Differences in Sequential Transform of Spontaneous Movements Revealed by Angular Acceleration and Angular Jerk of Elbow Flexion-extension Movements between Infants with Autism Spectrum Disorder and Healthy Infants

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Abstract : To clarify differences in sequential transforms of spontaneous movements between autism spectrum disorder (ASD) and healthy infants, angular acceleration and jerk root mean square (RMS) values of spontaneous movements of ASD infants and healthy infants were compared. Methods : Data of 18 premature infants were used : 3 had been diagnosed with ASD at elementary school entrance ; 15 had been diagnosed as having no central nervous system and musculoskeletal system disorder and the cardiopulmonary system disorder. During 36–56 weeks postmenstrual age (PMA), premature infants were examined every 4 weeks. A three-dimensional motion analyzer measured spontaneous movements of the upper right limb in the supine position. Upper limb position data were used to calculate the angular acceleration RMS and the angular jerk RMS. Those data were allotted into 36 and 40 week PMA (term I), at 44 and 48 week PMA (term II), and at 52 and 56 week PMA (term III). RMSs was calculated at each term. Results : For angular acceleration RMSs of healthy infants, term II were significantly lower than term I ($p<.05$). For angular acceleration RMS of the ASD infants, term III was significantly higher than term II ($p<.05$). For angular jerk RMSs of healthy infants, term II and term III were significantly lower than term I ($p<.05$). For angular acceleration RMS and angular jerk RMS of ASD tended to increase, although there was no significant difference. For angular acceleration and angular jerk RMSs, the ASD infant value was significantly larger than the healthy infant value at term III ($p<.05$). Discussion and Conclusion : Spontaneous movements of ASD showed more jerkiness than those of the healthy infant group, especially at term III. Increased angular acceleration and angular jerk RMSs are initial ASD symptoms related to prognosis.

Keywords : Autism spectrum disorder, Pre-mature infant, Spontaneous movements

1. Introduction

A large variety of spontaneous movement is found in early infancy. General movements (GMs) are spontaneous movements exhibited by infants who are placed supine [1].

GMs are observed as complex movements from an early fetal term. The fetus show such movements at 8–10 weeks post menstrual age (PMA). GMs continue to develop up to the fifth month after post-term age. From birth until the fifth month after post-term, GMs are part of this early spontane-

ous motor repertoire [1, 2].

Actually, GMs involve the entire body in a variable sequence of arm, leg, neck, and trunk movements. They wax and wane in intensity, force, and speed, and have a gradual beginning and end. Rotation along the limb axis and slight changes in the direction of movement makes them fluent and elegant and creates the impression of complexity and variation [1].

In addition, GMs are known to change sequence. The sequence changes are divisible into three : pre-term GMs, writhing GMs, and fidgety GMs. Regarding pre-term GMs, from their emergence until the due date, the GMs of a pre-term infant might occasionally have large amplitudes. They are often of high speed. For writhing GMs, from their emergence until the second month after post-term age, GMs involve the entire body and exhibit themselves in a variable sequence of arm, leg, neck, and trunk movements. They increase and decrease gradually in terms of intensity and speed. Rotations and frequent slight variations of the direction of motion make them appear to be complex and smooth. Regarding fidgety GMs, at the beginning of the third month, another pattern of GMs, the so-called 'fidgety GMs' emerges, lasting until the end of the fifth month. Fidgety GMs are small movements of the neck, trunk, all limbs in all directions, and showing varying acceleration [1, 3].

Assessment using changes in GMs is called general movement assessment (GMA). GMA is conducted in a visual Gestalt perception by the examiner. GMA has been used increasingly to predict motor dysfunction, especially cerebral palsy [4–11]. With sequential transformation of GMs, the prognosis of infants with disorders of the central nervous system can be predicted [12–14]. GMA is also useful for the prognosis of autism spectrum disorder (ASD) [15, 16]. Furthermore, the sequential transformation of GMs is reportedly different between ASD infants and healthy infants in a visual Gestalt perception by the examiner [15, 16].

