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Study on the Language Formation Process of Very-Low-Birth-Weight Infants in Infancy Using a Formant Analysis

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Expressive language development depends on anatomical factors, such as motor control of the tongue and oral cavity needed for vocalization, as well as cognitive aspects for comprehension and speech. The purpose of this study was to examine the differences in expressive language development between normal-birth-weight (NBW) infants and very-low-birth-weight (VLBW) infants in infancy using a formant analysis. We also examined the presence of differences between infants with a normal development and those with a high risk of autism spectrum disorder who were expected to exist among VLBW infants. The participants were 10 NBW infants and 10 VLBW infants 12-15 months of age whose speech had been recorded at intervals of approximately once every 3 months. The recorded speech signal was analyzed using a formant analysis, and changes due to age were observed. One NBW and 3 VLBW infants failed to pass the screening tests (CBCL and M-CHAT) at 24 months of age. The formant frequencies (F1 and F2) of the three groups of infants (NBW, VLBW and CBCL·M-CHAT non-passing infants) were scatter-plotted by age. For the NBW and VLBW infants, the area of the plot increased with age, but there was no significant expansion of the plot area for the CBCL·M-CHAT non-passing infants. The results showed no significant differences in expressive language development between NBW infants at 24 months old and VLBW infants at the corrected age. However, different language developmental patterns were observed in CBCL·M-CHAT non-passing infants, regardless of birth weight, suggesting the importance of screening by acoustic analyses.

INTRODUCTION

Advances in perinatal care have enabled many low-birth-weight (LBW; <2,500 g) infants to be saved in recent years. The birth rate of LBW infants accounted for about 10% of the total number of births in 2016, and the proportion of very-low-birth-weight (VLBW; <1,500 g) infants was 0.7%.[5]

Previous studies have revealed that the incidence of autism spectrum disorder (ASD) is higher in LBW infants than in those with higher birth weights. In a cohort study conducted by Limperopoulos et al. in corrected age VLBW infants at 18-24 months of age, 25% of VLBW infants scored positive on the Modified Checklist for Autism in Toddlers (M-CHAT) screening test.[16] In a survey conducted by Lampi et al. in Finland, the comparison of normal-birth-weight (NBW; ≥2,500 g) and VLBW infants showed that the incidence of ASD was more than threefold higher in VLBW infants.[14] In a study of 988 infants born before 28 weeks' gestation conducted by Kuban et al., the overall ASD prevalence was as high as 21%. In addition, even when studies are limited to infants without complications, such as cerebral palsy, intellectual disability, deafness, visual impairment, the positive rate was 10%.[12] If subjects were further restricted to infants born at <26 weeks' gestation, the overall positive rate increased to 41% and was 16.5% in infants without other disabilities.[17]

One of the characteristic related to the development of ASD is a delay in language development. Language development in infancy occurs through exposure to various stimuli in the environment while physical development of the oral cavity, such as the palate and vocal tract, and motor control of the tongue allows for the eventual creation of words. In order to produce words, it is necessary that a series of processes from the brain function properly, and ASD impedes this process, thereby resulting in the delayed development of language.[20]

Many studies on children's language development have been conducted, and formant frequencies are generally used as an index to capture the characteristics of acoustic change accompanying a child's vocal tract development. The vowels included in the words spoken by a person have a formant frequency which is the resonance of the vocal tract, and it is called the first formant (F1) and the second formant (F2) from the lower frequency side. It is possible to identify vowels using the F1 and F2 values. In addition, the average of frequency (F1 and F2) of all vowels is called the "neutral vowel", it is possible to determine the age of the target group from the frequency

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values.[2, 10] Kasuya et al. investigated the formant frequencies of 5 Japanese vowels of children (7-12 years of age), boys (13-15 years of age), female adults and male adults, and showed that formant frequency decreases with age (Table I).

Table I. Average formant frequency of each vowel and neutral vowel (children, boys, female adults and male adults).

		Average formant frequency (Hz)		Neutral vowel (Hz)	
	Vowels	F1	F2	F1	F2
Children	/a/	1072	1609	629	1981
	/i/	393	3215		
	/u/	428	1537		
	/e/	659	2468		
	/o/	593	1077		
Boys	/a/	805	1296	487	1615
	/i/	317	2622		
	/u/	339	1389		
	/e/	500	1900		
	/o/	475	868		
Female adults	/a/	888	1363	511	1801
	/i/	325	2725		
	/u/	375	1675		
	/e/	483	2317		
	/o/	483	925		
Male adults	/a/	775	1163	485	1460
	/i/	263	2263		
	/u/	363	1300		
	/e/	475	1738		
	/o/	550	838		

Kasuya et al. (1968):[8]

Similar to the formant frequency, there is a fundamental frequency (F0) called "pitch" used as an index to capture the change in the voice height. F0 represents the length of the vocal tract, and the numerical value decreases with the development of the vocal tract. The average F0 is about 120 Hz for male adults, about 225 Hz for female adults, about 300 Hz for children of either gender and about 400 Hz for infants, but it is possible for speakers to intentionally alter the height of their voice.[9]

The formant frequency and tongue position are also closely related. F1 corresponds to the tongue height, and the frequency decreases as the tongue position rises and increases as the tongue position drops. F2, by contrast, corresponds to the tongue advancement, and the frequency increases as the tongue moves closer to the lips and decreases as the tongue retreats toward the pharynx. By plotting the frequencies of F1 and F2 on the distribution map, it is possible to visually confirm the tongue position and phonation area during speech (Figure 1).

