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Original article

Reading difficulty in school-aged very low birth weight infants in Japan

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Abstract

Objective: To investigate the prevalence of and the perinatal risk factors related to reading difficulty in school-aged very low birth weight infants (VLBWI) with normal intelligence.

Methods: Subjects were 79 Japanese children in the second to fourth grade of elementary school who had been born at very low birth weight and who regularly visited a follow-up clinic at one of four hospitals. All members had a full-scale IQ score of 80 or higher. Perinatal information was obtained retrospectively from medical records. Each subject underwent four reading tasks, testing monomoratic syllable reading, word reading, non-word reading and short sentence reading. Subjects with an SD reading time score greater than 2.0 in two or more tasks were considered to have reading difficulty (RD). Furthermore we investigated the relations between RD and perinatal factors using logistic regression analysis adjusted for potential confounding factors.

Results: Twenty-five (31.6%) out of 79 subjects had RD. We discovered that treated retinopathy of prematurity (tRoP) was a significant risk factor (adjusted OR = 5.80, 95% confidence interval = 1.51–22.33).

Conclusion: The rate of RD in school-aged VLBWI was higher than the estimated prevalence of dyslexia in Japan. Even in children with normal intelligence, long-term developmental follow-up including support for reading skills is necessary for VLBWI. Further investigation is desired to elucidate the relations between visual problems and RD in school-aged children.

Keywords: Very low birth weight infant; Premature; Reading difficulty; Dyslexia

1. Introduction

A recent study showed that the survival rate of very low birth weight infants (VLBWI, less than 1500 g) in Japan has improved to more than 90% in the past 10 years [1]. Yet about 15% of VLBWI discharged from

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Japanese Neonatal Intensive Care Units (NICUs) exhibited developmental delay at 3 years of age [2]. Previous studies from abroad have shown that many school-aged preterm children without mental retardation have learning difficulties in reading, writing or mathematics [3]. Reading difficulty in school-aged preterm children has been particularly well studied in many countries, and a recent meta-analysis of English-speaking school-aged children showed that preterm children perform worse than peers born at term at both decoding and reading comprehension [4].

In Japan, however, there have been few studies about learning problems including reading difficulty in school-aged preterm children. More than 10 years ago, Hara et al. reported that 6 (14%) out of 44 children without major neurodevelopmental sequelae but with extremely low birth weight (less than 1000 g) had learning disabilities in the third grade (approximate age 8–9) [5]. Also, Koeda et al. reported that 3 (25%) out of 12 children born at very low birth weight (VLBW) had typical learning disabilities [6]. Because the methods of evaluating learning problems in those two studies were subjective, however, the authors of both studies noted the need for established methods for the objective assessment of learning problems in Japanese children.

Recently, a new set of Japanese guidelines for the diagnosis and treatment of specific developmental disorders [7] was published. In these guidelines, standardized objective tests for evaluating subjects' ability to read hiragana script were proposed. In the present study, using these objective evaluations, we aimed to estimate the prevalence of reading difficulty in school-aged children born at VLBW and to elucidate the perinatal risk factors for reading difficulty in children born at VLBW.

2. Methods

2.1. Subjects

Japanese children with normal intelligence in the second to fourth grades of elementary school (approximate age range 7–10) who had been born at VLBW and who regularly visited a follow-up clinic at one of the participating hospitals (Okayama Medical Center, Kyushu Medical Center, Saga Hospital and Mie Chuo Medical Center) were eligible for the study and were recruited prospectively between April 2013 and March 2015. Subjects had been scored according to the Wechsler Intelligence Scale for Children (WISC)-III or IV during preschool or later, and all participants had full-scale IQ scores of 80 or higher. Children with hearing difficulties, impaired visual acuity in spite of using eyeglasses, or articulatory disorders were excluded. Also, children in inappropriate educational settings were excluded. Written informed consent was obtained from all participants and/or their parents at the time of this study. This study was approved by the Ethical Committee of the National Hospital Organization (H25-0213005).

2.2. Reading tests

Each subject underwent all four of the reading tasks described below, in accordance with the methods previously reported by Ogino et al. [8]. All subjects were examined by experts on neuropsychology in quiet rooms. During each of the four tasks, we recorded the subjects' voices with an IC recorder.