Moreover, the sequential transform of spontaneous movements in the elbow flexion-extension movement of healthy infants has been elucidated by our earlier studies using the root mean square (RMS) of an angular acceleration and the RMS of an angular jerk [17].

The objective of this study is to clarify the difference in amounts of the RMS of an angular acceleration, and of the angular jerk between the ASD infant group and the healthy infant group.

2. Methods

2.1. Subjects

This study examined 18 cases. Three children (male 1, female 2) had been diagnosed as having ASD at the elementary school entrance. The three children had no central nervous system, musculoskeletal system, or cardiopulmonary system disorders other than ASD. Another 15 children (male 7,

Table 1 Case information

No.	M/F	PMA (week | day)	Barth weight (g)
Autism spectrum disorder infants group			
1	M	23w 4d	568
2	F	29w 0d	897
3	F	32w 3d	1,126
Healthy infants group			
1	M	22w 2d	410
2	F	25w 0d	668
3	M	25w 0d	800
4	F	30w 0d	1,307
5	F	30w 0d	1,409
6	M	30w 0d	1,449
7	M	30w 2d	864
8	F	30w 6d	1,024
9	M	30w 6d	1,395
10	F	30w 6d	1,449
11	F	30w 6d	1,576
12	M	34w 4d	1,414
13	M	35w 1d	1,950
14	F	35w 3d	2,071
15	F	35w 3d	2,497

M/F : male or female, PMA : postmenstrual age

female 8) had been diagnosed at the elementary school as healthy without problems of the central nervous system, the musculoskeletal system, and the cardiopulmonary system (Table 1). From 36 weeks post-menstrual age (PMA), the infants participated in this study. The infant data of these children were studied.

The infants were in a state of arousal. States such as crying or of non-arousal were unsuitable for assessments. For measurements, the room temperature was maintained as 28℃ (82.4℉). The infants wore thin clothes to maintain body temperature. Furthermore, the room was kept free of noise.

All infants' parents gave written informed consent to participate in this study, which was approved by the institutional review board of the Yamagata Prefectural Central Hospital (No. 29), and Tohoku University Hospital (2007-400).

2.2. Measurements

During 36-56 weeks PMA, the 18 premature infants were tested every 4 weeks. A three-dimensional motion analyzer (Fastrak® ; Polhemus Inc., USA) was used to measure spontaneous movements

of the upper right limb in a supine position.

For measurement of spontaneous movements of the upper right limb in the supine infants, a tear drop type (1 cm diameter, 2 g weight) sensor with 40 Hz frequency was used. The sensor was placed on the acromion, elbow, and forearm distal position edge back side.

Measurements of this study had been made between May 2008 and October 2009.

2.3. Analysis

Spontaneous movements of the upper right limb in supine infants were measured for 270 s. Upper right limb position data were used to calculate RMS for elbow flexion-extension movement. The RMS of angular acceleration in the elbow flexion-extension movement, and the RMS of angular jerk in the elbow flexion-extension movement were calculated using numerical analysis software (MATLAB® ; The Math Works, USA). A window of 180 s was applied to the RMS of angular acceleration time series data of 270 s using a zone that maximizes the value of the RMS of angular acceleration. Adoption of the RMS of angular jerk was done in the same zone as the zone to maximize the value of the RMS of angular acceleration.

The calculated data were allotted into three terms : 36-40 week PMA (term I), 44-48 week PMA (term II), and 52-56 week PMA (term III). The representative value was the mean value of each term.

3. Statistical Analysis

Missing data occurred when infants were in a state of crying or were not aroused. Missing data were imputed using MICE : packaged software for multivariate imputation by chained equation in R (R ver. 3.4.0) [18]. The initial value seed and the initial value m were used to run MICE in R. We used seed of 23,109 as an initial value for maintaining reproducibility. The variable value m is the number of imputed datasets. The value of m is shown in Table 2. Imputed datasets were analyzed statistically.

