Stress Brain and Behavior
Regional "Stress and Behavior" ISBS Conference
Vol.1, e019006, 2019
Journal homepage: www.isbsjapan.org

Research article

Preterm infant vocal behavior and SpO2, pulse rate modulation in neonatal intensive care unit

Ting Tao[1-2], Hayato Sakurai[2], Hiroko Kakei[2], Kayo Morita[2], Masakazu Honda[2], Yoshimasa Kamei[3], Hideo Yamanouchi[2], Tetsuya Kunikata[1], Mamiko Koshiba[1-2*]

[1] Graduate School of Science and Technology for Innovation, Yamaguchi University, Yamaguchi, Japan
[2] Department of Pediatrics, Saitama Medical University, Saitama, Japan
[3] Department of Obstetrics and Gynecology, Saitama Medical University, Saitama, Japan

Abstract

Background: The Japanese premature delivery number still keeps high and the preterm infants must be exposed absolutely different circumstances from the fetuses. In our neonatal intensive care unit (NICU), we focused on preterm infants' vocal behaviors in an incubator, expected possibly spontaneous nonverbal signals of the patient's general conditions and emotion. To seek any significant correlation in the vocal behaviors with the common markers of pathological physiology, this case study with a randomly selected participant was designed to compare the vocal behavior variation with oxygen saturation percentage (SpO2) and pulse rate (PR) longitudinally for several days, and to explore any modulation during feeding and clinical caring events.

Method: We complied with the approved contents by Institutional Review Board (IRB) Committee. Data from a preterm infant (weight: 1644g, height: 40.4cm, gestational age / recording corrected age: 31 weeks 5 days / 33 weeks 5 days to 34 weeks 2 days, born in July, 2017) were acquired by the longitudinal detector system. Acoustic data (sample rate 24 kHz) were analyzed by sound frequencies to identify crying and caring (suction in this case). SpO2 and PR were monitored at a limb.

Results and discussion: Acoustic frequency identification visualized the sounds over 500 Hz seemed intermittently repeated per appropriately three hours, like a life rhythm of crying during cares and intervention. Considering the mutual correlation in the serial peaks of "Cry", SpO2 and PR, it seemed all of them synchronized one another. SpO2 and PR tended to decrease and increase during crying, respectively. These trends in the patient suggested that there seemed three sequential states, "Stable", "Unstable" and "Recovery". In "Unstable" state, the periods between two adjacent peaks got longer and more variable. SpO2 histogram distribution shifted to suppression significantly in "Unstable" states. To screen causal possibilities, peak timing between "Cry" and either SpO2 or PR appeared simultaneous in "Stable" but the SpO2 and PR delayed to "Cry" in "Unstable" and "Recovery" states. These preliminary hypothetic results should be furthermore investigated to develop diagnostic intelligence by longitudinally monitoring of behavioral and physiological signals.

Keywords: Preterm infant, vocal behavior, oxygen saturation (SpO2), pulse rate (PR), Neonatal intensive care unit (NICU), developmental disorders.

Article history:
Received 7 September 2018
Received in revised 8 February 2019
Accepted 18 February 2019

*Open Access paper (available freely at www.isbsjapan.org)
*Corresponding author: Dr. Mamiko Koshiba, PhD, ISBS Fellow. Address: Yamaguchi University, 2-16-1, Tokiwadai ube-shi, Yamaguchi, 755-8611, Japan. Phone: +81-836-85-9814 or 9817; E-mail: koshiba@yamaguchi.ac.jp

1. Introduction

Every year, an estimated 15 million babies are born preterm (before 37 completed weeks of gestation) or low birth weight (less than 2500 grams), many survivors face lifetime of disabilities, including learning disabilities and visual and hearing problems [1]. The advances in neonatal medical treatment and nursing have significantly reduced the mortality rate from 55.3% (1980) to 15.2% (2000) in extremely low birth weight infants (500 g to 999 g) and from 20.7% (1980) to 3.8% (2000) in very low birth weight infants in Japan [2-3]. The prematurity has been reported its high risk of neurodevelopmental disorders including behavioral, cognitive and psychological impairments [25-28]. Early developmental intervention in NICU has been highlighted on preventative effect to these impairments [29-31].

Our previous studies in comparative biology described the essential bio-mechanisms of susceptible period learning for the neuronal development in specific infantile terms [4-13, 22-24]. The neuronal circuit formation in the earlier stages crucially affect physiological and psychological function including social adaptation in the latter stages [32-34]. The critical period learning systems have been addressed the regulation mechanisms by complex interaction between genetic and environmental factors. In particular, it was well-studied that sensory environments significantly impact the basic neuronal developments [4,5,7-16]. To consider preterm infant’s functional intervention in the NICU environments, quantitatively and comprehensively diagnostic approaches with physiological and behavioral monitoring have many clinical potentials for the next generation of preventative treatment [9, 35-37].