2.2.1. Monomoratic syllable reading task [7–9]

We defined 'mora' as the smallest rhythmic element into which a word can be divided. Subjects were instructed to read aloud 50 monomoratic syllables, including 20 contracted sounds, as quickly and as accurately as possible. Syllables were printed in hiragana on 210 × 297 mm white cards, arranged into five rows and 10 columns of syllables on each card. Before trial, subjects practiced with sample cards. The amount of time each subject required to read all 50 syllables was recorded.

2.2.2. Word reading tasks [7,8,10]

Subjects were instructed to read aloud 30 Japanese words of three to four moras each (e.g., "げんかん" [genkan] (entrance)) as quickly and as accurately as possible. Words were printed in hiragana on 210 × 297 mm white cards, arranged into three columns and 10 rows of words on each card. Before trial, subjects practiced with sample cards. The amount of time each subject required to read all 30 words was recorded.

2.2.3. Non-word reading tasks [7,8,10]

Subjects were instructed to read aloud 30 non-words of three to four moras each (e.g., "してぼう" [shitebou] (no meaning)) as quickly and as accurately as possible. These non-words were printed in hiragana on 210 × 297 mm white cards, arranged into three columns and 10 rows of non-words on each card. Before trial, subjects practiced with sample cards. The amount of time each subject required to read all 30 non-words was recorded.

2.2.4. Short sentence reading task [8,11]

Subjects were instructed to read aloud three short sentences of 23–27 moras each. Each sentence was printed in mixed hiragana and kanji on a 210 × 297 mm white card. Above the kanji letters, there were hiragana indicating the correct pronunciation of the kanji letters. Subjects were shown three cards in succession, and were instructed to read the short sentences aloud as quickly and as accurately as possible. The amount of time each subject required to read all of the sentences was recorded.

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Reading times were measured using DigiOnSound 5 Express (DigiOn, Inc., Fukuoka, Japan) voice analyzing software on a personal computer by a single researcher. Based on gender-segregated, grade-specific normative times required for comparable reading tasks [7], we calculated the Z scores of reading times of each reading task. Because the Japanese school year starts in April and the normative data was recorded in October, subjects who were tested on our reading tasks between April and September were scored relative to the normative data from the grade below [7]. According to the Japanese guidelines for the diagnosis and treatment of specific developmental disorder [7], we identified subjects with Z scores greater than 2.0 in two or more tasks as having reading difficulty (RD).

2.3. Perinatal information

Subjects' gestational age (GA), birth weight (BW), height at birth (HT), head circumference at birth (HC), and Apgar scores at 1 min (Aps1) and 5 min (Aps5) were collected retrospectively from their medical records. Also, presence or absence of intraventricular hemorrhage (IVH), symptomatic patent ductus arteriosus (sPDA), necrotizing enterocolitis (NEC), intestinal perforation, late circulatory collapse (LCC), treated retinopathy of prematurity (tRoP) and severe chronic lung disease (CLD36) was noted retrospectively from medical records. We defined CLD36 as oxygen dependence after 36 weeks of postconception age.

2.4. Data analysis

First, we analyzed the results of the reading tasks and calculated the prevalence of RD among our subjects. Then, to elucidate the perinatal risk factors for RD in school-age children born at VLBW, we performed logistic regression analysis adjusted for potential confounding factors to estimate the odds ratios (ORs) for RD.

3. Results

3.1. Prevalence of RD among school-aged children born at VLBW

The subjects were 79 Japanese children, specifically, 31 boys and 48 girls. Medians of GA and BW were 29 weeks 0 days (range: 23 weeks 3 days – 36 weeks 3 days) and 959 g (425–1498 g), respectively. Median age at the time of the reading test was 8 years 11 months (7 years 4 months – 9 years 11 months). The Z scores for each reading task are shown in Fig. 1. Twenty-five out of 79 subjects (31.6%) were judged to have RD. Detailed characteristics of subjects stratified by birth weight are shown in Table 1.