Table 2 Initial value "m"

	Amount of displacement	
	RMS of angular acceleration	RMS of angular jerk
ASD infants group	250	150
Healthy infants group	110	10

RMS : root mean square, ASD : autism spectrum disorder

Holm method was used for analysis of variance. The RMS of angular acceleration was compared among terms. Similarly, the RMS of angular jerk was compared among terms. Differences with a p value $<.05$ were inferred as statistically significant.

Welch's t-test was used to test the difference between the ASD infant group and the healthy infant group. The angular acceleration was divided for each term and was compared between groups. Similarly, the angular jerk was divided for each term and compared. Differences for which $p<.05$ were inferred as statistically significant.

4. Results

4.1. Differences in the RMS of angular acceleration with development (Table 3)

For the healthy infant group, term II were significantly less than term I.

For the ASD infant group, term III was larger than term II.

4.2. Differences in the RMS of angular jerk with development (Table 4)

For the healthy infant group, term II and term III were significantly less than term I. No significant difference was found between term I, term II, and term III at the ASD infants group. However, the

Table 3 Differences in the RMS of angular acceleration with development

property	Term I	Term II	Term III
	M [SE]	M [SE]	M [SE]
		$p = .036$	
Healthy infants	665.35 [29.20]	569.32 [23.17]	585.94 [24.80]
			$p = .032$
ASD infants	511.58 [71.84]	618.46 [34.06]	750.08 [21.91]

M : mean, SE : standard error

Table 4 Differences in the RMS of angular jerk with development

property	Term I	Term II	Term III
	M [SE]	M [SE]	M [SE]
		$p = .0035$	
		$p = .041$	
Healthy infants	33,396.9 [1,209.05]	30,050.5 [850.66]	28,542.1 [848.17]
ASD infants	29,700.3 [1,121.21]	31,163.3 [1,760.30]	32,105.8 [699.24]

M : mean, SE : standard error

RMS of angular jerk showed a tendency to increase from term I to term III.

4.3. Differences in the RMS of angular acceleration between healthy infants and ASD infants in the each Term (Table 5)

Regarding the RMS of an angular acceleration at term III, the value of the ASD infant group was significantly larger than the value of the healthy infant group.

4.4. Differences in the RMS of angular jerk between healthy infants and ASD infants in the each Term (Table 6)

Regarding the RMS of an angular jerk at term III, the value of the ASD infant group was significantly larger than the value found for the healthy infant group.

5. Discussion

In this study, the larger value of angular acceleration indicates greater forcefulness of the spontaneous movement. Furthermore, the larger value of angular jerk indicates lower smoothness of the

Table 5 Differences in the RMS of angular acceleration between Healthy infants and ASD infants in the each Term

Term	RMS of angular acceleration		
	Healthy infants	ASD infants	
	M [*SE*]	*M* [*SE*]	
Term I	665.35 [29.20]	511.58 [71.84]	*n.s.*
Term II	569.32 [23.17]	618.46 [34.06]	*n.s.*
Term III	585.94 [24.80]	750.08 [21.91]	$p = .011$

M : mean, *SE* : standard error, *n.s.* : no significant

Table 6 Differences in the RMS of angular jerk between Healthy infants and ASD infants in the each Term

Term	RMS of angular jerk		
	Healthy infants	ASD infants	
	M [*SE*]	*M* [*SE*]	
Term I	33,396.89 [1,209.05]	29,700.31 [1,121.21]	*n.s.*
Term II	30,050.48 [850.66]	31,163.27 [1,760.30]	*n.s.*
Term III	28,542.09 [848.17]	32,105.75 [699.24]	$p = .0096$

M : mean, *SE* : standard error, *n.s.* : no significant

spontaneous movement.

The amounts of RMSs of angular acceleration, and of angular jerk in term II and term III were lower than term I in the healthy infant group. The result indicates that the spontaneous movement changed to calm and smooth movements along with healthy infant growth.