In the current study, we suggest a daily diagnostic monitoring system quantitatively in a NICU incubator by co-analyzing a preterm patient’s behaviors, physiological and the surrounding environments. We explored to infer the patient’s clinical condition featuring his/her vocal behavior, particularly “cry” that is supposable as his/her spontaneous expression of negatively emotional signals. The sound data in a NICU incubator were recorded for five days, followed by screening of the characteristic frequencies to discriminate the patient’s crying behaviors. We further searched SpO2 and PR correlation with respiratory relevant behavior, crying. Pulse oximeters display both vital signs, SpO2 and PR, expressing respirator, neurological or any other disorder problems with diagnostic algorithms in newborns [20-21]. They have become generally critical tools in determining need for oxygen in sick newborns. Routine use of these tools may also aid identification of infants with clinically unrecognized respiratory abnormalities, making it necessary to establish pulse oximeter performance in the neonatal population [19].

2. Methods

2.1. Participant and Measurements

We complied with the approved contents by Saitama Medical University Hospital Institutional Review Board (IRB) Committee. A male participant whose parents agreed was randomly selected for this case study in very preterm patients (28~31 weeks). His birth weight/height and gestational week-age/recording corrected age were 1644g/40.4cm and 31 weeks 5 days / 33 weeks 5 days to 34 weeks 2 days. We observed from July 21st to 25th in year 2017.

2.2. Measurements and data analysis

The acoustic data were longitudinally acquired by a sound level meter (Rion NL-42, Japan, sample rate 24 kHz) in the closed incubator, under non-contact and non-invasive condition. The SpO2 and PR data at the limb were simultaneously recorded by a clinical pulse oximetry system (N-BSJ, Convidien Nellcor). The sound data collected from preterm infants’ data were performed automatic frequency analysis by Matlab customized application. We preliminarily visualized the original sound wave forms of typical “Cry” normalized to scale of [-1, 1] (Figure 1(a)) and processed them into harmonic spectrogram components in the time-frequency graph by fast Fourier transform (FFT) analysis, (Figure 1(b)). Based on our confirmation of the first components generally around 500Hz (a red arrow in Figure 1(b)), the sound over 500Hz was processed by the 6th-order Butterworth high-pass filter, mostly regarded as “Cry” behavioral expression.

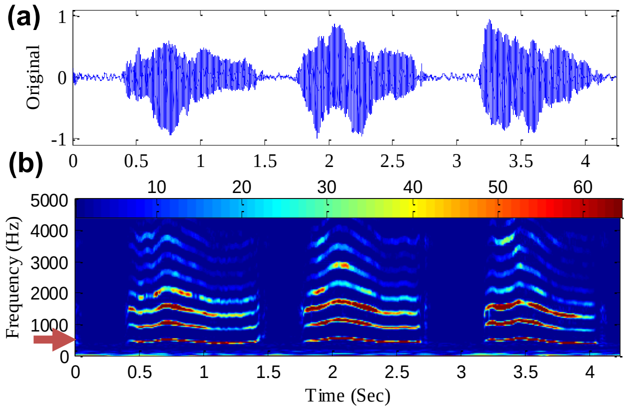

Figure 1. The “Cry” wave forms and the harmonic spectrogram examples of the preterm infant in time-domain and spectrogram.
Note an arrow at 500 Hz around the first component for “Cry” differentiation.

To eliminate further interference noises, the collected duration of sound presence over the minimum threshold, determined from the average per 600 seconds was expressed in a trend graph (Figure 2(a)). To ensure accuracy of this sound detection, we checked the sound data acoustically by our ears.

The SpO2 and PR were simultaneously monitored at the patient’s limb per 4 seconds by a pulse oximeter (Convidien Nellcor) and were made line graphs per 600 seconds (Figure 2(b, c)).

The sound presence duration peaks more than 100 seconds were visually defined and numbered in Figure 2(a).

2.3. Statistics

We used One-way ANOVA (ANalysis Of VAriance) with post-hoc Tukey HSD (Honestly Significant Difference) Test Calculator by R language (Version: R x64 3.5.1, Platform: x86_64-w64-mingw32/x64 (64-bit)). This test is a post-hoc test based on the studentized range distribution, can be used to compare 'Stable', 'Unstable' and 'Recovery' states, to find out which specific group's means (compared with each other) are different. The test compared all possible pairs of means. The statistics results of SpO2 and PR differences in the three states were summarized in Table 2.