Here, we showed two representative cases with RD. Case 1 was a boy born at 24 weeks of GA. His BW and HT were appropriate for GA. He was mechanically ventilated for 35 days due to prematurity. He had a mild (grade I) IVH. LCC occurred when he was 20 days old and dexamethasone was administered intravenously for several days. He did not have sPDA, NEC, intestinal perforation or CLD36 during his clinical course. Laser retinal photocoagulation was done bilaterally for treatment of RoP. After discharge from the NICU, his developmental milestones were not delayed. He used eyeglasses because of myopia of the left eye. At school, he was not good at taking notes or learning Japanese kanji, although he had no significant difficulties understanding his studies. In the third grade of elementary school (8 years of age) WISC-III and kana reading tests was done. His full-scale intelligence quotient (FIQ), performance intelligence quotient (PIQ) and verbal intelligence quotient (VIQ) were 98, 93 and 103, respectively. His verbal comprehension (VC), perceptual organization (PO), freedom from distractibility (FD) and processing speed (PS) were 103, 95, 97 and 106, respectively. On kana reading tests, he scored below −2.0 SD in three of four reading tasks, and was judged to have RD.

Case 2 was a girl born at 30 weeks of GA. She was a SGA infant. She did not have IVH, sPDA, NEC, intestinal perforation, LCC or CLD36 during her clinical course. Although she had mild RoP, treatment was not needed. After discharge from the NICU, her developmental milestones were not delayed. At school, she did not like reading long text, and she was not good at reading Japanese kanji, although she had no significant difficulties with understanding her studies. In the fourth grade of elementary school (9 years of age) WISC-III and kana reading tests were done. Her FIQ, PIQ and VIQ were 87, 87 and 89 respectively. Her VC, PO, FD and PS were 86, 85, 94 and 103, respectively. On kana reading tests, she scored below −2.0 SD in two of four reading tasks, and was judged to have RD.

3.2. Perinatal risk factors for RD

Significant differences were seen in the morbidity of tRoP (OR = 4.52, 95% CI = 1.30–15.72 $p = 0.018$) between the RD group ($n = 25$) and the non-RD group ($n = 54$) (Table 2). Aps5 was mildly related to the morbidity of both tRoP and RD, and was adopted as a confounding factor. Adjusted OR of tRoP for RD was 5.80 (95% C.I., 1.51–22.33). Although GA had no relation to RD, GA was significantly related to the morbidity of tRoP. Accordingly, we divided subjects into two subgroups according to GA, with the cutoff point set as the median GA for the entire subject population (29 weeks 0 days). In the low-GA group (less than

