Medical Sciences

Effects of Bronchopulmonary Dysplasia on Swallow:Breath Interaction and Phase of Respiration with Swallow During Non-nutritive Suck

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Objectives: The objective of this study is to describe swallow:breath interaction (SwBr) and phase of respiration incident to swallow (POR) during non-nutritive suck in infants with bronchopulmonary dysplasia and determine if speech-language intervention can modify the characteristics of non-nutritive suck in these infants.

Methods: Logistic regression models were used to describe SwBr and POR in 16 low-risk preterm (LRP) infants and 43 infants with bronchopulmonary dysplasia. Infants with bronchopulmonary dysplasia were randomized to receive individualized intervention from a speech-language pathologist (BPDwithTX) or standard care (BPDnoTX).

Results: No significant differences were noted between low-risk infants and either group of BPD infants for the distribution of SwBr types. Infants with bronchopulmonary dysplasia showed minor differences in the progression of POR. Speech-Language intervention did not change the progression of SwBr or POR in infants with bronchopulmonary dysplasia.

Conclusion: Infants with bronchopulmonary dysplasia can improve the progression of SwBr through practice as effectively as low-risk preterm infants can. The minor differences in POR in infants with bronchopulmonary dysplasia are consistent with dysmature development as seen with other feeding studies of infants with this disease. Speech-Language intervention did not modify the developmental progression of swallow:breath interaction or phase of respiration incident to swallow.

Infant Feeding | Suck Swallow Breath | Bronchopulmonary Dysplasia

Introduction

Efficient suckle-feeding can be considered to be the most complex skill a newborn infant must master to attain independent survival. However, feeding problems are frequent in preterm infants and can lead to prolonged hospital stays[1-5]. Feeding problems have been identified as sequelae of hypoxic-ischemic injury[6] and later neurologic deficits such as cerebral palsy[7-8]. Mild disruptions of the rhythmicity of suckle-feeding can indicate less severe injury[9] and may predict subsequent neurologic problems[10]. Poor feeding in the neonatal period may be an early indicator of neurologic injury[11,12] and has been linked to language delay later in life[13-15].

The development of efficient suckle-feeding is dependent on the maturation and coordination of neuronal central pattern generators (CPGs) controlling suck, swallow and breath[16]. Coordination among these CPGs is also activated, to a lesser degree, during non-nutritive suck (NNS). During NNS, babies must intermittently swallow as their own secretions collect in the oral cavity. As these swallows occur, there is an abrupt cessation of respiratory airflow, called deglutition apnea, followed by resumption of continuous respiration[17]. Since babies are capable of NNS much earlier than nutritive feeding, the study of swallow and deglutition apnea during NNS may provide an earlier marker of intact neurodevelopment than nutritive feeding. We have previously used our method to study NNS in Low-Risk Preterm (LRP) infants[18] and infants with Neonatal Abstinence Syndrome[19]. We have shown that the interaction of swallow and breath (SwBR) develops in a predictable pattern in LRP infants toward more swallows occurring in a "mature" fashion which is affected by practice (or learning). The phase of respiration (POR) incident to swallow progresses toward swallows occurring at points in the respiratory cycle that minimize aspiration into the airway. This progression is not affected by opportunities to practice. Term infants affected by Neonatal Abstinence Syndrome are more similar to low-risk preterm infants than term babies with no substance exposure.

Bronchopulmonary dysplasia (BPD), a chronic lung disease associated with preterm infants, has been shown to impact the mechanics of suckle-feeding[20] and delay attainment of full oral feeding[21]. We hypothesized that BPD will affect the characteristics of SwBr and POR during NNS and that these differences may be modifiable by interventions directed by a Speech-Language Pathologist.

Methods

The study population consisted of 16 Low-Risk Preterm (LRP) infants and 43 infants deemed to be "likely to develop" bronchopulmonary dysplasia (BPD). Infants affected by BPD were randomized to receive individualized intervention by a certified Speech-Language Pathologist (BPDwithTX; n=22) or standard care (BPDnoTX; n=21). We originally enrolled 25 infants in each group. For various reasons, not all studies provided interpretable data, leaving the final study population. All study participants were born and evaluated between 2007-2010. LRP was defined as being born prior to 35 completed weeks of gestation, having no intraventricular hemorrhage (IVH) of Grade 3 or 4, no congenital anomalies and being "not likely to develop" bronchopulmonary dysplasia (BPD). Babies in the BPD group were also born before 35 weeks gestation, with no IVH of Grade 3 or 4 and no congenital anomalies. Because these babies