3. Results

Figure 2 expresses the longitudinal trend results of the sound presence duration (a) with both the SpO2 (b) and PR (c) recorded from the preterm infant cared in a NICU incubator during the five admitted days. The analyzed sound trend firstly seems rhythmic with peaks repeated intermittently per appropriate 180 minutes from 21st to the morning of 23rd and 25th but not from the afternoon of 23rd to 24th. We acoustically confirmed the peaks mostly derived from the infant's crying voice ("Cry"), partially including environmental sounds that were mainly of suction cares given by the nurse at feeding per three hours. Furthermore, the SpO2 and PR trend peaks generally appeared mutually syntonic and well-correlated reciprocally and directly with the "Cry" presence duration peaks, respectively (Figure 2). The summaries of means ± variances in periods between adjacent peaks of "Cry", the values of SpO2 and PR were 2.8±0.5 [hour], 97.73±2.60 [%] and 165.41±11.62 [bpm], respectively. Meanwhile, the trends of "Cry" and SpO2 possibly suggested three different states, as "Stable", "Unstable" and "Recovery" in turn in Figure 2.

In order to investigate the relevance of the crying behavior with SpO2 and PR, we numbered the "Cry" major peaks more than 100 seconds serially from No.1 to 27 (Figure 2(a)). To consider the causal sequence between vocal behavior, "Cry" and physiological parameters, SpO2 and PR, we compared the peak timing difference as delays of SpO2 ($D_{SpO2\text{-}Cry}$) or PR ($D_{PR\text{-}Cry}$) from "Cry" (Table 1) in the three states. In result, we found the "Cry" peaks almost occurred simultaneously with SpO2 and PR peaks in the stable state, however, afterwards in the unstable and recovery states, the "Cry" peaks occurred generally more than 10 minutes before SpO2 or PR peaks. Concerning the frequency period of peaks' occurrence of "Cry", SpO2 and PR, it was suggested around 180 minutes, i.e., near three hours, with the variances about 20 minutes in the stable and recovery states, whereas, longer than three hours (near 200 minutes) with much longer variances during the unstable state.

In further to characterize SpO2 and PR in these three states, we summarized the peak value distribution histograms in Figure 3 and the P-values of One-way ANOVA with post-hoc Tukey HSD test in round robin state comparison in Table3. Consequently, SpO2 value distributions in 85-100% contributed to significant difference (P-value<0.05) in comparisons of "Recovery"-"Unstable" and "Stable"-"Unstable". The patient's notable symptoms were confirmed in the clinical logs as stridor, nasal obstruction, stertor sound and retractive breathing in the unstable state at ① and ② of Figure 2.

To search any environmental factors to induce the crying behaviors, we listened to all the original audio files at each peak (No.1~27), and confirmed this patient's crying mostly accompanied by the initial suction sound, with the crying voice lasting for a while frequently after the suction ended.

4. Discussion

The nonverbal expression "Cry", expected as a certain emotional and socio-functional signal in distress [38-39] were attempted to be utilized for the preterm infant's diagnostic intelligence with seeking physiological evaluation in the current clinical report. Frequency filtering trials in the longitudinally recorded sound data, enabled us to elucidate appropriately 180-minute (3-hour) periodic modulation in the NICU incubator in the frequency window over 500 Hz. We acoustically confirmed the peak sound sources were dominated by the infant's crying voices with the nurse's initial sucking at feeding, generally per 3 hours consistently with convention [40]. That said, to hear the self-crying sound and to receive cares led the preterm infant meet much different experiences from the same aged normal fetuses during interactively learning period in the surrounding environments [4-13, 22-24]. For instance, there must be crucial difference of acoustic environments for preterm infants from fetuses at high-frequency sound reduction over 500Hz, that occurred supposedly by uterine structures [16-18]. Since the early developing brainstem dysfunction was reported relevance to later behavioral inhibition as a risk factor for developmental psychopathology [41], the current behavioral, emotional and acoustic environmental monitoring technology may contribute to its preventive intervention for the fundamental neurodevelopment in NICU [42-44]. Simultaneously, this technology has a potential to visualize holistic rhythmicity in life environments and biological functions [45, 47] by the simple methodology. One of the representative early life event rhythms is oral feeding, generally per 3-4 hours [46] during initial development of circadian time-keeping neuro-mechanisms to influence high-risks of psychiatry or any diseases in later life [48].