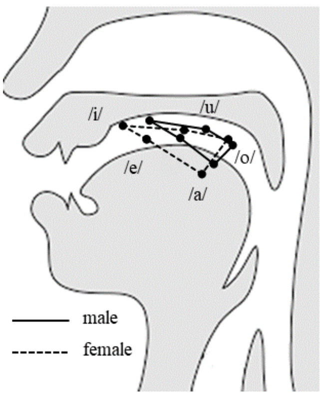

Figure 1. Five Japanese vowels and tongue positions corresponding to F1 and F2.

Infants' voices are very unstable. However, Serkhane et al. showed that despite having a vocal-tract configuration in which infants can make discriminable sounds in their study using an infant's articulatory model, they did not use the entire range of the phonation area.[18] This is because infants cannot fully control the movement of their tongue; however, as the vocal tract and articulatory functions develop with age, it is possible for them to enlarge their phonation area. Indeed, a longitudinal study conducted by Lieberman showed that the phonation area of five infants expanded with age.[15]

The purpose of the present study was to examine the differences in expressive language development between NBW and VLBW infants in infancy using a formant analysis. In addition, we examined the presence of differences between infants with a normal development and those with a high risk of ASD who were expected to exist among VLBW infants.

MATERIALS AND METHODS

Participants

The participants were 10 NBW infants and 10 VLBW infants at a corrected age of 12-15 months. The inclusion criteria were as follows: NBW infants with a birth weight of 2,500-4,000 g and born at 37-41 gestational weeks, VLBW infants with a birth weight of <1,500 g and born at <37 gestational weeks. In addition, VLBW infants were recruited from among subjects who had participated in a child-rearing support classes for infants with a birth weight <1,500 g.

None of the VLBW infants had congenital abnormalities or MRI findings suggestive of intraventricular hemorrhaging (IVH) or periventricular leukomalacia (PVL).

Procedure

Voice recording was performed longitudinally up to 24 months of age approximately once every 3 months. The number of recordings was 5 times for infants who were 12 months of age at the start of recording and 4 times for infants who were 15 months of age at the start of recording, but there were cases of postponement or cancellation of a recording due to a poor physical condition or hospitalization. The Child Behavior Checklist (CBCL) and M-CHAT were performed for each infant around 24 months of age.

Positivity on the M-CHAT was defined as non-passage of 3 fails of 23 items or 2 fails of 6 important items. In addition, we used the Language Development Survey (LDS) of CBCL in this study. The LDS consists of 8 questions and 310 spontaneous words. The screening criteria of LDS was defined as non-passage with a Vocabulary Score ≤15th percentile among 310 spontaneous words combined with 5 other words.

Apparatus

For audio recordings, we used a portable recorder (set to 24 bit, 44.1 kHz) and asked parents of subjects to record speech utterances for about 20 minutes of recording time or about 50 words in a quiet environment. The recorded speech signal was excised as "*.wav" data for each word using freely downloadable "spwave" software programs as the audio file editor. At this time, we excluded the subjects' cries and laughter from the speech signal to be excised. We also excluded cases where speech signals other than the target infant and strong noises surrounding the subject overlapped.

A formant analysis of the extracted *.wav data was further performed with the freely downloadable "Praat" software programs as a voice analysis in order to calculate the fundamental frequency (F0), F1 and F2 for each mora (phoneme). The distribution map of F1 and F2 was created in each infant at each recorded time. The expansion of the frequency was analyzed by age. In addition, the variance in the F1 and F2 for each age group was determined, and multiple comparison studies were performed using the SPSS software program for Windows, version 24.0 (IBM Inc., Tokyo, Japan), and the Kruskal-Wallis rank test.

Ethical approval

This study was approved by the Ethics Committee of Kobe University Graduate School of Health Sciences in accordance with the World Medical Association Declaration of Helsinki (approval date: March 20, 2014). All parents of the infants were informed of the details of the research, and their written informed consent was obtained.

RESULTS

Table II shows the average birth weights and gestational ages of the NBW and VLBW infants. The average birth weight in the NBW infant group was 3.55 times that in the VLBW infant group. The average weeks of gestation in the VLBW infant group was 12 weeks earlier than in the NBW infant group. For VLBW infants, the survey was conducted in terms of the corrected age based on the scheduled delivery date.

Table II. Birth weight and gestational age average of target infants (NBW and VLBW).

	NBW infant (n=10)	VLBW infant (n=10)
Birth weight (g)	3087.9±313.5	871±351.8
Gestational age (weeks)	39.5±1.1	27.5±3.7

Values are shown as the mean ± standard deviation.
Normal-birth-weight (NBW), very-low-birth-weight (VLBW)

Table III shows the sex, recorded age and data cut among 10 NBW and 10 VLBW infants. In the NBW infant group, 4 out of the 10 infants had their speech recorded 5 times, and in VLBW infant group, 5 out of the 10 infants had their speech recorded 5 times. The first recording was made at 12 months of age, the second at 15 months of age, and the fifth (final) at 24 months of age as a guide.

The formant analysis showed that F0, representing the length of the vocal tract, was higher in the VLBW infant group at 24 months of age than in the NBW infant group by 50 Hz, and a significant difference was observed between the two groups by the Mann-Whitney U test. Focusing on the neutral vowels, an indicator of vocal tract development similar to F0, the calculated average frequencies of F1 and F2 in both groups were higher than the child data (7-12 years of age) obtained by Kasuya et al. This was because the vocal tract development was age-appropriate, but there were no significant differences between the NBW and VLBW infant groups (Table IV).

Table III. Characteristics of 10 NBW and 10 VLBW infants.