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were enrolled in the study prior to being old enough to meet the standard criteria for a diagnosis of BPD, a definition for "not likely to develop" BPD had to be created. The amount of respiratory support on day-of-life (DOL) 28 was selected as an important point in this definition, regardless of gestational age at birth or age at enrollment. Those babies with no respiratory support or nasal cannula flow at less than 1.5 liters per minute, regardless of FiO2, on DOL 28 were classified as "not likely to develop" BPD, although we recognized that some of these babies may go on to develop BPD. Babies who required any type of mechanical ventilation, CPAP or nasal cannula of 1.5 liters per minute (or higher) flow, regardless of FiO2, on DOL 28 were categorized as "likely to develop" BPD, accepting the fact that some of these babies may ultimately not go on to not meet the accepted definition of BPD.

Infants with BPD were randomly assigned to receive standard care (BPDnoTX) or an individualized treatment by a certified Speech-Language Pathologist (BPDwithTX) at the time of enrollment by opening a sealed envelope containing the assignment. Speech-Language Interventions were developed and administered by one of the authors (G.C.), a certified Speech-Language Pathologist, and consisted of provision of external chin and/or cheek support, variations of nipple characteristics (thickness, size of opening, compressibility, shape, etc.), oral sensory motor stimulation, and other common interventions. Intervention programs were individualized to the patient. Patients were formally evaluated at least once per week, during which time individualized intervention plans were developed. Intervention plans were given to the parents and bedside nurses to be implemented with each feeding time.

Patients were identified when the medical team indicated that infant was ready to begin oral feeding. The first study for each infant occurred within a few days of this feeding as we did not want to interfere with the parents giving the baby his/her first bottle feeding. Infants were studied weekly until discharged from the NICU.

Informed consent was obtained from the parent(s) of each infant prior to participation in the study. The project complied with all applicable HIPAA standards and was approved by the Institutional Review Board of the University of Kentucky.

We have previously published the specific method for preparing the babies for the study and data collection[18]. To summarize the salient portion of the study for this project, the infant study participants were prepared in the following manner:

- A 5F naso-pharyngeal catheter was placed and connected to a pressure transducer (Transpac IV Neonatal/Pediatric Pressure Monitoring Kit, Hospira Inc., Lake Forrest IL) to measure swallow pressure. The catheter was placed by measuring the distance from the nose to the lower portion of the ear and then to the angle of the mandible.
- A second catheter was placed through a pacifier (Phillips, Soothie) so that the catheter tip was flush with the nipple and connected to a transducer to measure suction pressure.
- Respiratory effort was measured with a stretchable band placed around the infant's chest (Pneumotrace II, Model 1132, UFI, Morro Bay, CA).
- Nasal airflow was measured with a small thermistor bead (Omega 44030, Omega Engineering Inc., Stamford, CT) in a custom assembly placed at the opening of the nares.
- Other biometric data (ECG, SpO2), 2 types of acoustic data, and short- and long-term developmental outcomes were collected for use in other studies.

With the equipment in place, the infant was offered the pacifier for one minute of NNS just prior to a nutritive feeding. The 1-minute interval was arbitrarily chosen because it could be expected to create a data set for each infant that was long enough to be meaningful, but no so long as to be overwhelming during processing[18].

Data were collected and displayed as multi-channel linear graphs, using the Windaq Acquisition System and Waveform Browser (Dataq Industries, Akron OH). A sample data set is included in Figure 1. The entire one-minute sequence was canvassed for swallow events, noted as deflections in the naso-pharyngeal pressure recording. The type of swallow:breath interaction (SwBr) and phase of respiration incident to swallow (POR)were classified, as described below. The individual responsible for categorizing the swallows was blinded to the demographic data associated with each study, but not the group assignment.