The current investigated relations between the possibly identified crying behaviors and oxidative saturation and pulse rates significantly suggested hypothetical dependency on the preterm infant's clinical conditions. It was defined as three serially different states, "Stable", "Unstable" and "Recovery" by comparing each period between two adjacent peaks of Figure 2 (Table 1,2 and Figure 3). The peak timing analysis of respiratory-dependent behavior "Cry" with cardiovascular and respiratory parameters SpO2/PR further visualized more than ten-minute delay of SpO2/PR peaks after "Cry" in the 'Unstable" and "Recovery" states. This result might inspire a certain biological intermodulation due to developmental or etiological mechanisms [49-53]. Concerning the neonatal OxyCardioRespiroGram, it is simultaneously recording of respiration rate, respiration waveform, instantaneous heart rate, transcutaneous oxygen tension, and relative skin perfusion or "blood flow" from newborn infants [54]. If the OxyCardioRespiroGram is added for the current vocal behavior monitoring evaluation, it must support to obtain the various useful signals.

Such monitoring of multiple kinds of parameters and their mutual correlation with vocal behaviors and physiology may be supportive for novel clinical comprehension in unknown preterm processes much differently from full-term ones [55].

5. Conclusion

The current preliminary evaluation report of longitudinal monitoring system with the preterm infant would attribute to propose a non-invasive intelligence possibility for high-risk premature infants' developmental diagnosis and future preventive treatments although further investigation and analyses should follow in multiple and variable cases.

Figure 2. A preterm infant's vocal behaviors and SpO2, PR modulation in NICU for 4 days (21st ~25th).
(a) Sound presence duration, mainly vocal behavior "Cry", (b) SpO2, (c) PR. According to the trend intermodulation in "Cry" and SpO2, it was tentatively divided into three different states, "Stable", "Unstable" and "Recovery" in each green dotted box. Notable symptoms: ①Wheezing and nasal obstruction at 22:00 on 23rd. ② Retractive breathing and obvious constriction sounds, SpO2 decrease in spite of nasal high flow (NHF) setting at 1:30, 7:59, 15:59 on 24th . ③ SpO2 recovers and stertor sound disappeared after using 30% of oxygen at 16:20 on 24th

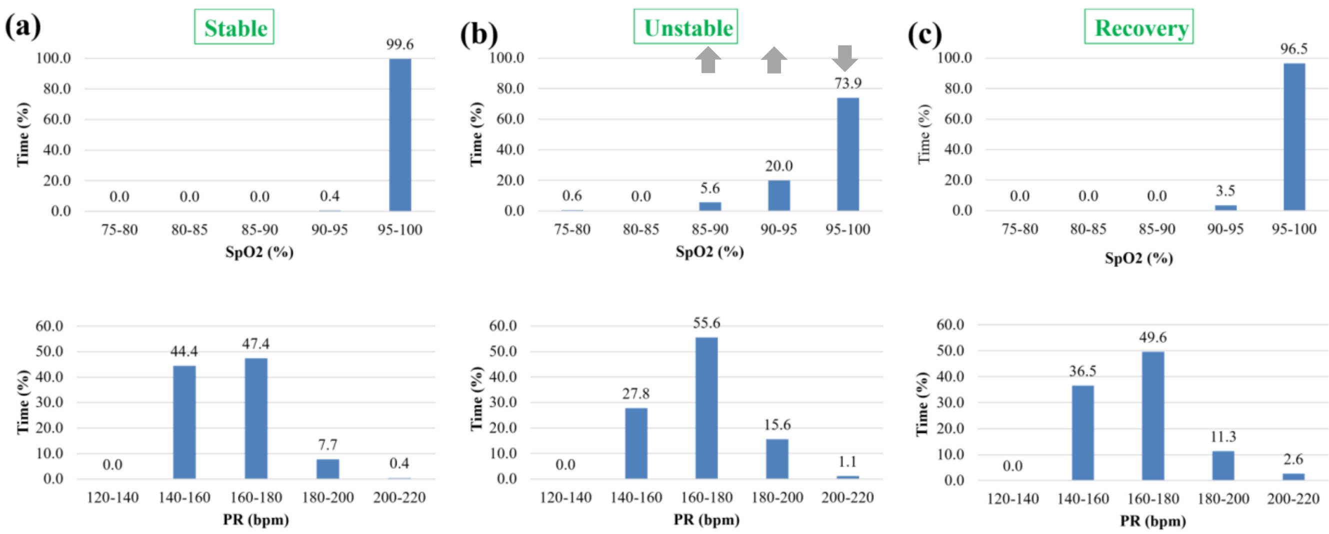

Figure 3. SpO2 and PR distribution histograms in the three states, "Stable", "Unstable" and "Recovery".
In "Unstable" state, SpO2 distributions of 95~100 [%] decreased and ones of 85~95 [%] increased significantly (gray arrows in (b)) while PR histograms expressed no significant changes.

