RELATIONSHIPS BETWEEN ORAL CHARACTERISTICS AND EATING/SWALLOWING FUNCTIONS IN PATIENTS WITH RETT SYNDROME OF VARIOUS AGES

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ABSTRACT

This study was conducted to clarify the actual status of oral symptoms related to the *systemic* and eating/swallowing functions, and the effect of ageing for those conditions in patients with Rett syndrome. The subjects were 38 females aged from 4 to 63 years diagnosed with Rett syndrome. The examination items were age, nutritional status, gross motor functions, history of epileptic seizures, antiepileptic drugs use, history of pneumonia, respiratory status (apnea, hyperventilation, and aerophagia), ingested food type, eating/swallowing functions, dysphagia symptom, occlusal condition, eating independence level, palate shape, and bruxism. Using Pearson's correlation coefficient, no significant correlation between age and nutritional status was observed (Rohrer index: $p=0.12$, BMI: $p=0.22$). When the other inter-item relationships were evaluated by the χ square test and Fisher's exact test, a significant correlation was recognized between gross motor functions and oral functions ($p < 0.01$), between gross motor functions and swallowing function ($p < 0.05$), and between respiratory status and oral functions ($p < 0.05$). The investigation of the characteristics of patients with Rett syndrome suggested that decreased gross motor functions, such as gait function, and the appearance of respiratory status might herald the development of eating/swallowing dysfunction.

KEY WORDS: Rett syndrome; Eating/swallowing functions; Ageing; Nutritional status; Respiratory status

INTRODUCTION

Rett syndrome is a neuro-developmental disease caused by mutation of the MECP2 gene on the X chromosome, which results in intellectual impairment, an autistic feature, varying degrees of movement impairment, epilepsy and other disorders (Amir, Van den Veyver, Wan, Tran, Francke, Zoghbi, 1999). It occurs in one out of every 10,000 females. There are no abnormalities during the perinatal period, and nearly normal mental development is seen until 6 months after birth, but thereafter muscle tension gradually increases with aging, eventually resulting in spastic paralysis and intellectual impairment (Suzuki & Hirayama, 2005). Furthermore, stereotypical hand movements are characteristically seen, autonomic disorder, and eating/swallowing dysfunction reportedly develops in many cases (Suzuki et al, 2005; Matsuishi, 2013; Fuertes-González, Silvestre, Almerich-Silla, 2011). However, only few reports have referred to eating/swallowing dysfunctions accompanying the progression of symptoms specific to Rett syndrome (Oddy, Webb, Baikie, Thompson, Relly, Fyfe, Young, Anderson, Leonard, 2007; Tommessen, Kase, Heiberg 1992; Morton, Bonas, Minford, Tarrant, Ellis,1997), and the actual status of these functions has not yet been sufficiently examined. On the other hand, it was thought that Rett syndrome with malocclusion and bruxism as they are considered likely to be associated with orofacial muscle, some of their eating/swallowing dysfunctions might be improved by orofacial myofunctional therapy. Therefore, this study was conducted to clarify the actual status of symptoms related to the systemic, oral and eating/swallowing functions

in patients with Rett syndrome, and to investigate the influences of aging on these functions.

MATERIALS AND METHODS

Subjects

For the survey, the subjects were 38 females diagnosed with Rett syndrome who lived in the Kanto area in Japan (age range: 4-63 years, mean: 23.9 ± 14.2 years). Rett syndrome was genetically diagnosed by gene examination in 8 subjects and clinically diagnosed based on symptoms in the other 30 subjects. Referrals had been made by an attending physician for 31 subjects and by an acquaintance for 7 subjects. When classified according to living circumstances, 28 subjects lived at home, 7 at an institution for the disabled, and 3 at medical institutions.

Methods

Examination methods

Concerning the past history and present illness of each subject, information was obtained from medical records and from interviews with their guardians. One dentist, specialized in dysphagia rehabilitation, visited each subject at their home or the institution where they were housed, and evaluated eating/swallowing functions by observation according to Kaneko's evaluation criteria while eating lunch (Kaneko, Mukai, Omoto,1987; Tamura, Kikutani, Machida, Takahashi, Nishiwaki, Yaegaki. 2011).

Examination items

Four categories were examined: 1. Age; 2. Systemic Condition items; 3. Diet Items; and 4. Oral Environment items. The details of the later three categories included are described below. Inter-item correlations were investigated in each category.