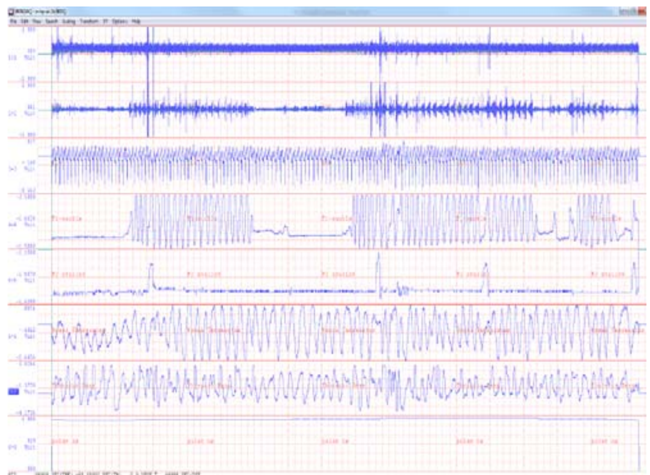

Figure 1. Sample raw data set from 1 minute of non-nutritive suck showing 8 channels of linear data. From the top: 1: accelerometer, 2: microphone, 3: ECG, 4: Suckle Pressure, 5: Swallow Pressure, 6: Nasal Airflow, 7: Chest Wall Movement, 8: Pulse Oximeter. For this study only Channels 4-7 are used.

Three types of SwBr were identified and classified as Central Apnea (CA), Obstructive Apnea (OA), or Attenuated Respiration (AR), a term we created to describe the slight deflection of the slope of the respiratory line on the graph. We identified five types of POR: Beginning Expiration (BE), Mid-Expiration (ME), End-Expiration (EE), Mid-Inspiration (MI) and Apnea (AP). Swallows can occur during any point in the respiratory cycle[12]. We have previously published figures showing examples of each type of SwBr and POR[18].

Independent variables for this analysis included gender, Birth Weight, Gestational Age, Postmenstrual Age, number of Swallows in the study, Weeks *Before*-First Nipple feed (time between birth and start of nipple feeding), and Weeks *Post*-First Nipple feed (time between first nipple feed and day of study). Day-of-Life is not used because it becomes redundant since postmenstrual age can be considered to be a function of Day-of-Life and Gestational Age.

We used SAS v9.1 (SAS Institute, Cary NC) to construct logistic regression models relating the odds of each type of SwBr and POR to the independent variables defined above. Statistical inferences were made via generalized estimating equations[22] with an exchangeable structure to take into account the correlations inherent to repeated assessments on the same baby, except when the generalized estimating equation did not yield valid results. In those cases, ordinary maximum likelihood was used.

Results

Table 1 shows characteristics of the study populations. LRP infants had significantly higher Gestational Age and Birth Weight and younger Day-of-Life than either group of BPD infants. Among NICU patients, it can be expected that the smaller, more preterm infants are more likely to experience complications of prematurity, in this case BPD. It would also follow that low-risk (healthier) infants would be stable for oral feedings at an earlier age than the pathologic group. Thus, it would be quite difficult to collect a group of low-risk infants with the same Gestational Age, Birth Weight and Day-of-Life as the pathologic group. Even with that limitation, the groups reflect a clinically reasonable way to sort the infants according to respiratory symptoms. In LRP infants, there were 176 swallows in 35 NNS periods among 16 infants. In BPDnoTX infants, there were 186 swallows in 40 NNS studies among 21 infants. In BPDwithTX infants, there were 212 swallows in 48 NNS studies among 22 infants.

Table 2 shows the distribution of SwBr and POR in each of the groups. Neither the distribution of SwBr nor POR was statistically different among the three groups.

Table 1. Patient Demographics.

	LRP	BPD no TX	BPD with TX
Infants	16	21	22
Studies	35	40	48
Swallows	176	186	212
Gestational Age @ Birth*	28.7 + 2.5	26.6 + 1.2	25.7 + 1.3
Birth Weight (grams)*	1056 + 338	803 + 172	758 + 166
Gender	9 males 7 females	9 males 12 females	12 males 10 females
Postmenstrual Age @ Study	35.2 + 2.5	35.8 + 1.6	36.3 + 1.6
Day-of-Life @ Study*	50 + 19	67 + 15	74 + 14
Weeks *Before*-First Nipple Feed	4.3 + 2.2	6.9 + 1.7	7.4 + 1.7
Weeks *Post*-First Nipple Feed	4.9 + 5.5	2.7 + 1.7	3.2 + 1.5
Swallows per Study (median)	4	4	4

"*" indicates statistically significant differences between groups.