	ID	Sex	Recorded age (months)					Number of data excluded
			1st	2nd	3rd	4th	5th	
NBW	N1	m		15	18	21	24	276
	N2	m	13	16	19	22	25	460
	N3	f		15	19	21	24	222
	N4	m	12	15	18	21	25	585
	N5	m		14	17	20	23	416
	N6	f		16	19	22	25	342
	N7	m	13	16	19	22	25	365
	N8	m		15	18	21	24	360
	N9	m	12	15	18	21	24	520
	N10	m		15	18	21	24	380
VLBW	V1	m		14	18	21	24	384
	V2	m	13	16	19	22	25	422
	V3	m	12	16	19		25	463
	V4	f		14	17	20	23	394
	V5	m	11	14	18	21	33	491
	V6	f	13	16	19	22	25	552
	V7	m		15	18	22	25	223
	V8	m		15	18	22	25	452
	V9	f	12	15	18	21	24	595
	V10	f	14	16	19	22	25	377

Table IV. A comparison of the average F0, F1 and F2 values between NBW and VLBW infants at 24 months of age.

	NBW (n=10)	VLBW (n=10)	*P*-value	
F0 (Hz)	337±48.6	386±48.2	0.035	*
F1 (Hz)	753±80.8	766±86.8	0.631	
F2 (Hz)	2301±190.2	2338±201.4	0.393	

*$p<0.05$, **$p<0.01$ (Mann-Whitney U test)

Two types of developmental assessment were conducted for all infants at 24 months of age (corrected age in VLBW infants). In the LDS of CBCL, infants whose parents checked the item that their parents were concerned about their child's language development, and the Vocabulary Score of spontaneous words were ≤15th percentile were detected 1 in NBW infant group and 3 VLBW infant group. In M-CHAT, 1 non-passing infant was detected in each of the NBW and VLBW infant groups (Table V).

Table V. Results of LDS (CBCL) and M-CHAT (NBW and VLBW groups).

NBW ID	Vocabulary Score (%ile)	Worried about development	M-CHAT	VLBW ID	Vocabulary Score (%ile)	Worried about development	M-CHAT
N1	20	no	pass	V1	≤15	yes	pass
N2	40	no	pass	V2	≤15	no	pass
N3	20	no	pass	V3	≤15	no	pass
N4	60	no	pass	V4	45	yes	pass
N5	65	no	pass	V5	＞85	no	pass
N6	45	no	pass	V6	55	no	pass
N7	20	no	pass	V7	≤15	yes	pass
N8	≤15	no	pass	V8	55	no	pass
N9	50	no	pass	V9	45	no	pass
N10	≤15	yes	fail	V10	≤15	yes	fail

The shaded areas indicate infants with LDS ≤15th percentile and language worries, and M-CHAT were non-passing.

The frequencies of F1 and F2 were analyzed from the speech data extracted from each target infant, and a distribution map was created by plotting the frequencies of F1 and F2 for each recorded age. However, in order to correspond to the oral cavity sectional view shown in Figure 1, we made a distribution map in which the coordinate axes of F1 and F2 were reversed.

Figure 2 is an enlarged view of the F1-F2 plot diagram, with the vertical axis showing the frequency of F1 and the horizontal axis the frequency of F2. The results of the F1-F2 plot diagram were divided among three groups: nine NBW infants, seven VLBW infants and four CBCL·M-CHAT non-passing infants (Figures 3, 4 and 5). In the NBW and VLBW infants, the F1-F2 plot region expanded with age, with the expansion tending to become stronger after the third recording (around 18 months of age). However, there were some infants of NBW and VLBW group who continued to show poor changes even at the fifth recording (around 24 months of age). In the CBCL·M-CHAT non-passing infant group, all age-specific changes in the F1-F2 plot region were poor.

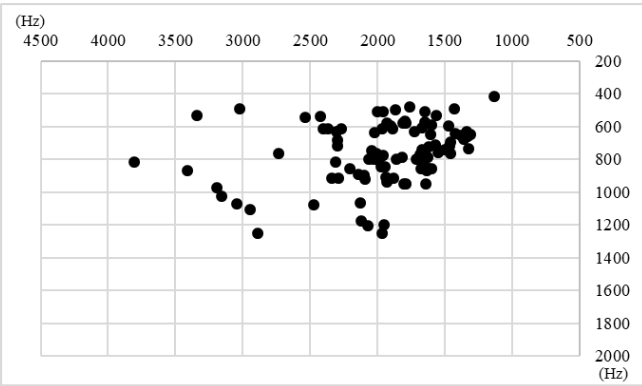

Figure 2. Enlarged view of F1-F2 plot diagram. The vertical axis shows the frequency of F1, and the horizontal axis shows the frequency of F2.