Earlier studies of GMs using surface electromyography (EMG) revealed shorter burst durations of phasic activity, attenuation of burst amplitude, and lower tonic background activity with age [19]. Surface EMG provides a gross measure of muscle activity. Therefore, our study results support those of earlier studies [19] and those of visual gestalt perception by the examiner [1, 3].

In the RMSs of angular acceleration and of angular jerk at term III, the value of the ASD infant group was higher than the value found for the healthy infant group. The result indicates that the spontaneous movement remained to jerky and rough movements though with ASD infant growth. The previous study of ASD or Rett syndrome based on the visual Gestalt perception revealed abnormalities in the GMs. An individual with a later diagnosis of ASD had abnormal writhing and fidgety GMs. Abnormal GMs show insufficient variation, complex and not fluent movements [15]. Our study results might quantitatively elucidate the characteristics of abnormal GMs found quantitatively in earlier studies.

Regarding the RMS of angular acceleration in term III, the value of the ASD infant group was significantly greater than the value of healthy group. Furthermore, regarding the RMS of angular jerk in term III, the value of the ASD infant group was significantly greater than the value of the group of the healthy children. These results demonstrate that the spontaneous movements of the ASD infants included more jerky movements at term III.

Infants diagnosed with ASD are said to have a high risk of abnormal spontaneous movement in term III (i.e., abnormal fidgety GMs) [15]. Furthermore, the sequential transforms of GMs from writhing GMs to fidgety GMs are regarded as caused by organizational changes of the nervous system [20]. The amount of serotonin in the brain of ASD children is known to be small [21]. The function of the raphe nucleus of the midbrain was found to be low in a study of mice with the same genomic abnormality as humans [22]. Abnormal behavior induced by ASD strongly suggests a lack of serotonin production [23]. Serotonin deficiency in the cerebellum is known to cause ataxia movement [24]. Thus, the spontaneous movements in early infancy with ASD might present a developmental coordination disorder.

Our investigation revealed differences in the sequential transform of spontaneous movements between ASD infants and healthy infants by using the RMSs of angular acceleration and angular jerk. This result might have captured the initial signs of voluntary movement abnormalities with ASD infants due to central nervous system disorders.

There have been no useful quantitative parameters to predict the expression of ASD. It might be possible to infer from the results of this study that the developmental abnormalities of the central nervous system by observing the transition of the RMSs angular acceleration and angular jerk.

The present study also suggests that the method of using the RMSs of angular acceleration and of angular jerk could distinguish spontaneous movements between ASD infants and healthy infants at term III. Deviations of the RMSs for angular acceleration and angular jerk of the spontaneous movements at term III might reflect abnormalities of spontaneous movement in ASD infants. However, developmental coordination disorders are likely to be indicated by other diseases too. Therefore, further studies are necessary to identify ASD specific abnormalities in sequential transforms of spontaneous movement including investigation of other movement related parameters. Future research must be conducted to clarify the predictive value for these parameters and to determine a cutoff value for detecting signs of ASD.

6. Conclusion

This study compared spontaneous movements of the upper limbs of ASD infants with the spontaneous movement of the upper limbs of healthy infants using the RMS of angular acceleration and the RMS of angular jerk.

The spontaneous movements in healthy infants began to move smoothly with development, although spontaneous movements in ASD infants remained jerky.

Especially in the term III, the values of ASD infants were larger than the values healthy infants at the RMS of angular acceleration and the RMS of angular jerk.

The study found that the difference between ASD and continuous changes in upper limb locomotor activity in healthy infants can be distinguished by the RMS of angular acceleration and the RMS of angular jerk in the term III.

This method of assessing spontaneous movements in early infancy using angular acceleration RMS and angular jerk RMS provides a useful parameters for elucidating the changes in central nervous system function in ASD infants.

Conflict of interest statement

The author declare that no conflict of interests exists. The author has seen and approved the final version of the manuscript. The manuscript has solely been submitted to TFU Journal for review and possible publication.

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