Table 2. Distribution of SwBr and POR among the three study groups

Swallow:Breath Interaction	LRP	BPDnoTX	BPDwithTX
Swallows	176	186	212
Attenuated Respiration	74 (42%)	60 (32%)	90 (42%)
Obstructive Apnea	60 (34%)	62 (33%)	87 (41%)
Central Apnea	42 (24%)	64 (34%)	35 (17%)
Phase of Respiration	**LRP**	**BPDnoTX**	**BPDwithTX**
Swallows	176	186	212
Beginning Expiration	41 (23%)	37 (20%)	53 (25%)
Mid-Expiration	16 (9%)	19 (10%)	17 (8%)
End Expiration	81 (46%)	73 (39%)	92 (43%)
Mid-Inspiration	12 (7%)	25 (13%)	23 (11%)
Apnea	26 (15%)	32 (17%)	27 (13%)

Table 3 shows the results of our analysis comparing SwBr to the independent variables. Statistically significant association within each group are shown in ***bold/italics/red font***. There were no significant differences between any of the three groups.

Table 4 shows the significant relationships between POR and the independent variables. Statistically significant associations within each group, and between groups (BTWN), are shown in ***bold/italics/red font***. In the BPDnoTX group, BE is positively associated with Postmenstrual Age. AP is negatively associated with Postmenstrual Age. ME is negatively associated with, and AP is positively associated with, the number of Swallows per study. In the BPDwithTX group, BE is negatively associated with Male gender and Postmenstrual Age and positively associated with Weeks *Post*-First Nipple Feed. EE is positively associated with Male gender. AP is positively associated with Weeks *Post*-First Nipple Feed and Postmenstrual Age. ME is positively associated with the number of Swallows per study. Between group differences were noted for BE/Weeks *Post*-First Nipple Feed (p-value = 0.002), BE/Postmenstrual Age (p-value = 0.002), ME/Weeks *Before*-First Nipple Feed (p-value = 0.05), EE/male (p-value = 0.019) and EE/ Weeks *Before*-First Nipple Feed (p-value = 0.003).

Table 3. SwBr interactions between the dependent and independent variables for each of the three study groups.

		Attenuated Respiration		Central Apnea		Obstructive Apnea	
		OR	p-value	OR	p-value	OR	p-value
Male	LRP	1.185	0.761	2.745	0.118	***0.436***	***0.011***
	BPDnoTX	0.622	0.367	1.382	0.506	0.948	0.905
	BPDwithTX	1.579	0.191	0.78	0.632	0.709	0.321
Weeks *Before*-First Nipple Feed	LRP	1.074	0.449	0.88	0.365	1.032	0.801
	BPDnoTX	0.884	0.298	1.006	0.971	1.122	0.212
	BPDwithTX	1.139	0.458	***0.68***	***0.011***	1.092	0.439
Weeks *Post*-First Nipple Feed	LRP	***1.562***	***<0.0001***	0.813	0.32	***0.683***	***<0.0001***
	BPDnoTX	1.118	0.242	1.178	0.502	1.006	0.971
	BPDwithTX	1.062	0.512	0.885	0.268	0.848	0.106
Postmenstrual Age	LRP	***1.28***	***0.036***	0.85	0.321	0.873	0.177
	BPDnoTX	1.104	0.304	1.151	0.684	0.974	0.879
	BPDwithTX	1.022	0.802	0.922	0.301	0.898	0.339
Gestational Age	LRP	0.914	0.287	1.066	0.559	1.038	0.749
	BPDnoTX	1.173	0.486	1.143	0.536	***0.76***	***0.048***
	BPDwithTX	0.806	0.21	***1.759***	***0.011***	0.86	0.259
Birth Weight	LRP	1.024	0.623	1.015	0.909	0.967	0.611
	BPDnoTX	1.018	0.896	1.012	0.929	0.967	0.747
	BPDwithTX	0.92	0.434	1.029	0.879	1.065	0.539
Swallows per Study	LRP	0.969	0.585	1.065	0.084	0.98	0.5
	BPDnoTX	1.023	0.634	0.878	0.121	1.099	0.302
	BPDwithTX	***0.817***	***0.007***	1.046	0.697	***1.202***	***0.025***

Note: ***Bold/Italics/[red font]*** entries are statistically significant.

Table 4. POR interactions between the dependent and independent variables for each of the three study groups.