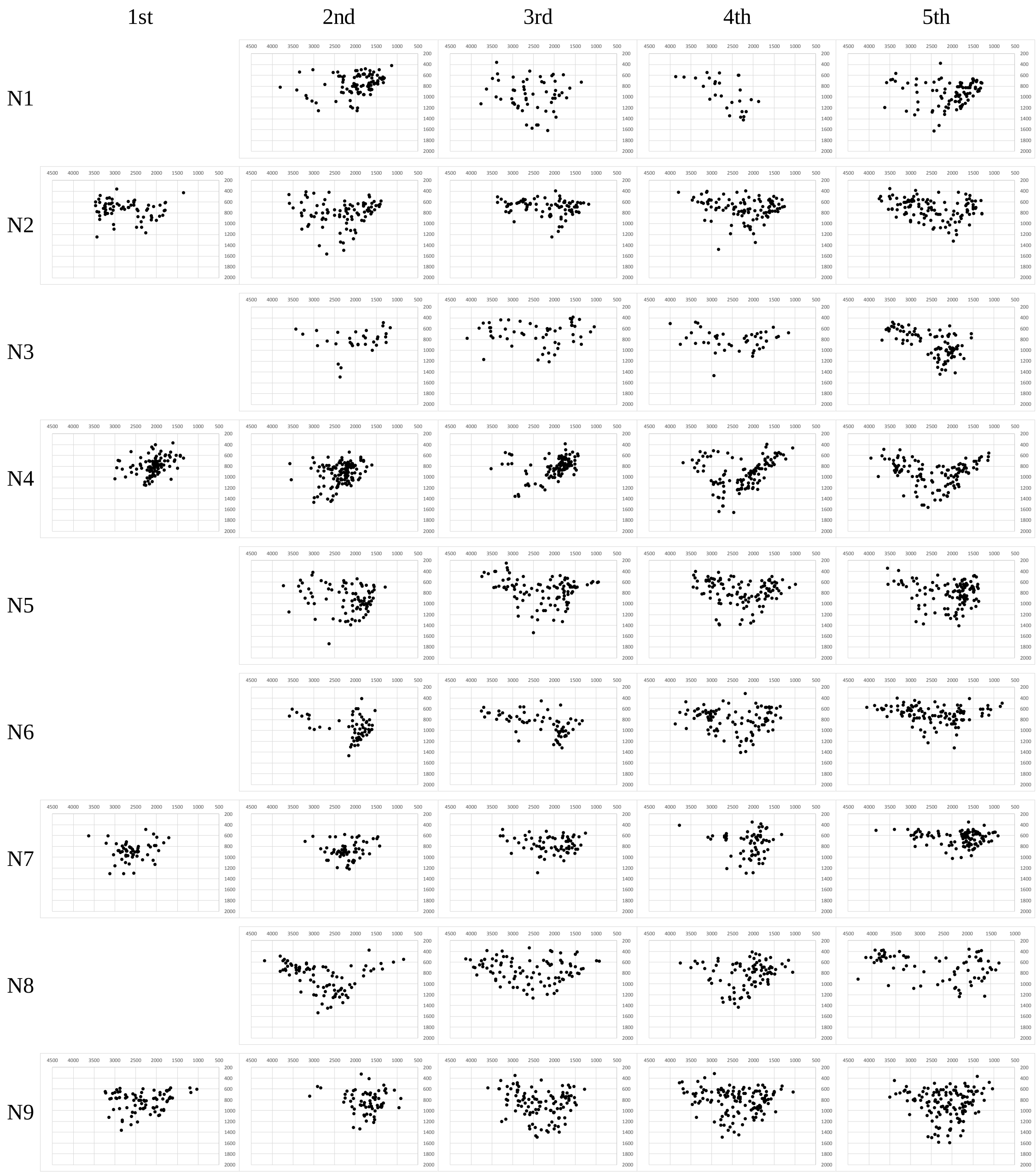

Figure 3. Age-specific changes in the F1-F2 plot diagram of the 9 infants in the NBW group.