Category 2 Systemic Condition items:

1) nutritional status (Body Mass Index [BMI] (Waard, 1987), targeting an age ≥ 19 years, and Rohrer Index (Kitagawa, 1974), targeting an age ≤ 18 years);
2) gross motor functions such as gait function: walking without limitations (walking), walking with limitations (walking with L) , sitting without limitations (sitting), sitting with limitations (sitting with L),and bedridden (unable to maintain antigravity head and trunk postures) according to part of Gross Motor Functions Classification System (GMFCS) (Allen & Alexander,1990),
3) presence/absence of epileptic seizures,
4) antiepileptic drug/s use,
5) history of pneumonia,
6) respiratory status: apnea, hyperventilation, and aerophagia (Suzuki et al, 2005).

Category 3 Diet items:

1) ingested food type: regular and purred,
2) eating/swallowing functions such as chewing ability - munching, diagonal rotary chew, and circular rotary chew, (Morris & Klein, 2000) and tubal feeding,
3) dysphagia symptom: presence or absence of choking during eating; and
4) eating independence level - independent, partially independent, total assistance.

Category 4 Oral Environment items:

1) occlusal condition - normal, maxillary prognathism, and cross bite (Ribeiro, Romano, Birman, Mayer,1997),
2) palate shape (Riberio et al,1997) and
3) presence/absence of bruxism (Magalhães, Kawamura , Araújo, 2002)

Statistical Analysis

SPSS Ver. 18 (windows) was used for all statistical analyses. The relationship between age and nutritional status was evaluated employing Pearson's correlation coefficient, and other inter-item relationships were evaluated by the χ squared test and Fisher's exact test.

Ethical Considerations
Before the start of this study, the purpose was explained to the guardians of each subject orally and in writing, and consent for participation in this study was obtained. This study was conducted after obtaining approval from the Ethics Committee, Nippon Dental University School of Life Dentistry (Approval No. NDU-T2010-41).

RESULTS

The basic information of age, systemic condition items, diet items and oral environment items are provided in Table 1.

Age
There were 16 (42.1%) subjects under 18 years old. There were 22 (57.9%) subjects over 19 years old.

Systemic condition items
Regarding nutritional status, malnutrition was seen in 27 (71.1 %) subjects. There were 23 (60.5%) subjects who were able to walk (including limited walking). There were 30 (78.9%) subjects taking an antiepileptic drug), but 20 (52.6%) subjects being free of epileptic seizures. There were 27 (71.1%) subjects who had no history of pneumonia. As to respiratory status: 20 (52.6%) subjects had apnea, 11 (28.9%) subjects had hyperpnea, and 8 (21.1%) subjects had aerophagia.

Diet items
The ingested food type was a regular diet in 27 (71.1%) subjects, and purred diet in 11 (28.9%) subjects. As to oral functions, 24 (63.2%) subjects were able to chew although often not completely. As to dysphagia symptoms, 24 (63.2%) subjects choked when eating. The eating independence level was total assistance in 29 (76.3%) subjects.

Oral environment items
The occlusal condition was normal in 20 (52.6%) subjects, and the palate was U-shaped in 36 (94.7%) subjects. There were 27 (71.1%) subjects who had bruxism.

Table 1. Basic Information

		Nutritional status		Presence/Absence of epileptic seizures		Eating independence level		History of pneumonia	
		Malnutrition	Good nutrition	No	Yes	Independent/Partially independent	Total assistance	No	Yes
Antiepileptic drugs use	No	4	4	8	0	5	3	8	0
	Yes	21	9	15	15	4	26	19	11
		p=0.032		p=0.025		p=0.004		p=0.042	

Relationship between age and nutritional status
Using, Pearson's correlation coefficient, no significant correlation was observed between the age and nutritional status (Rohrer index: r=-0.4 p=0.12, BMI: r=0.27 p=0.22).

Investigation of other inter-item relationships
When the other inter-item relationships were evaluated by the χ square test, a significant correlation was recognized between nutritional status and eating independence level ($p < 0.01$) (Table 2). There were significant relationships between gross motor functions and ingested food type ($p < 0.05$), eating swallowing functions ($p < 0.01$), and dysphagia symptom ($p < 0.05$) (Table 3). There was a significant relationships between antiepileptic drug use and nutritional status ($p < 0.05$), presence/absence of epileptic seizures ($p < 0.05$), history of pneumonia ($p < 0.05$), and eating independence level ($p < 0.01$) (Table4). There was a significant relationship between occlusal condition and bruxism ($p < 0.05$) (Table5).