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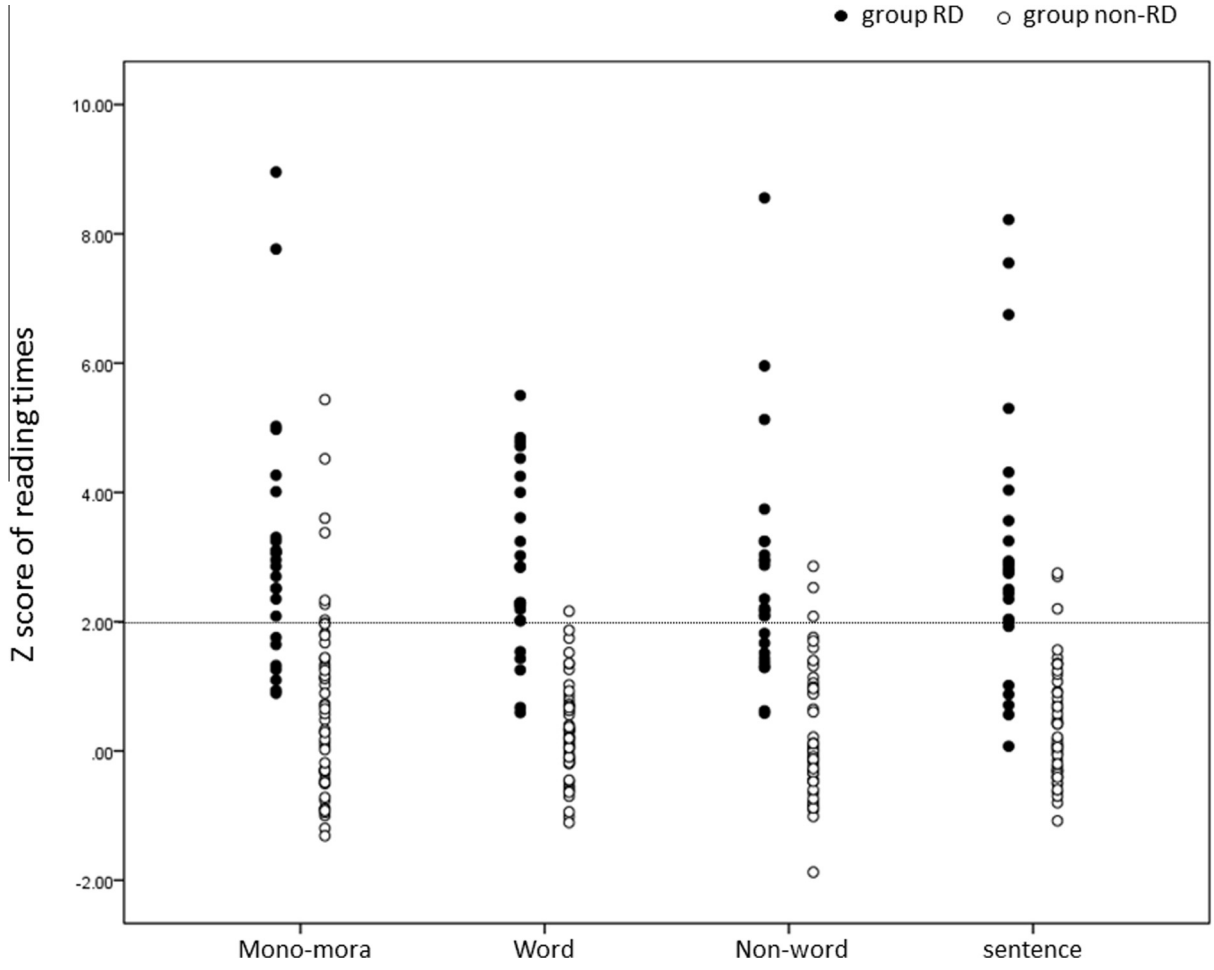

Fig. 1. Distributions of Z scores for each reading task. Based on gender-segregated, grade-specific normative times required for comparable reading tasks, we calculated the Z scores of the reading times of each reading task. Subjects judged to have RD (scored 2.0 SD or higher in two or more reading tasks) were shown as filled circle (group RD), and subjects without RD was shown as open circle (group non-RD). The horizontal line was drawn at 2.0 SD.

Table 1
Detailed characteristics of the subjects stratified by birth weight.

	Birth weight			
	<750 g ($n = 17$)	750–999 g ($n = 25$)	1000–1249 g ($n = 17$)	1250–1499 g ($n = 20$)
Gestational age[a]	27w1d (23w3d–31w4d)	27w6d (24w5d–34w2d)	29w3d (26w5d–33w6d)	32w1d (29w0d–36w3d)
Birth weight[a]	674 g (425–738)	891 g (750–990)	1108 g (1004–1224)	1393 g (1250–1498)
Male	7 (41.2%)	10 (40.0%)	6 (35.3%)	8 (40.0%)
Apgar score 1 min	4 (1–6)	4.5 (1–9)[c]	5 (1–9)	8 (2–9)
Apgar score 5 min	7 (1–9)[b]	7 (1–10)	8 (4–9)	9 (6–10)
Small for gestational age	8 (47.1%)	11 (44.0%)	6 (37.5%)[b]	6 (30.0%)
Intraventricle hemorrhage	2 (11.8%)	3 (12.0%)	1 (6.3%)[b]	1 (5.0%)
Necrotizing enterocolitis	0	0	0[b]	0
Intestinal perforation	0	1 (4.0%)	0[b]	0
Symptomatic PDA	11 (64.7%)	13 (52.0%)	6 (37.5%)[b]	2 (10.0%)
Late circulatory collapse	3 (17.6%)	8 (32.0%)	2 (12.5%)[b]	0
Severe CLD	3 (17.6%)	4 (16.0%)	2 (12.5%)[b]	1 (5.0%)
Treated RoP	5 (29.4%)	5 (20.0%)	3 (18.8%)[b]	0
Reading difficulty	6 (35.3%)	8 (32.0%)	5 (29.4%)	6 (30.0%)

PDA, patent ductus arteriosus; CLD, chronic lung disease; RoP, retinopathy of prematurity.
[a] Median (min–max).
[b] $n = 16$.
[c] $n = 24$.

