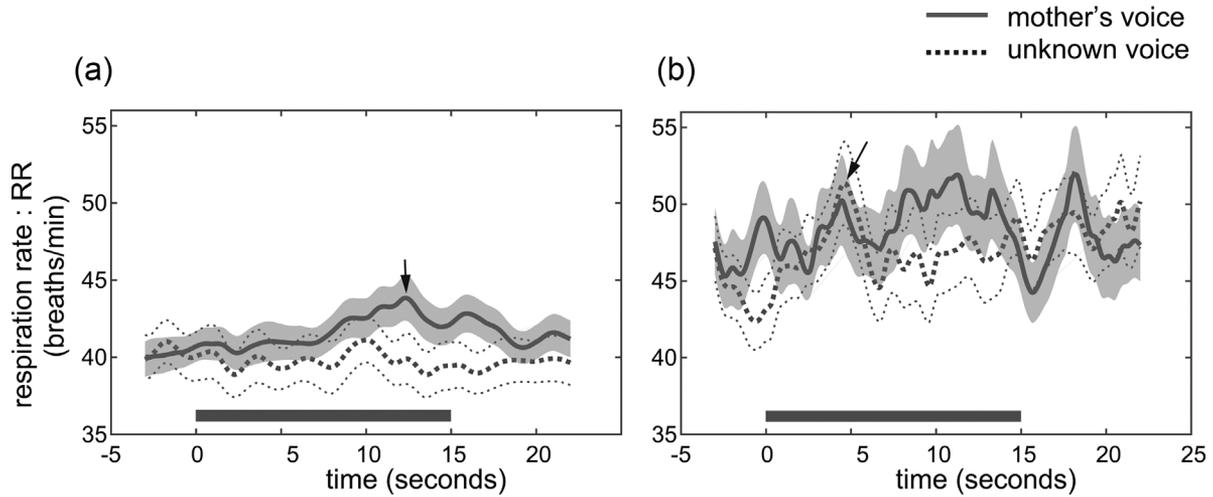


FIGURE 4 Average time courses of the RR for (a) small SDRR blocks and (b) large SDRR blocks. In (a), the maximum peak of the RR for the mother's voice condition (12.4 s), indicated with an arrow, was significantly higher than the baseline ($p < .05$). In (b), the maximum peak of the RR for the unknown voice condition (4.4 s), indicated with an arrow, was also significantly higher than the baseline ($p < .05$). The gray horizontal thick line between 0 s and 15 s at the bottom of (a) and (b) indicates the voice stimulus duration. The average time courses for the mother's voice condition are shown with a solid line, while the 95% confidence interval (CI) is shown as a gray shadow. The average time courses for the unknown voice condition are shown with a dashed line, while the 95%CI is shown as a thin dashed line

signed-rank test, $p = .028$, $r_{es} = .454$) when the participants listened to the mother's voice (Figure 4a). In the larger SDRR group, the average RR rapidly increased (with a maximum peak latency of 4.4 s), compared with the baseline average (Wilcoxon signed-rank test, $p = .0075$, $r_{es} = .570$), when the participants listened to an unknown voice (Figure 4b).

We also examined the effects of the voice stimuli and electrode locations on the max-IA δ . The max-IA δ was detected during the period from the stimulus onset (0 s) to t_{peakRR} (12.4 s). As shown in Figure 5a, there was a significant main effect of the stimuli (rank-based robust ANOVA, $p = .015$, $r_{es} = .309$), and the max-IA δ in the frontal and

parietal areas (Fz and Pz, respectively) were greater when the participants listened to the mother's voice than when participants listened to an unknown voice in smaller SDRR blocks. In larger SDRR blocks (Figure 5b), there were significant main effects of the stimuli (rank-based robust ANOVA, $p = .009$, $r_{es} = .304$) and the electrode locations ($p = .008$, $r_{es} = .304$), and the max-IA δ was higher in the frontal area (Fz) when listening to the mother's voice, compared to when listening to an unknown voice.