		Beginning Expiration		Mid-Expiration		End Expiration		Mid-Inspiration		Apnea	
		OR	p-value	OR	p-value	OR	p-value	OR	p-value	OR	p-value
Male	LRP	1.69	0.313	0.49	0.322	0.671	0.257	0.916	0.91	2.684	0.092
	BPDnoTX	0.742	0.386	0.829	0.804	0.593	0.103	1.821	0.214	3.229	0.092
	BPDwithTX	***0.434***	***0.027***	2.78	0.131	***1.655***	***0.027***	0.854	0.812	0.817	0.71
	BTWN		0.123		0.198		***0.019***		0.613		0.289
Weeks *Before*-First Nipple Feed	LRP	1.04	0.778	1.387	0.069	***0.751***	***0.0007***	1.284	0.348	1.088	0.499
	BPDnoTX	1.019	0.849	1.646	0.317	1.043	0.726	0.875	0.354	0.771	0.272
	BPDwithTX	1.007	0.955	0.877	0.393	1.107	0.312	0.866	0.248	0.94	0.719
	BTWN		0.983		***0.05***		***0.03***		0.442		0.508
Weeks *Post*-First Nipple Feed	LRP	***1.432***	***0.009***	1.019	0.919	0.918	0.146	***0.657***	***0.048***	***0.775***	***0.046***
	BPDnoTX	***1.22***	***0.002***	1.029	0.843	0.917	0.287	1.059	0.638	0.84	0.162
	BPDwithTX	0.89	0.129	0.939	0.786	1.004	0.956	0.972	0.849	***1.26***	***0.009***
	BTWN		***0.002***		0.939		0.665		0.245		0.133
Postmenstrual Age	LRP	***1.328***	***0.0003***	0.968	0.835	0.91	0.094	0.787	0.12	0.816	0.052
	BPDnoTX	***1.213***	***0.016***	1.194	0.371	0.97	0.699	1.024	0.859	***0.734***	***0.032***
	BPDwithTX	***0.844***	***0.026***	0.903	0.662	1.108	0.146	0.906	0.336	***1.247***	***0.015***
	BTWN		***0.002***		0.595		0.159		0.486		0.078
Gestational Age	LRP	1.104	0.443	0.703	0.056	1.149	0.21	0.755	0.217	0.859	0.272
	BPDnoTX	0.961	0.772	0.546	0.062	1.003	0.987	1.208	0.361	1.233	0.545
	BPDwithTX	1.013	0.934	1.01	0.97	0.948	0.609	0.99	0.358	1.122	0.655
	BTWN		0.752		0.304		0.481		0.38		0.542
Birth Weight	LRP	1.007	0.937	0.983	0.822	***1.107***	***0.007***	0.945	0.617	0.904	0.208
	BPDnoTX	0.872	0.063	***0.634***	***0.021***	1.036	0.677	1.093	0.509	1.279	0.197
	BPDwithTX	0.899	0.459	0.993	0.955	0.979	0.783	0.991	0.95	1.175	0.332
	BTWN		0.571		0.177		0.379		0.742		0.25
Swallows per study	LRP	0.934	0.203	0.826	0.127	1.001	0.969	0.867	0.076	***1.128***	***0.0001***
	BPDnoTX	0.971	0.719	***0.803***	***0.013***	0.982	0.761	1.106	0.075	***1.112***	***0.011***
	BPDwithTX	1.079	0.155	***1.313***	***0.009***	0.922	0.155	0.833	0.069	1.087	0.093
	BTWN		0.303		***0.0495***		0.245		0.168		0.868

Note: ***Bold/Italics/[red font]*** entries are statistically significant. BTWN= Between groups. For example: There is a significant association between Beginning Expiration and Male gender in the BPDwithTX group, but no differences between the 3 groups. There is a significant association between End Expiration and Male gender in the BPDwithTX ***and*** there is a significant difference between groups.

Discussion

We have previously used our technique to describe SwBr and POR in Low-Risk Preterm infants and babies with Neonatal Abstinence Syndrome[18,19]. With this method, a significant relationship for only Weeks *Post*-First Nipple feed suggests that practice or "learning" is important in the progression of what is being described. Significant relationships in the same direction for the variables Gestational Age, Weeks *Before*- and Weeks *Post*- First Nipple feed, support a maturational model for the development, rather than learnable skills.

In our previous work with NNS in low-risk infants[18], we showed that SwBr progresses from more frequent central apnea to more frequent attenuated respiration. The associations were consistent with our model of practice or learning being an important factor in the progression of SwBr. When considering POR in LRP infants, there was a maturational progression of these parameters, unrelated to practice, toward swallows occurring at points in the respiratory cycle that minimize the chance of airway aspiration (Beginning Expiration, Mid-Expiration and Apnea). In the current work, we investigate the effects of BPD on SwBr and POR and if therapeutic interventions can modify these characteristics of deglutition apnea.