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Table 2
Differences of patient characteristics between group RD and group non-RD.

			Logistic regression	
	Group RD ($n = 25$)	Group non-RD ($n = 54$)	OR (95% CI)	p value
Gestational age[a]	29w3d (24w0d–36w3d)	28w6d (23w3d–34w2d)		0.483
Birth weight[a]	959 g (425–1498 g)	961.5 g (573–1492 g)	0.99 (0.99–1.00)	0.557
Male	7 (28.0%)	24 (44.4%)	0.49 (0.17–1.36)	0.168
Apgar score at 1 min	6 (1–9)	5 (1–9)[b]	1.12 (0.93–1.35)	0.229
Apgar score at 5 min	8 (1–10)	8 (1–10)[b]	1.21 (0.92–1.59)	0.165
Small for gestational age	12 (48.0%)	19 (35.8%)[b]	1.65 (0.63–4.34)	0.308
Intraventricle hemorrhage	2 (8.0%)	5 (0.4%)[b]	0.84 (0.15–4.63)	0.836
Necrotizing enterocolitis	0 (0%)	0 (0%)[b]	–	–
Intestinal perforation	1 (4.0%)	0 (0%)[b]	–	1.000
Symptomatic PDA	10 (41.5%)	22 (40.0%)[b]	0.94 (0.36–2.48)	0.899
Late circulatory collapse	4 (16.0%)	8 (15.1%)[b]	1.07 (0.29–3.96)	0.918
Severe CLD	4 (16.0%)	6 (11.3%)[b]	1.49 (0.38–5.85)	0.566
Treated RoP	8 (32.0%)	5 (9.4%)[b]	4.52 (1.30–15.72)	0.018

PDA, patent ductus arteriosus; CLD, chronic lung disease; RoP, retinopathy of prematurity; RD, reading difficulty.
[a] Median (min–max).
[b] $n = 53$.

Table 3
Adjusted odds ratios of treated RoP for RD in two subgroups stratified by gestational age.

			Logistic regression	
			OR (95% CI)[a]	p value
Gestational age >= 29w0d	Group RD ($n = 15$)	Group non-RD ($n = 25$)		
Treated RoP	2 (13.3%)	1 (4.0%)	3.81 (0.31–46.10)	0.294
Gestational age < 29w0d	Group RD ($n = 10$)	Group non-RD ($n = 28$)		
Treated RoP	6 (60.0%)	4 (14.8%)	8.93 (1.51–52.64)	0.016

RoP, retinopathy of prematurity; RD, reading difficulty.
[a] Adjusted for Apgar score at 5 min.

29 weeks 0 days), adjustedOR of tRoP for RD was 8.30 (95% C.I., 1.51, 52.64). In the high-GA group (more than 29 weeks 0 days), on the other hand, adjustedOR of tRoP for RD was 3.81 (95% C.I., 0.31, 46.10, $p = 0.294$) (Table 3).

4. Discussion

According to the results of our Japanese kana reading tests, we judged that 25 (31.6%) out of 79 study participants had RD. In contrast, a previous large study in Japan estimated that the prevalence of dyslexia, including suspected cases, in the general population of Japan was 0.7–2.2% [7]. Though it is difficult to compare directly the results of the present study with those of the previous dyslexia study, it seems clear that the rate of RD is higher in school-aged Japanese VLBWI than in the general population of Japan. In Sweden, Samuelsson et al. previously reported that 31% of school-aged VLBWI had low reading skill scores in reading comprehension tests [12]. The rate of poor reading skills in Samuelsson's study in Sweden are comparable with that in the present study in Japan.

In the present study, we found that treated RoP was the most significant risk factor for RD in school-aged VLBWI. No significant relation between CLD36 and RD was shown in the present study, though a relation between co-morbid chronic lung disease (CLD) and low academic achievement among children born with ELBW has been reported previously [13].