The number of participants and the number of blocks for each SDRR type are shown in Table 1. The means of the trial numbers

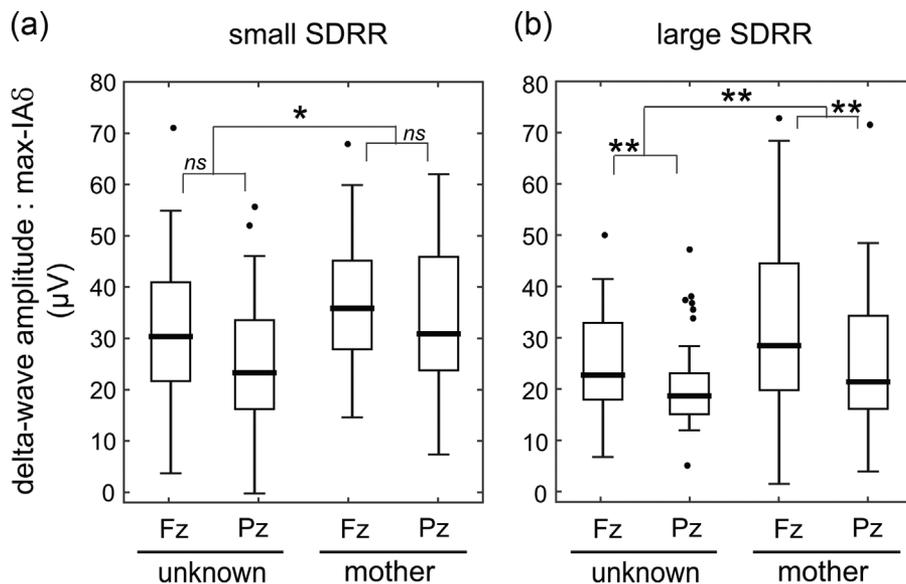


FIGURE 5 Effects of voice stimuli and electrode locations on EEG delta wave amplitude (max-IA δ). (a) Max-IA δ for small SDRR. (b) Max-IA δ for large SDRR. The boxes and error bars indicate the 25–75% range and the 3–97% range, respectively. The bold horizontal line in each box indicates the median max-IA δ for each condition, while the dots indicate the outliers. * and ** indicate statistically significant difference probabilities ($p < .05$ and $p < .01$, respectively)

TABLE 1 Sample numbers for each SDRR condition and voice stimulus

	Small SDRR		Large SDRR	
	Unknown	Mother	Unknown	Mother
Number of involved participants	14	14	14	15
Total trial number of all participants	43	47	44	47
Trial number per one participant (mean \pm s.d)	3.07 \pm 1.64	3.62 \pm 2.36	3.14 \pm 1.51	3.13 \pm 1.64

among the participants were not significantly different between the vocal stimuli (Wilcoxon rank-sum test, $p > .8$, $r_{es} < .04$).

The respiratory autonomic index of the SDRR functions highly correlated with the cardiac autonomic index of the CSI (Pearson's correlation coefficient, $r = .535$, $p < .0001$ for the mother's voice; $r = .594$, $p < .0001$ for an unknown voice) (Figure 6a) but not that of the CVI (Figure 6b). As shown in Figure 6c–e, the medians of the SDRR, CSI, and CVI did not significantly differ between the voice stimuli (Wilcoxon rank-sum test, $p > .21$, $r_{es} < .12$).

4 | DISCUSSION

The objective of this study was to understand how RR are affected by the basal ANS state and cortical functions when neonates hear the mother's voice and an unknown voice. To this end, we examined how RR is related to SDRR and EEG delta wave. As stated in the introduction section, changes in heart rates have been typically characterized as one of two types: transient changes with peak latency after stimulus onset of ≤ 6 s or sustained changes with longer peak latency (Porges, 1976, 1995; Porges et al., 1973). The present study demonstrated that the peak latency of changes in RR were also characterized into two types. The transient increase in RR appeared within a latency of approximately 5 s after the onset of an unknown voice in blocks with a large SDRR (see Figure 4b), and the sustained increase in RR appeared within a latency of 10 s after the onset of the mother's voice in blocks with a small SDRR (see Figure 4a). According to Smith et al. (2007), whereas transient changes in the heart rates appeared after the onset of mother's voice and an unknown voice during both high and low cardiac vagal tones, a sustained decrease in heart rates appeared only when fetuses heard the mother's voice during high cardiac vagal tones. A comparison between our results and that of Smith et al. (2007) suggests that transient changes in RR can be suppressed by hearing the mother's voice under the basal ANS state with large SDRR, whereas transient changes in heart rates occur irrespective of the voice stimulus and the basal ANS state.