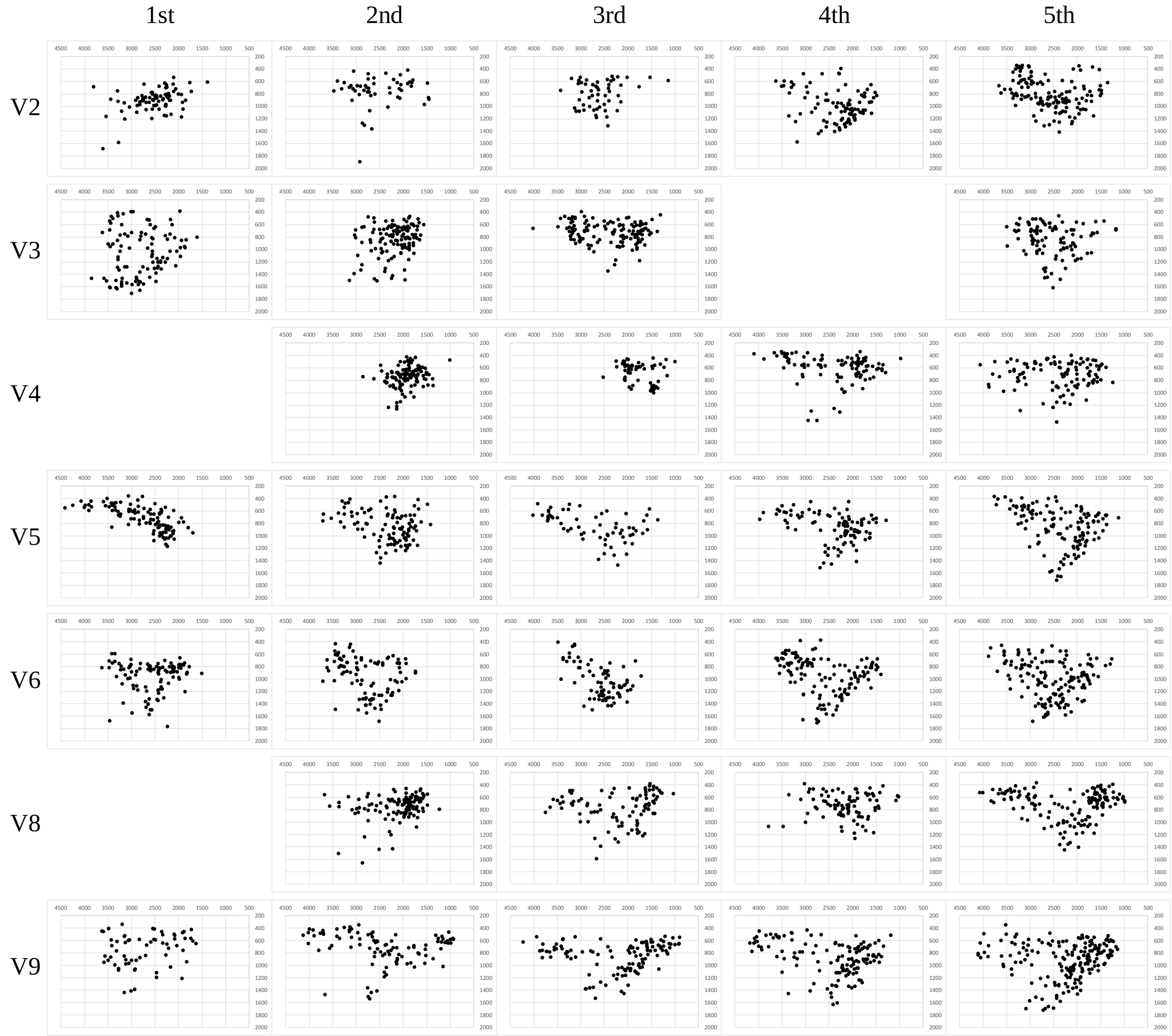

Figure 4. Age-specific changes in the F1-F2 plot diagram of the 7 infants in the VLBW group.

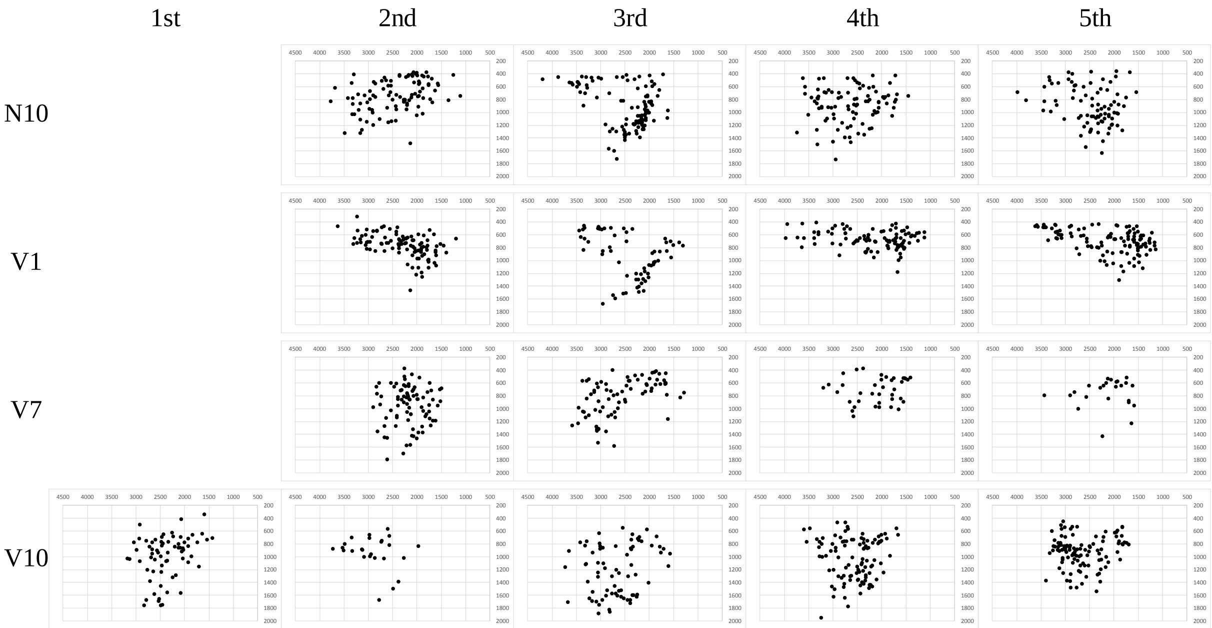

Figure 5. Age-specific changes in the F1-F2 plot diagram of the 4 infants in the CBCL·M-CHAT non-passing group.

The variance in the F1 and F2 frequencies were calculated to compare the expansion of the F1-F2 plot region. We examined the 2nd to the 5th recording in which all the target infants participated. Regarding the variance in the F1, there were four NBW infants, six VLBW infants and two CBCL·M-CHAT non-passing infants whose variance at the 5th recording was higher than that at the 2nd recording. Regarding the variance in the F2, there were seven NBW infants, six VLBW infants and three CBCL·M-CHAT non-passing infants whose variance at the 5th recording was higher than that at the 2nd recording (Table VI).

Table VI. Variance in the F1 and F2 frequency (NBW, VLBW and CBCL·M-CHAT non-passing infant groups).

	Variance in the F1					Variance in the F2			
	2nd	3rd	4th	5th		2nd	3rd	4th	5th
NBW (n=9)	34323	79963	80801	47635	NBW (n=9)	257638	305224	235597	333600
	54170	20396	39072	36443		344305	344489	372136	450373
	44973	44504	32646	54863		351797	658330	507401	306083
	36058	32744	73492	51878		107835	201030	336102	479735
	61717	55934	49220	49543		312574	462358	384208	309616
	44006	38486	47195	25970		272164	438985	447563	500986
	25421	22613	50613	15432		121837	253164	177660	329947
	65934	45752	58353	47469		473555	637747	302588	908141
	40747	65954	53142	71257		161395	276034	361317	266846
VLBW (n=7)	64442	45178	62964	59241	VLBW (n=7)	285609	171435	274549	304968
	59095	28567		65847		131508	367132		245652
	27186	28891	51128	47350		79422	99755	479723	442769
	59800	50376	54194	99207		277771	519586	369478	356946
	89567	70282	88439	91731		240610	168203	381955	326229
	40390	64542	39612	56540		245853	481613	280807	633495
	68906	54208	71357	85933		737211	712315	612178	509487
CBCL M-CHAT non-passing (n=4)	62538	107390	74936	88785	CBCL M-CHAT non-passing (n=4)	331131	296733	293940	247540
	34174	120693	19506	34536		267174	327783	489489	503686
	92746	83120	39748	48266		113696	357116	234406	214282
	64188	148220	105676	56609		178611	245648	174151	196886

The shaded areas indicate infants whose variance in the 5th recording was higher than that in the 2nd recording.