Table 1. The peaks' time of crying, SpO2 and PR under three states

States	Peak No.	Peak time [*10 minutes]			Difference of peak time [*10 minutes]			Delay time [*10 minutes]	
		Cry	SpO2	PR	Cry	SpO2	PR	$D_{SpO2-Cry}$	D_{PR-Cry}
Stable	1	35	36	36				1	1
	2	52	52	52	17	16	16	0	0
	3	73	72	71	21	20	19	-1	-2
	4	89	89	89	16	17	18	0	0
	5	110	111	111	21	22	22	1	1
	6	125	125	126	15	14	15	0	1
	7	143	142	143	18	17	17	-1	0
	8	161	160	161	18	18	18	-1	0
	9	180	180	179	19	20	18	0	-1
	10	197	197	197	17	17	18	0	0
	Mean				18.0	17.9	17.9	-0.1	0.0
	Stdv				2.1	2.4	2.0	0.7	0.9
Unstable	11	269	267	269	72	70	72	-2	0
	12	286	286	286	17	19	17	0	0
	13	307	311	307	21	25	21	4	0
	14	324	325	325	17	14	18	1	1
	15	338	340	340	14	15	15	2	2
	16	346	346	347	8	6	7	0	1
	17	352	353	353	6	7	6	1	1
	18	362	363	363	10	10	10	1	1
	19	379	379	381	17	16	18	0	2
	20	399	402	401	20	23	20	3	2
	Mean				20.2	20.5	20.4	1.0	1.0
	Stdv				18.9	18.5	18.9	1.7	0.8
Recovery	21	415	418	416	16	16	15	3	1
	22	431	431	432	16	13	16	0	1
	23	448	450	449	17	19	17	2	1
	24	467	471	468	19	21	19	4	1
	25	485	487	487	18	16	19	2	2
	26	502	504	504	17	17	17	2	2
	27	521	524	524	19	20	20	3	3
	Mean				17.4	17.4	17.6	2.3	1.6
	Stdv				1.3	2.8	1.8	1.3	0.8

Table 2. The SpO2 and PR differences in the three states analyzed by One-way ANOVA with post-hoc Tukey HSD Test.

P-value	SpO2(%)					PR(bpm)				
	95~100	90~95	85~90	80~85	75~80	200~220	180~200	160~180	140~160	120~140
Recovery-Unstable	0.00002*	0.00203*	0.04938*	-	0.51544	0.89277	0.84698	0.76405	0.80941	-
Stable-Unstable	0*	0.00001*	0.01890*	-	0.40623	0.72736	0.17455	0.46082	0.13286	-
Stable-Recovery	0.33918	0.33035	1	-	1	0.48422	0.53682	0.93765	0.50097	-

- ;no data, *; significant (p<0.05).

Conflict of interest

The authors declare no conflicts of interest

Acknowledgements

This research was supported by JSPS (P16307, 5J06978, 17K18648, 25282221, 21200017, 25119509), JST-ALCA, JST-a-step and SCOPE. We would like to thank all the doctors and nurses from Saitama Medical University Hospital for their assistances.

References

[1] Hamilton, B., Martin, J., Osterman, M., Curtin, S., Mathews, T. Births: Final Data for 2014. *Natl Vital Stat Rep* **64**, 1-63 (2015).

[2] Horiuchi, T., Itani, Y., Ohno, T. Studies on the States of Care for High Risk Neonates and Neonatal Mortality in Our Country (year 2000). *The Journal of the Japan Pediatric Society* **106**, 603-613 (2002).

[3] Shimizu, A., Matsuo, H. Sound Environments Surrounding Preterm Infants Within an Occupied Closed Incubator. *Journal of Pediatric Nursing* **31**, 149-154 (2016).

[4] Senoo, A., Okuya, T., Sugiura, Y., Mimura, K., Honda, Y., Tanaka, I., Kodama, T., Tokuno, H., Yui, K., Nakamura, S., Usui, S., Koshiba, M. Effects of Constant Daylight Exposure during Early Development on Marmoset Psychosocial Behavior. *Progress in Neuro-Psychopharmacology & Biological Psychiatry* **35**, 1493-1498 (2011).

[5] Koshiba, M., Shirakawa, Y., Mimura, K., Senoo, A., Karino, G., Nakamura, S. Familiarity Perception Call Elicited under Restricted Sensory Cues in Peer-social Interactions of the Domestic Chick. *Plos One* **8**, 1-8 (2013).

[6] Mimura, K., Nakamura, S., Koshiba, M. A Flexion Period for Attachment Formation in Isolated Chicks to Unfamiliar Peers Visualized in a Developmental Trajectory Space through Behavioral Multivariate Correlation Analysis. *Neuroscience Letters* **547**, 70-75 (2013).