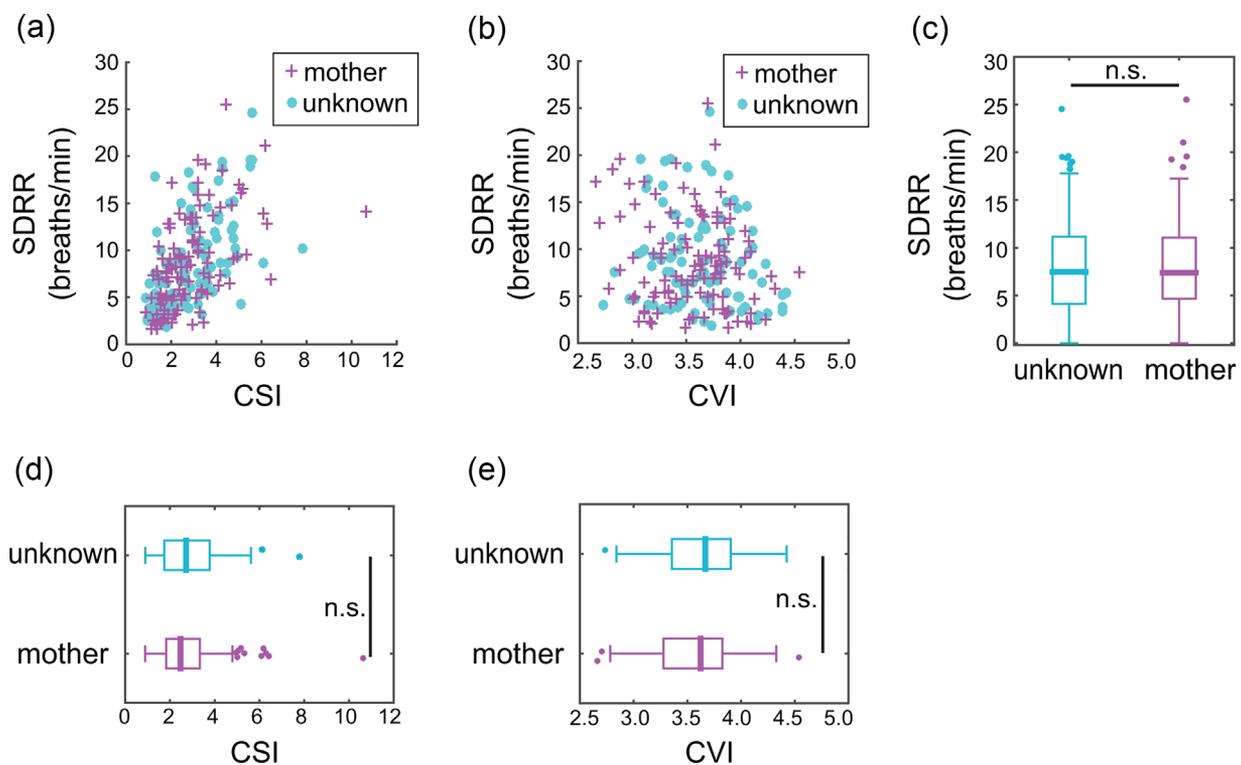


FIGURE 6 Correlation between the respiratory autonomic function index (SDRR) and the cardiac autonomic function indices (CSI and CVI). (a) The relationship between the SDRR and the CSI. (b) The relationship between the SDRR and the CVI. The magenta crosses and cyan circles indicate the mother's voice and an unknown voice, respectively. The SDRR did not significantly correlate with the CVI, whereas the SDRR showed a positive correlation with the CSI under both voice conditions. The autonomic function index of SDRR (c), the CSI (d), and the CVI (e) did not differ between the vocal stimuli. The boxes and error bars indicate the 25–75% range and the 3–97% range, respectively. The bold line within each box indicates the median, while the dots indicate the outliers

Additional comparison of these results indicates that sustained changes in both RR and heart rates are frequently formed by mother's voice under the basal ANS state with small SDRR and high cardiac vagal tones. Similar sustained changes in RR appear during various cognitive tasks, including the discrimination task of speech stimuli for neonates (Fifer & Moon, 1994) as well as the attention task for adults (Vlemincx, et al., 2011). Hence, sustained changes in RR may be associated with the voice recognition function and attention processes, which are facilitated by hearing familiar voice.