In Figure 6, the variance in the F1 and F2 frequency obtained from the 2nd to 5th recordings was graphed over time. The variance in the F1 frequency increased for the NBW and VLBW infant groups from the 3rd (around 18 months of age) to the 5th (around 24 months of age) recordings. In contrast, the variance in the F1 frequency in the CBCL·M-CHAT non-passing infant group was higher only at the 3rd recording and returned to normal by the 4th (around 21 months of age) and 5th recordings. The variance in the F2 frequency for the NBW and VLBW infant groups showed repeated fluctuation of increasing and decreasing, whereas the CBCL·M-CHAT non-passing infant group showed poor age-specific changes, and the dispersion tended to be consistently low until the 5th recording.

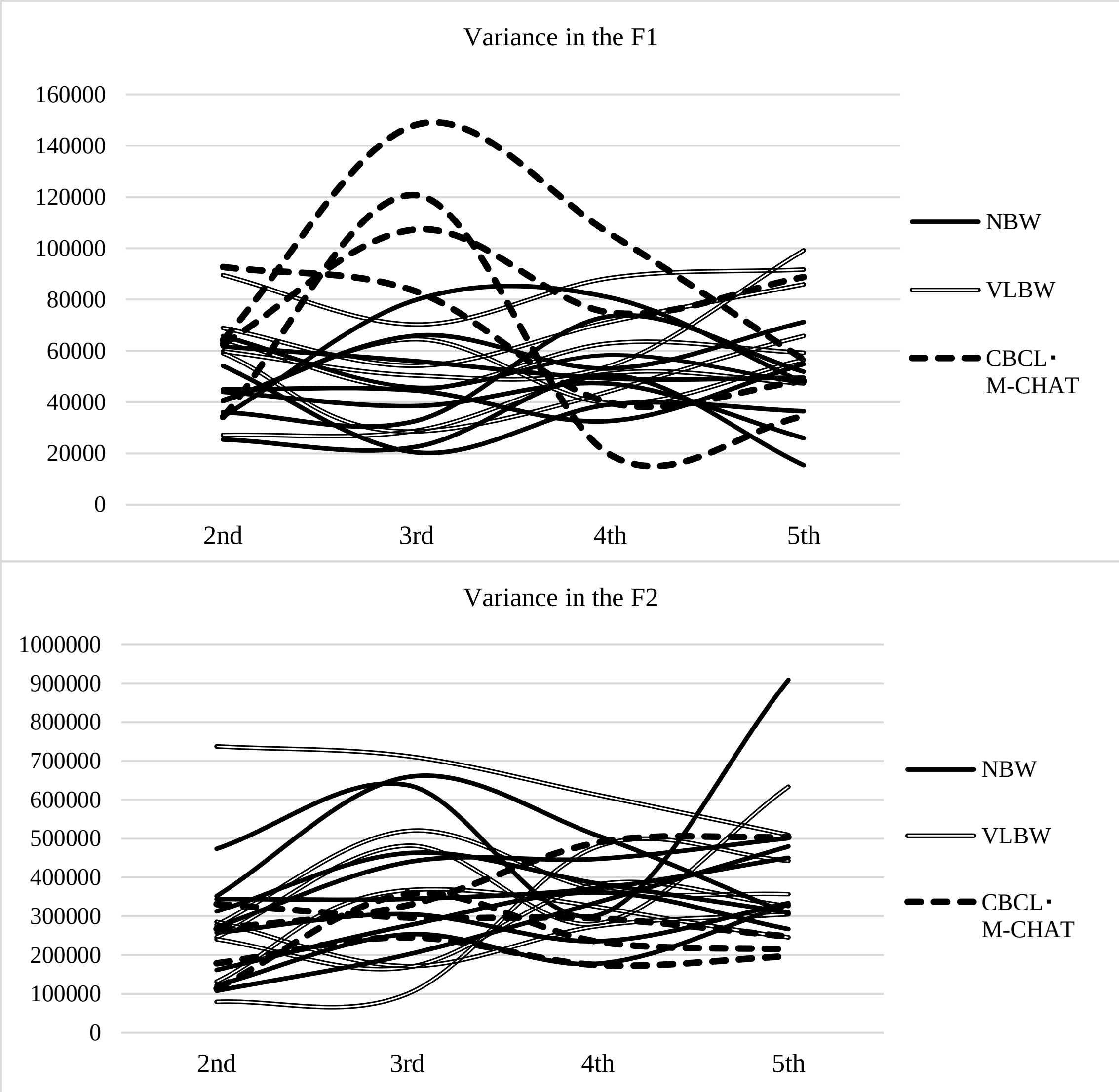

Figure 6. Variance in the F1 and F2 frequency (NBW and VLBW and CBCL·M-CHAT non-passing infant groups).

On comparing the variance in F1 and F2 using the Kruskal-Wallis test, significant differences among NBW and VLBW and CBCL·M-CHAT non-passing infant groups were observed at the 3rd recording of F1. In addition, since significant differences were observed among the groups, Dunnet's multiple comparison test with Bonferroni correction was performed. As shown in Table 7, significant differences were observed between the NBW and CBCL·M-CHAT non-passing infant groups and between the VLBW and CBCL·M-CHAT non-passing infant groups.