Infants in our BPDwithTX group showed a significant negative association between CA and Weeks *Before*-First Nipple Feed and a positive association with Gestational Age, similar to LRP infants. For infants in the BPDnoTX, OA has a negative association with Gestational Age, similar to LPR infants. No differences were found for SwBr among the 3 study groups. We conclude that the presence of bronchopulmonary dysplasia does not affect the infant's ability to "learn" how deglutition apnea should occur.

Turning our attention to POR in the BPD groups, the pattern of statistically significant relationships for infants in the BPD groups did not fit our previously described learning/maturation theme. However, the 5 statistically different relationships we found only occurred in POR (not in SwBr), which we have previously suggested represented maturational progression in LRP infants rather than a learning model. Thus, by this technique, infants effected by BPD have a dysmature pattern of development of deglutition apnea during NNS, which is consistent with other studies of feeding in infants with bronchopulmonary dysplasia. Mizuno[20], et al, showed that infants effected by BPD have lower pressure and lower frequency of rhythmic suck and shorter duration of suckle bursts than unaffected controls. They also had lower frequency of swallows, longer deglutition apneas and lower feeding efficiency. Gewolb, et al, in their studies of rhythmic feeding found decreased suckle rhythm stability and shortened length of suckle and swallow runs[21] in infants affected by BPD compared to control infants. Similarly, they found diminished dyadic stability, a measure of the integration of suck and swallow rhythms or how suck and swallow work together, in infants with BPD[23,24]. Even the stability of the sounds of infant swallow collected via cervical auscultation have been shown to be affected by BPD[25]. Thus, dysmaturity is a pervasive finding in the study of feeding infants with BPD, regardless of technique.

We were also interested in the effect of Speech-Language intervention on NNS. If the intervention has an effect, we would predict that the BPDnoTX group would be different from the LRP infants, and the BPDwithTX group would be more similar to LRP infants. However, we only found the predicted relationship in 1 of the 5 POR comparisons (BE/ Weeks *Post*-First Nipple Feed). In fact, in 3 of the 5 cases (BE/ Weeks *Before*-First Nipple Feed, ME/ Weeks *Before*-First Nipple Feed and EE/Male), the LRP group looked more like the BPDnoTX group than the BPDwithTX group, suggesting that the treatment may have made the infants less normal. In one case (EE/ Weeks *Before*-First Nipple Feed), the two BPD groups looked more similar to each other than either looked like the LRP group. In summary, an individualized speech-language intervention did not affect the parameters of NNS that we studied. That is not to say speech therapy is not effective for improving other aspects of newborn oral feeding. Oral support and oral stimulation have been shown to decrease transition time from gavage feeds and increase feeding efficiency[26,27]. In Mizuno's study of BPD infants, they suggested that speech therapy, specifically jaw and chin support, "might be helpful to support the weak intraoral pressure" during suck. However, increasing the swallow frequency and swallow volume resulted in decreased minute ventilation[20], which is likely detrimental to infants with BPD.

It is unclear how or if infants with BPD overcome this type of developmental dysmaturity. The current study investigates deglutition apnea during NNS in relatively newborn infants, which is almost entirely reflexive. Eventually, infant feeding becomes volitional. Therefore, it is possible that rhythmic NNS and feeding reflexes are extinguished before these infants can exhibit catch-up development. Certainly, this type of dysfunctional development, and subsequent inefficient feeding, will contribute to the increased metabolic needs common for infants with BPD.

Conclusion

We have expanded our understanding of deglutition apnea during non-nutritive suck by describing the relationships of swallow and breath in infants with bronchopulmonary dysplasia. Development of SwBr, which has been shown to be affected by practice in low-risk preterm infants was not different in infants with bronchopulmonary dysplasia. There were differences noted in POR, which is controlled more by maturation and less affected by learning. This dysmature pattern of development is common in studies of feeding infants affected by bronchopulmonary dysplasia. Individualized intervention by a Speech-Language Pathologist had no effect on the progression of SwBr or POR in our study groups.

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Abbreviations

Sw:Br: Swallow:Breath Interaction, POR: Phase of Respiration Incident to Swallow, BPD: Bronchopulmonary Dysplasia, LRP: Low-Risk Preterm, NNS: non-nutritive suck, CA: central apnea, OA: obstructive apnea, AR: Attenuated Respiration, BE: Beginning Expiration, ME: Mid-Expiration, EE: End-Expiration, MI: Mid-Inspiration, AP: Apnea

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