Table 2. Nutritional status and Eating Independence

		Nutritional status		
		Malnutrition	Good nutrition	
Eating independence level	No	5	6	p = 0.001
	Yes	22	5	

Table 3. Gross motor functions and significant associations

		Gross motor functions					p-value
		Walking	Walking with L	Sitting	Sitting with L	Bedridden	
Ingested food type	Regular	14	4	7	2	0	p = 0.036
	Purred	1	4	3	1	2	
Oral functions	Circular rotary chew	7	1	4	0	0	p = 0.001
	Diagonal rotary chew	6	4	0	2	0	
	Munching	2	3	6	1	0	
	Tubal feeding	0	0	0	0	2	
Dysphagia symptom	Presence	10	6	8	0	0	p=0.035
	Absence	5	2	2	3	2	

Table 4. Antiepileptic drugs use and significant associations

		Antiepileptic drugs use		p-value
		No	Yes	
Nutritional status	Malnutrition	4	21	p=0.032
	Good nutrition	4	9	
History of epileptic seizures	Presence	0	15	p=0.025
	Absence	8	15	
History of pneumonia	Presence	0	11	p=0.042
	Absence	8	19	
Eating independence level	Independent/Partially independent	5	4	p=0.004
	Total assistance	3	26	

Table 5 Occlusal condition and significant associations

		Occlusal condition				p-value
		Normal	Maxillary prognathism	Cross bite	Other	
Bruxism	Presence	1 7	7	3	0	p=0.03
	Absence	3	2	5	1	

DISCUSSION

Rett syndrome is a neuro-developmental disorder showing mental retardation and a tendency for autism, and the severity of impairments is known to have a broad spectrum (Suzuki et al, 2005). It was reported that Rett syndrome is accompanied simultaneously by hand wringing, stereotyped movements such as grinding of the teeth, respiratory abnormalities such as apnea, convulsions, peripheral blood vessel movement impairment, spinal scoliosis, etc., and eating/swallowing dysfunction is also seen in many cases (Morton et al, 1997). As in the preceding study, the patients were quite thin and showed a tendency for malnutrition. Normal growth is reportedly seen in these patients until 6 months after birth (Suzuki et al, 2005). Observing the diet items revealed that 27 subjects (71.1%) ingested regular food. However, 24 subjects (63.2%) experienced choking while eating, suggesting decreased eating/swallowing functions.

In the present study, correlations were recognized among history of pneumonia, oral functions, and eating independence level. All of the subjects with a history of pneumonia were taking an antiepileptic drug. Antiepileptic drugs are said to be associated with a tendency for somnolence and hypotonic muscles as adverse reactions, which may both have adverse influences on eating/swallowing functions. In addition, antiepileptic drugs use is also related to the presence/absence of chewing functions and the need for full aid when eating. It is reasonable to speculate that the tendency for somnolence and hypotonic muscles are contributory factors, diminishing the ability to eat independently.

Since the items representing the eating/swallowing functions (i.e., ingested food type), swallowing functions and oral functions, did not correlate with age, it hardly bears mentioning that eating/swallowing functions would worsen with aging, observations different from those made in the preceding studies (Morton, et.al, 1997; Suzuki et al, 2005). However, the fact two subjects were on tube feeding, both of whom were older than 40 years and bedridden, suggested that eating/swallowing functions may possibly deteriorate simultaneously with decreases in gross motor functions such as gait function, which diminish markedly beyond age 40 years. Many subjects capable of eating a regular diet food could walk independently, and many such subjects were also able to chew as an eating/swallowing function (Nakane, Shishikura, Mukai, Kaneko,1996; Tamura, Shishikura, Mukai, Kaneko,1999). Therefore, the items serving as indices of eating/swallowing functions (i.e., ingested food type and oral functions) correlated significantly with gross motor functions such as gait function. In addition, ingested food type and eating/swallowing functions both showed a significant correlation with respiratory status (aerophagia). Other respiratory status items such as apnea and hyperpnea occurring during diet may result in cessation of eating, but the influences on eating/swallowing functions themselves were considered to be small. On the other hand, since aerophagia causes air retention in the abdomen possibly leading to difficulty in swallowing, loss of appetite and

dyspepsia (Morton, Pinnington, Ellis, 2000; Cigrang, Hunter, Peterson, 2006), aerophagia is considered to influence eating/swallowing functions.

Significant correlation was recognized between occlusal condition and habitual bruxism. The bruxism seen in Rett syndrome is considered to be induced by spastic muscle tension (Kuroshita, Nakagawa,Takamori, Wtanabe, 2007). Persons with an overbite or an underbite may also have similar jaw movements, but the fact that the contact surface between the upper and lower teeth is large in persons with a normal occlusion may also account for this result. In this connection, a high-arched palate is also reported to frequently be seen in Rett syndrome patients, but a high-arched palate was recognized in only 2 subjects in this study, and there were no correlations with other items (Marina, Juliana, Luiz, 2002). From these findings, the decrease in gross motor functions such as gait function or the appearance of aerophagia was considered to possibly herald the development of eating/swallowing dysfunction.