Table VII. Statistical results of variance in F1 and F2 (NBW and VLBW and CBCL·M-CHAT non-passing infant groups).

	Average rank (F1)				
	2nd	3rd		4th	5th
NBW (n=9)	8.22	8.00		8.89	7.33
VLBW (n=7)	12.00	9.14		11.50	14.57
CBCL·M-CHAT non-passing (n=4)	13.00	18.50		10.25	10.50
Chi-squared	2.498	9.290		0.785	5.894
Degree of freedom	2	2		2	2
P-value	0.287	0.010	*	0.675	0.053

*p<0.05, **p<0.01 (Kruskal-Wallis one-way analysis of variance)

	Average rank (F2)			
	2nd	3rd	4th	5th
NBW (n=9)	11.44	11.44	10.22	11.78
VLBW (n=7)	10.00	10.29	11.67	11.43
CBCL· M-CHAT non-passing (n=4)	9.25	8.75	7.00	6.00
Chi-squared	0.458	0.589	1.677	2.907
Degree of freedom	2	2	2	2
P-value	0.795	0.745	0.432	0.234

**p*<0.05, ***p*<0.01 (Kruskal-Wallis one-way analysis of variance)

	Test statistic	*P*-value	
NBW-VLBW	-0.383	1.000	
NBW-CBCL· M-CHAT non-passing	-2.953	0.009	**
VLBW-CBCL· M-CHAT non-passing	-2.523	0.035	*

**p*<0.05, ***p*<0.01 (Dunnet's multiple comparison, Bonferroni correction)

DISCUSSION

In the present study, the language development of NBW and VLBW infants was compared using a formant analysis. Language development in early childhood is a major concern for parents, and the development evaluation of CBCL in the present study confirmed that parents of VLBW infants worried about their child's language development particularly frequently. However, given that the developmental process of language differs among individuals, with differing nurturing circumstances and gender-based differences influencing outcomes, we considered that, rather than a cross-sectional survey, a longitudinal survey tracking language development of each target infant over time would be most appropriate. In addition, the development of language must be examined from both an anatomical aspect and a cognitive functional aspect. This study confirmed that frequency analyses of the length of the vocal tract and the position of the tongue at the time of utterance can be used to analyze the anatomical aspect. Developmental assessments, such as the LDS of CBCL and M-CHAT, were also confirmed to be useful for evaluating the cognitive function.

The development of child behavior is variable, and most pediatric neurologists consider the accurate diagnosis of ASD to be impossible before two years of age. We detected 3 ASD high-risk infants among the 10 VLBW infants in this study. As the participants' birth weight and gestational age were extremely low, the incidence of ASD high-risk infants was considered to be a reasonable one. In addition, one NBW infant was diagnosed as having a high risk of ASD incidentally. Many infants with LBW have issues in the perinatal period and are often born before 37 weeks' gestation, so it is best to evaluate the development of the infant in terms of the corrected age. On comparing the frequency of F0 between the NBW and corrected VLBW infant groups in the present study, the F0 of the VLBW infant group was about 50 Hz higher than that of the NBW infant group. Considering that the difference in the F0 frequency average of infants and young children is about 100 Hz, it is generally presumed that the vocal tract length of VLBW infants is shorter than that of NBW infants, even after age correction. However, considering that the length and shape of the vocal tract rapidly develops at two years after birth and that the F0 frequency analysis in infancy is very unstable, it is difficult to evaluate the development of the vocal tract of an infant based solely on the F0 frequency.

In the English language, the F0 frequency of /i/ and /u/ is higher than that of other vowels, so the characteristics of the F0 frequency vary among vowels.[3] If we can evaluate the F0 frequency of each vowel longitudinally and along with formant frequencies, such as F1 and F2, it may be possible to acoustically examine the development of the vocal tract in infancy. However, it is difficult to accurately label vowels in the speech of an infant who cannot speak the requested word.

In the present study, the changes over time in the frequencies of F1 and F2 were compared among three groups. In early childhood, the "first words" emerge from about 12 months of age, and most children can speak about 50 meaningful words by 18 months of age. After 18 months of age, the acquisition of vocabulary proceeds rapidly, and an explosive increase in vocabulary (roughly 8 to 10 words acquired per day) called the "vocabulary spurt" can be seen.[11] The results of the present study suggested that the range of the front and back movement and up and down movement of the tongue became rich, since the variance in the F1 and F2 of NBW and VLBW infants increased after 18 months of age. We may have thus captured the increased vocabulary as acoustic features. However, the CBCL·M-CHAT non-passing infant group showed distinctive characteristics of language development, such as a significantly increased variance in the F1 at 18 months of age followed by an increase and decrease similar to the NBW and VLBW infant groups. Some infants with ASD have “knick type” autism in which they lose their acquired abilities during the first few years of life.[4, 7] In a study of 261 ASD infants, Kurita reported that 96.9% of the disintegrative phenomenon involved the loss of meaningful words, and the median age at the onset was 18 months. In addition, it is also reported that the age of the emergence of meaning words was significantly earlier than that of non-knick-type autism infants. However, Kurita states that such a disintegrative phenomenon is seen not only in infants with ASD but also in those with mental retardation.[13] The different variance in the F1 in CBCL-M-CHAT non-passing infants from NBW and VLBW infants might be related to the autistic regression seen in infants with ASD. Unfortunately, the pathogenesis of autistic regression remains unclear, despite extensive studies. The knick type was reported to account for about one-third of all ASD cases.[6] Larger-scale studies will be needed in the future, although a formant analysis may be able to detect the change more sensitively.