Next, we investigated the relation between the basal ANS state and EEG delta wave amplitudes ($\max\text{-IA}\delta$) in the frontal (Fz) and parietal (Pz) areas while hearing the mother's voice and an unknown voice. As shown in Figure 5, the $\max\text{-IA}\delta$ in these areas varied widely, and the sample size was not large enough to detect clear differences between the voice stimuli and the cortical areas. However, the $\max\text{-IA}\delta$ showed a significantly greater increase when the neonates heard the mother's voice, rather than when they heard an unknown voice, in each condition of large SDRR and small SDRR. This significant increase in $\max\text{-IA}\delta$ appeared in both the frontal and parietal lobes during small SDRR. However, it appeared more frequently in the frontal area than in the parietal area during large SDRR. These results suggest that a functional difference occurs between the frontal and parietal areas, depending on the basal ANS state. Sustained increases in RR to mother's voice during small SDRR may be associated with the function of both frontal and parietal cortices. On the other hand, suppressed transient changes in RR to the mother's voice during large SDRR may be associated with the function of the frontal cortex. Siddappa et al. (2004) and Therien et al. (2004) reported that, for pre-term infants at a menstrual age of 38–42 weeks, both of the frontal and parietal areas showed an increase in the PSW component (which matches the delta wave component) when hearing the mother's voice. Beauchemin et al. (2010) reported that, for neonates, the positive mismatch negativity, with 100–525 ms latency (including the delta wave component) in the frontal and parietal areas, was higher for the mother's voice than for an unknown voice. They interpreted the frontal and parietal lobes were involved in the voice recognition or attention processes. The results of the present study are consistent with these previous findings, based on the increase in the delta wave amplitude in the frontal and parietal areas while hearing mother's voice. Additionally, our present study indicated that this phenomenon appeared during small SDRR. Thus, we speculated that the basal state of ANS with small SDRR would promote the activity of frontal and parietal cortices associated with the voice recognition and attention processes.

However, the present study indicated that the delta wave component was amplified more in the frontal area than in the parietal area, while hearing the mother's voice under the condition of large SDRR. Thus, it is important to explain the functional difference between the frontal and parietal areas. In previous studies that focused on functional magnetic resonance imaging (fMRI) and used near-infrared spectroscopy (NIRS) to record the hemodynamic changes in the brain during electrical activity, the infants' cortical areas responsible for the recognition of the mother's voice were examined. More specifically, the medial prefrontal and orbitofrontal cortices related to emotion processing showed a stronger hemodynamic

response to the mother's voice among 2-month-old infants in a fMRI study (Dehaene-Lambertz et al., 2010) and 6–9-month-old infants in two NIRS studies (Imafuku, Hakuno, Uchida-Ota, Yamamoto, & Minagawa, 2014; Naoi et al., 2012). In adults, the medial prefrontal cortex played roles in the autonomic regulation and representation of somatic-emotional states in two additional fMRI studies (Critchley, Corfield, Chandler, Mathias, & Dolan, 2000; Lane, Reiman, Ahern, & Thayer, 2001). Increased delta amplitude was observed in the frontal area during the passive task of perceiving angry voices and in the parietal area during the active task of paying attention to angry voices among adults (Del Giudice et al., 2016). Increased delta amplitude in the frontal area is associated with inhibition of sensory afferents that interfere with internal concentration (Harmony, 2013; Harmony et al., 1996). No studies have investigated the development and functional specialization of emotional-voice recognition functions in the frontal cortex of neonates (e.g., Lagercrantz & Changeux, 2014; Leppänen & Nelson, 2009). No studies have reported that the EEG delta wave index in the neonatal frontal area is associated with attentional or orienting process. Yet, we speculated that the neonatal increased delta amplitude observed in the present study reflects the inhibition of sensory afferents in the frontal lobe. In addition, the delta wave amplification in the frontal area was accompanied by an inhibited transient increase in RR when hearing the mother's voice during large SDRR. This result raises the possibility that the neonatal frontal cortex regulates the orienting response of RR depending on the basal ANS state.

In the present study, to more explicitly investigate the basal ANS state derived from the RR in relation to that from the heart rates, the CSI and the CVI (Toichi, Sugiura, Murai, & Sengoku, 1997) were derived from the heart rates for each block. The findings show that the SDRR was highly correlated with the CSI but not the CVI (see Figures 6a and 6b). This result suggests that a larger SDRR (or smaller SDRR) indicates a basal state when the RR are more strongly (or less strongly) influenced by the sympathetic nerve and that SDRR does not reflect vagal nerve activity. Thus, the basal state of sympathetic nerve, rather than the vagal tone condition, maybe a factor contributing to the suppression of transient changes in RR while hearing the mother's voice. Beyond that, we found that the SDRR did not differ between the two stimulus conditions, i.e., hearing the mother's voice or an unknown voice (see Figure 6c). Thus, we interpreted that the SDRR was used as a reliable and voice-independent index of the respiratory basal ANS state, specifically indicating the sympathetic nerve activity.

Finally, we demonstrated that the transient or sustained changes in RR which appear depending on the familiarity of voice stimuli were associated with the activity of the frontal and parietal cortical region and the basal state of the sympathetic nerve. These unprecedented and significant findings contribute to our knowledge of the respiratory responses of infants to the mother's voice.

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