CONCLUSION

Investigating the characteristics of 38 patients with Rett syndrome revealed a decrease in gross motor functions such as gait function or the appearance of aerophagia to possibly herald the development of eating/swallowing dysfunction.

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REFERENCES

Allen MC, Alexander GR. (1990). Gross motor milestones in preterm infants: correction for degree of prematurity. *Journal of Pediatrics* Jun;116(6):955-9.

Amir RE, Van den Veyver IB, Wan M, Tran CQ, Francke U, Zoghbi HY. (1999). Rett syndrome is caused by mutations in X-linked MECP2, encoding methyl-CpG-binding protein 2. *Nature Genetics* .23:185-8.

Cigrang JA, Hunter CM, Peterson AL. (2006). Behavioral treatment of chronic belching due to aerophagia in a normal adult. *Behavior Modification*. 30:341-51.

Fuertes-González MC, Silvestre FJ, Almerich-Silla JM. (2011). Oral findings in Rett syndrome: a systematic review of the dental literature. *Medicina Oral Patologia Oral y Cirugia Bucal*.16:37-41.

Kaneko Y, Mukai Y, Omoto K. (1987). *Impairment of Eating Functions*. Tokyo. Ishiyaku Publishers.

Kato N, Murata M, Kawano M, Taniguchi T, Otake T. (2004). Standards of body development in children aged 0 - 18 years—From the report of "Conference on Sound Growth of Children through Food Life"– *The Journal of Child Health*. 63:345-8.

Kitagawa K. (1974). Critica lexamination of Rohrer's index in relation to the body density and the allometry equation for young male adults *Japanese Society of Physical Education NII-Electronic Library Service* 19(1)41-45

Kuroshita R, Nakagawa K, Takamori K, Wtanabe S. (2007). Care of pediatric patients with Rett syndrome accompanied by bruxism and their masseter muscle activities. *Journal of Japanese Society for the Disability and Oral Health*. 28:500.

Magalhães MH, Kawamura JY, Araújo LC.(2002) General and oral characteristics in Rett syndrome. *Special Care in Dentistry*. Jul-Aug; 22(4):147-50.

Marina H, Juliana Y, Luiz C. (2002). General and oral characteristics in Rett syndrome. *Special Care in Dentistry*. 22(4):147-150.

Matsuishi T. (2013). Rett syndrome: the state of research, and future perspectives. Japan Clinical. 11(71):2043-2053.

Morris SE, Klein MD. (2000). Pre-Feeding Skills–A Comprehensive Resource for Mealtime Development, 2nd ed. Tucson, AZ: Therapy Skill Builders, 87.

Morton RE, Bonas R, Minford J, Tarrant SC, Ellis RE. (1997). Respiration patterns during feeding in Rett syndrome. *Developmental Medicine & Child Neurology*. 39:607-13.

Morton RE, Pinnington L, Ellis RE. (2000). Air swallowing in Rett syndrome *Developmental Medicine & Child Neurology* . 42:271-5.

Nakane F, Shishikura J, Mukai Y, Kaneko Y. (1996). Respiratory and circulatory dynamics in meal ingestion by persons with severe and multiple disabilities. *Journal of Japanese Society for the Disability and Oral Health*. 17:211-28.

Oddy WH, Webb KG, Baikie G, Thompson SM, Relly S, Fyfe SD, Young D, Anderson AM, Leonard H. (2007). Feeding experiences and growth status in a Rett syndrome population. *Journal of Pediatric Gastroenterology and Nutrition*. 45:582-90.

Ribeiro,R.A., Romano, A.R. Goldenberg. E., Mircia, B., Alves Mayer, P. (1997) Oral manifestations in Rett syndrome: a study of 17 cases. *Pediatric Dentistry*. 1997 Jul-Aug;19(5):349-52.

Suzuki H, Hirayama Y. (2005). Understanding of and support to Rett syndrome. *Disability Welfare General Research Project*. Ministry of Health, Labour and Welfare

Tamura F, Kikutani T, Machida R, Takahashi N, Nishiwaki K, Yaegaki K. (2011). Feeding therapy for children with food refusal. *International Journal Orofacial Myology*. Nov;37: 57-68.

Tamura F, Shishikura J, Mukai Y, Kaneko Y. (1999). Arterial oxygen saturation in severely disabled people: effect of oral feeding in the sitting position. *Dysphagia*.14: 204-11.

Thommessen M, Kase BF, Heiberg A. (1992). Growth and nutrition in 10 girls with Rett syndrome. *Acta Paediatrica*. 81:686-90.

Waard F. (1978). Body Mass Index. *Journal of Chronic Diseases*. 31:129.

Zerin, JM, Blane CE. (1994). Sonographic assessment of renal length in children: a reappraisal. *Pediatric Radiology*. 24:101-6.