We noted a high positivity rate for M-CHAT among VLBW infants at the beginning of this study. In the present study, one NBW infant and one VLBW infant failed to pass the M-CHAT, but as M-CHAT is being developed as a primary screening to avoid false negatives, we consider that M-CHAT enhances the positive rate of ASD. In addition, LBW infants has the weak region such as joint attention action, it should be careful to diagnose ASD only with M-CHAT. Increasing the accuracy by conducting additional screening with other development evaluations in combination with M-CHAT will lead to the early detection and early support of ASD high-risk infants.

In the present study, the language development delay, which is a core feature of ASD infants from an acoustic point of view, was analyzed, and the obtained findings suggest the utility of a formant analysis. Studies in the field of speech analysis are progressing daily, and speech translation using speech recognition systems and writing with automatic dictation using a speech input interface or similar mechanic are being put into practical use. However, such advances have been made possible because vast amounts of vocabulary data have already been obtained, and it is difficult to apply the language acquisition of an infant who does not possess any vocabulary at birth. To understand language development, we must also consider the generation of speech, the function of the cerebral cortex related to perception and the anatomical structure of articulatory organs. Furthermore, in order to examine the development of articulatory movement, it is necessary to construct a speech production database in Japanese. Hashi created an articulatory movement database for adults using X-ray microbeams.[1] As a result, since the normal range of utterances can be limited, it has become possible to evaluate pathological articulatory movements, such as dysarthria. However, the development of an articulatory movement database for infants has only just begun, and further development will be needed in order to facilitate the evaluation of language development delay due to the presence of individual differences and developmental disorders.

Shriberg et al. investigated the prosody and voice characteristics of adult ASD patients and suggested the need for instrumental studies.[19] In order to detect ASD high-risk infants early, we must capture more specific changes in the early stage of the language acquisition process. By improving the accuracy of the frequency analysis, capturing the differentiation of the five Japanese vowels over time in infancy and labeling the speech of infants, we hope to improve the screening process of ASD infants.

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REFERENCES

1. **Hashi, M.** 2000. The x-ray microbeam speech production database in Japanese. Journal of the Phonetic Society of Japan. **4(2)**: 31-35
2. **Hattori, S.** 1986. Phonetics, p.132-133. Iwanami Press, Tokyo, Japan
3. **Honda, K.** 2018. Experimental speech science: In search of the generative processes of speech events, p.21. In Acoustical Society of Japan. (ed.). Korona Press, Tokyo, Japan
4. **Ishii, T.** 1971. Diagnosis and treatment of infantile autism. Japan Medical Journal. **2459**: 27-30
5. **Kamiya, K.** 2018. Maternal and child health statistics of Japan, p.44-45. In Mothers’& Children’s Health & Welfare Association. (ed.). Mothers’& Children’s Health Organization, Tokyo, Japan
6. **Kamizono, S.** 2015. Current review and future prospects about autistic regression. Bulletin of Faculty of

Education University of the Ryukyus. **(87)**:147-166
7. **Kanner, L.** 1943. Autistic disturbances of affective contact. Nerv Child. **2**: 217-250
8. **Kasuya, H., Suzuki, H., and Kido, K.** 1968. Changes in pitch and first three formant frequencies of five Japanese vowels with age and sex of speakers. Acoustical Society of Japan. **24(6)**: 355-364
9. **Kent, R.D., and Read, C.** 1996. The acoustic analysis of speech, p.21-191. Kaibundo Press, Tokyo, Japan
10. **Ibid.**, p.117
11. **Koyama, T.** 2008. Development at a period of early language acquisition, p.12-18. Nakanishiya Press, Kyoto, Japan
12. **Kuban, K.C., O'Shea, M., Allred, E.N., et al.** 2009. Positive screening of the modified checklist for autism in toddlers (M-CHAT) in extremely low gestational age newborns. J Pediatr. **154**: 535-540
13. **Kurita, H.** 1983. Specificity of "disintegrative phenomenon" in infantile autism. I. description of the phenomenon, antecedent factors and early development. Clinical Psychiatry. **25(9)**: 953-961
14. **Lampi, K.M., Lehtonen, L., Tran, P.L., et al.** 2012. Risk of autism spectrum disorders in low birth weight and small for gestational age infants. J Pediatr. **161(5)**: 830-836
15. **Lieberman, P.** 1980. On the development of vowel production in young children, p.113-142. In Yeni-Komshian, G.H., Kavanagh, J.F., Ferguson, C.A. (eds.). Child Phonology volume1. Academic Press, New York, USA
16. **Limperopoulos, C., Bassan, H., Sullivan, N.R., et al.** 2008. Positive screening for autism in ex-preterm infants: Prevalence and risk factors. Pediatrics **121(4)**: 758-765
17. **Moore, T., Johnson, S., Hennesyssy, E., et al.** 2012. Screening for autism in extremely preterm infants: problems in interpretation. Dev Med Child Neurol. **54**: 514-520
18. **Serkhane, J.E., Schwartz, J.L., Boë, L.J., et al.** 2007. Infants' vocalizations analyzed with an articulatory model: A preliminary report. Journal of Phonetics **35**: 328-329
19. **Shriberg, L.D., Paul, R., and McSweeny, J.L.** 2001. Speech and prosody characteristics of adolescents and adults with high-functioning autism and asperger syndrome. Journal of Speech, Language, and Hearing Reseach. **44**: 1097-1115
20. **Tallal, P.** 2003. Language learning disabilities: Integrating research approaches. Current Directions in Psychological Science. **12(6)**: 206-211