[7] Koshiba, M., Karino, G., Senoo, A., Mimura, K., Shirakawa, Y., Fukushima, Y., Obara, S., Sekihara, H., Ozawa, S., Ikegami, K., Ueda, T., Yamanouchi, H., Nakamura, S. Peer Attachment Formation by Systemic Redox Regulation with Social Training after a Sensitive Period. *Scientific Reports* **3**, 1-10 (2013).

[8] Koshiba, M., Senoo, A., Mimura, K., Shirakawa, Y., Karino, G., Obara, S., Ozawa, S., Sekihara, H., Fukushima, Y., Ueda, T., Kishino, H., Tanaka, T., Ishibashi, H., Yamanouchi, H., Yui, K., Nakamura, S. A Cross-species Affective Structure Revealed by a Model-free Data-driven Approach. *Scientific Reports* **3**, 1-20 (2013).

[9] M. Koshiba, H. Kakei, M. Honda, G. Karino, M. Niitsu, T. Miyaji, H. Kishino, S. Nakamura, T. Kunikata, H. Yamanouchi, Early-infant Diagnostic Predictors of the Neuro-behavioral Development after Neonatal Care, *Behavioral Brain Research* **276**, 143-150 (2015).

[10] Karino, G., Tsugawa, W., Sode, K., Murakoshiz, T., Kunikata, T., Yamanouchi, H., Koshiba, M. Common Marmosets' Developing Generation Specific Peer Social Experiences Might Affect Their Adult Bodyweight Adaptation to Climate. *Stress, Brain & Behavior* **1**, 1-6 (2015).

[11] Koshiba, M., Nakamura, S., Mimura, K., Senoo, A., Karino, G., Amemiya, S., Miyaji, T., Kunikata, T., Yamanouchi, H. Socio-emotional Development Evaluated by Behavior Output Analysis for Quantitative Emotional State Translation (BOUQUET) Towards Early Diagnosis of Individuals with Developmental Disorders, *OA Autism* **1**, 1-8 (2013).

[12] Koshiba, M., Senoo, A., Karino, G., Ozawa, S., Mmimura, K., Tanaka, I., Honda, Y., Usui, S., Kodama, T., Nakamura, S., Kunikata, T., Yamanouchi, H., Tokuno, H. Susceptible Period of Socio-emotional Development Affected by Constant Exposure to Daylight, *Neuroscience Research* **93**, 91-98 (2015).

[13] Koshiba, M., Karino, G., Mimura, K., Nakamura, S., Yui, K., Kunikata, T., Yamanouchi, H. Psycho-Cognitive Intervention for ASD from Cross-Species Behavioral Analyses of Infants, Chicks and Common Marmosets. *CNS & Neurol Disorders-Drug Targets* **15**, 578-586 (2016).

[14] Mimura, K., Kishino, H., Karino, G., Nitta, E., Senoo, A., Ikegami, K., Kunikata, T., Yamanouchi, H., Nakamura, S., Sato, K., Koshiba, M. Potential of a Smartphone as a Stress-free Sensor of Daily Human Behavior. *Behavioral Brain Research* **276**, 181-189 (2015).

[15] Karino, G., Murakoshi, T., Nakamura, S., Kunikata, T., Yamanouchi, H., Koshiba, M. Timing of Changes from a Primitive Reflex to a Voluntary Behavior in Infancy as a Potential Predictor of Socio-psychological and Physical Development During Juvenile Stages among Common Marmosets. *Journal of King Saud University - Science* **27**, 260-270 (2015).

[16] Tao, T., Sakurai, H., Kakei, H., Morita, K., Honda, M., Jiang, Z., Yamanouchi, H., Kunikata, T., Koshiba, M. Longitudinal Recording Revealed Preterm Infants' Circadian Vocal Behaviors Influenced by Care Events, *The International Stress and Behavior Society (ISBS)*, 18 (2017).

[17] Kellam, B., Bhatia, J. Sound Spectral Analysis in the Intensive Care Nursery: Measuring High-Frequency Sound, *Journal of Pediatric Nursing* **23**, 317-323 (2008).

[18] Tao, T., Sakurai, H., Kakei, H., Morita, K., Honda, M., Jiang, Z., Yamanouchi, H., Kunikata, T., Koshiba, M. Longitudinal Recording Revealed Preterm Infants' Acoustic Experiences Per Individual in Clinical Environments. *Inovation Application Reseasrch and Education (ICIARE2017)*, 123-126 (2017).