The relation between RoP and reading problems in VLBWI has not been reported previously as far as we know. The negative impacts of RoP on visual function in childhood, such as strabismus, abnormal refraction and abnormal contrast sensitivity, have been previously reported, however [14]. Similarly, Larsson et al. reported that the peripheral visual field is constricted in children who have undergone cryotreatment [15]. Therefore it is possible that tRoP has a direct negative impact on visual function despite the exclusion of subjects with impaired visual acuity from the present study.

In many languages, including Japanese, the primary cause of dyslexia is thought to be a problem in decoding function [16,17]. Yet Samuelsson has reported that weaknesses in orthographic (spelling-based) reading skills were more prominent relative to weaknesses in

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phonological (sound-based) skills in the VLBW group than in the normal-birth-weight controls [18,19]. Recently, the crowding phenomenon attracted attention as a basis of reading disorders [20]. Crowding refers to the interference of flanking letters in the recognition of target letters [20]. Larsson et al. showed that prematurely born children, especially those with severe untreated RoP or cryotreated RoP, had poor crowding acuity compared with full-term children [21]. The crowding phenomenon might contribute to the relation between treated RoP and RD discovered in the present study.

Also, the increased risk of reading difficulty in children with very low birth weight is reportedly associated with periventricular white matter injury [22]. The portion of periventricular white matter that is sometimes injured in premature infants is part of the visual cognition pathway [23]. Therefore the mechanism by which reading difficulty occurs might differ between VLBWI and children born at full term. Problems with visual cognition, in addition to phonological weakness, might play an important role in reading difficulty in school-aged VLBWI.

Among the subjects of the present study, four children received special-needs education a few hours each week, and three of these had RD. Though we did not investigate the reasons why these children were receiving special-needs education, it is likely that they exhibited learning problems or behavioral problems such as attention deficit hyperactivity disorder (ADHD) or autism spectrum disorder (ASD). A high prevalence of RD in patients with ADHD or ASD in Japan has been shown in a previous study [24].

The present study had two major strengths. First, this was a multicenter study, reducing the possibility that the therapeutic characteristics of any particular hospital affected our results. Second, we adopted an objective reading evaluation; this was the first report on reading difficulty in school-aged VLBWI in Japan in which the data was collected using an objective test. On the other hand, this study had some limitations. First, we could not eliminate the possibility of selection bias because the follow-up rates at two of the four participating hospitals were too low. Moreover, we could not recruit all potential subjects followed in the developmental outpatient clinics at each hospital. Second, tests of precise visual acuity, detailed visual field tests and refraction tests at the time of the reading test were not available, because not all of the patients received ophthalmologic examinations after admission into elementary school. Further large prospective studies, including brain imaging, detailed ophthalmologic examinations at school age, tests for phonological processing, neuropsychological evaluations for visual cognition such as the Frostig developmental test of visual perception [25] or Rey–Osterrieth Complex Figure [26] and behavioral evaluations able to detect ADHD and ASD are desired.

Although Samuelsson et al. reported that the reading skills of school-aged VLBWI improved over time until, by the age of 15 years [19], there was no significant difference between VLBWI and normal control subjects, it is thought that reading difficulty in the lower grades of elementary school might have a negative impact on academic achievement throughout a child's school career. Accordingly, it is important to diagnose reading difficulties and provide appropriate educational environments as early as possible. Long-term developmental follow-up for VLBWI including support for reading skills is necessary even for VLBWI of normal intelligence, and cooperation with schools and specialized institutions for educational and behavioral problems is very important.

5. Conclusions

About 30% of school-aged VLBWI with normal intelligence and no significant visual problems had a possible reading disorder. This rate is higher than the estimated prevalence (0.7–2.2%) of dyslexia in the Japanese general population. In spite of normal intelligence, long-term developmental follow-up for VLBWI including support for reading skills is needed. Moreover, we discovered that treated RoP was a significant risk factor for reading difficulties among school-aged VLBWI. Further investigation is desired to elucidate the relations between visual problems and RD in school-aged VLBWI.

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