[19] Morgan, M., Maina, B., Waiyego, M., Mutinda, C., Aluvaala, J., Maina, M., English, M. Oxygen saturation ranges for healthy newborns within 24 hours at 1800 m, *ADC Fetal & neonatal* **102**, F1-F3 (2017).

[20] Knapp, A.A., Metterville, D.R., Kemper, A.R., Prosser, L., Perrin, J.M. Evidence review: Critical congenital cyanotic heart disease. Health Resources and Services Administration, Maternal and Child Health Bureau.http://www.hrsa.gov/advisorycommittees/mchbadvisory/heritabledisorders/nominatecondition/reviews/cyanoticheart.pdf Published September 3, 2010. Accessed February 25, 2015.

[21] Kattwinkel, J., Perlman, J.M., Aziz, K. Part 15: neonatal resuscitation: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation* **122**, S909-S919 (2010).

[22] Koshiba, M., Nakamura, S., Deng, C., Rogers, L.J. Light-dependent development of asymmetry in the ipsilateral and contralateral thalamofugal visual projections of the chick. *Neuroscience Letters* **336**, 81-84 (2003).

[23] Koshiba, M., Yohda, M., Nakamura, S. Topological relation of chick thalamofugal visual projections with hyper pallium revealed by three color tracers. *Neuroscience Research* **52**, 235-242 (2005).

[24] Koshiba, M., Mimura, K., Sugiura, Y., Okuya, T., Senoo,

A., Ishibashi, H., Nakamura, S. Reading marmoset behavior 'semantics' under particular social context by multi-parameters correlation analysis. *Prog Neuro-psychopharmacol Biol Psychiatry* **35**, 1499-1504 (2011).

[25] Soleimani, F., Zaheri, F., Abdi, F. Long-term neurodevelopmental outcomes after preterm birth. *Iran Red Crescent Med J* **16**, e17965 (2014).

[26] Jarjour, I.T. Neurodevelopmental outcome after extreme prematurity: a review of the literature. *Pediatr Neurol* **52**, 143-152 (2015).

[27] Schieve, L.A. Tian, L.H., Rankin, K., Kogan, M.D., Yeargin-Allsopp, M., Visser, S., Rosenberg, D. Population impact of preterm birth and low birth weight on developmental disabilities in US children. *Ann Epidemiol* **26**, 267-274 (2016).

[28] Pierrat, V., Marchand-Martin, L., Arnaud, C., Kaminski, M., Resche-Rigon, M., Lebeaux, C., Bodeau-Livinec, F., Morgan, A.S., Goffinet, F., Marret, S., Ancel, P.Y. EPIPAGE-2 writing group. Neurodevelopmental outcome at 2 years for preterm children born at 22 to 34 weeks' gestation in France in 2011: EPIPAGE-2 cohort study. *BMJ*, 358:j3448 (2017).

[29] Spittle, A., Orton, J., Anderson, P.J., Boyd, R., Doyle, L.W. Early developmental intervention programmes provided post hospital discharge to prevent motor and cognitive impairment in preterm infants. *Cochrane Database Syst Rev* **24**, CD005495 (2015).

[30] Spittle, A., Treyvaud, K. The role of early developmental intervention to influence neurobehavioral outcomes of children born preterm. *Semin Perinatol* **40**, 542-548 (2016).

[31] Pelc, K., Daniel, I., Wenderickx, B., Dan, B.; Primebrain group. Multicentre prospective randomised single-blind controlled study protocol of the effect of an additional parent-administered sensorimotor stimulation on neurological development of preterm infants: Primebrain. *BMJ Open* **7**, e018084 (2017).

[32] Aagaard, H., Uhrenfeldt, L., Spliid, M., Fegran, L. Parents' experiences of transition when their infants are discharged from the Neonatal Intensive Care Unit: a systematic review protocol. *JBI Database System Rev Implement Rep* **13**, 123-132 (2015).

[33] Pickler, R.H., Wetzel, P.A., Meinzen-Derr, J., Tubbs-Cooley, H.L., Moore, M. Patterned feeding experience for preterm infants: study protocol for a randomized controlled trial. *Trials*, 6:255 (2015).

[34] Bhutta, A.T., Anand, K.J. Vulnerability of the developing brain. Neuronal mechanisms. *Clin Perinatol* **29**, 357-372 (2002).

[35] Khalesi, N., Khosravi, N., Ranjbar, A., Godarzi, Z., Karimi, A. The effectiveness of earmuffs on the physiologic and behavioral stability in preterm infants. *Int J Pediatr Otorhinolaryngol* **98**, 43-47 (2017).

[36] Maitre, N.L., Ballard, R.A., Ellenberg, J.H., Davis, S.D., Greenberg, J.M., Hamvas, A., Pryhuber, G.S. Prematurity and Respiratory Outcomes Program.Respiratory consequences of prematurity: evolution of a diagnosis and development of a comprehensive approach. *J Perinatol* **35**, 313-321 (2015).

[37] Als, H., Butler, S., Kosta, S., McAnulty, G. The Assessment of Preterm Infants' Behavior (APIB): furthering the understanding and measurement of neurodevelopmental competence in preterm and full-term infants. *Ment Retard Dev Disabil Res Rev* **11**, 94-102 (2005).

[38] Young, K.S., Parsons, C.E., Jegindoe Elmholdt, E.M., Woolrich, M.W., van Hartevelt, T.J., Stevner, ABA., Stein, A., Kringelbach, M.L. Evidence for a Caregiving Instinct: Rapid Differentiation of Infant from Adult Vocalizations Using Magnetoencephalography. *Cereb Cortex* **26**, 1309-1321 (2016).

[39] Esposito, G., Valenzi, S., Islam, T., Bornstein, M.H. Three physiological responses in fathers and non-fathers' to vocalizations of typically developing infants and infants with Autism Spectrum Disorder. *Res Dev Disabil* **43-44**, 43-50 (2015).

[40] Underwood, M.A. Human milk for the premature infant. *Pediatr Clin North Am* **60**, 189-207 (2013).

[41] Geva, R., Schreiber, J., Segal-Caspi, L., Markus-Shiffman, M. Neonatal brainstem dysfunction after preterm birth predicts behavioral inhibition. *J Child Psychol Psychiatry* **55**, 802-810 (2014).

[42] Colombo, G., De Bon, G. Strategies to protect sleep. *J Matern Fetal Neonatal Med* **24,** 30-31 (2011).

[43] Vandenberg, K.A. State systems development in high-risk newborns in the neonatal intensive care unit: identification and management of sleep, alertness, and crying. *J Perinat Neonatal Nurs* **21**, 130-139 (2007).

[44] Allen, M.C. Assessment of gestational age and neuromaturation. *Ment Retard Dev Disabil Res Rev* **11**, 21-33 (2005).

[45] Bueno, C., Menna-Barreto, L. Environmental factors influencing biological rhythms in newborns: From neonatal intensive care units to home. *Sleep Sci* **9**, 295-300 (2016).

[46] Kish, M.Z. Improving preterm infant outcomes: implementing an evidence-based oral feeding advancement protocol in the neonatal intensive care unit. *Adv Neonatal Care* **14**, 346-353 (2014).

[47] Bueno, C., Menna-Barreto, L. Development of sleep/wake, activity and temperature rhythms in newborns maintained in a neonatal intensive care unit and the impact of feeding schedules. *Infant Behav Dev* **44**, 21-28 (2016).

[48] Serón-Ferré, M., Torres-Farfán, C., Forcelledo, M.L., Valenzuela, G.J. The development of circadian rhythms in the fetus and neonate. *Semin Perinatol* **25**, 363-370 (2001).

[49] Barr, R.G., Chen, S., Hopkins, B., Westra, T. Crying patterns in preterm infants. *Dev Med Child Neurol* **38**, 345-55 (1996).

[50] Lester, B.M. Developmental outcome prediction from acoustic cry analysis in term and preterm infants. *Pediatrics* **80**, 529-534 (1987).

[51] Rautava, L., Lempinen, A., Ojala, S., Parkkola, R., Rikalainen, H., Lapinleimu, H., Haataja, L., Lehtonen, L; PIPARI Study Group. Acoustic quality of cry in very-low-birth-weight infants at the age of 1 1/2 years. *Early Hum Dev* **83**, 5-12 (2007).

[52] Akhnikh, S., Engelberts, A.C., van Sleuwen, B.E., L'Hoir, M.P., Benninga, M.A. The excessively crying infant: etiology and treatment. *Pediatr Ann* **43**, e69-75 (2014).

[53] Minowa, H., Bando, Y., Yasuhara, H., Ebisu, R., Ohgitani, A. Timing of injury in utero causing respiratory inhibition after crying. *Pediatr Int* **54**, 370-374 (2012).

[54] Neuman, M.R., Huch, R., Huch, A. The neonatal oxycardiorespirogram. *Crit Rev Biomed Eng* **11**, 77-112 (1984).

[55] Manfredi, C., Bocchi, L., Orlandi, S., Calisti, M., Spaccaterra, L., Donzelli, G.P. Non-invasive distress evaluation in preterm newborn infants. *Conf Proc IEEE Eng Med Biol Soc* **2008**, 2908-2911 (2008).