Quantitative Evaluation of Pronation and Supination for Children with ADHD

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Quantitative Evaluation of
Pronation and Supination for Children with ADHD

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Abstract

Pronation and supination are motor tasks for soft neurological signs (SNS). SNS are minor abnormalities or developmental deviations of the central nervous system, and are used to help diagnose Attention Deficit Hyperactivity Disorder (ADHD) which is one of the developmental disorders. A diagnosis of SNS is an important assessment in which pediatricians observe the child's behavior directly in a clinical setting. Currently, most tests for SNS involve visual inspection by pediatricians. These tests for SNS are not quantitative. It is desirable to establish quantitative tests for SNS, as this will enable quantification of the progress of and the effect of treatment on ADHD symptoms. The aim of this thesis was to develop a portable, quantitative evaluation method for pronation and supination that can be used in children with ADHD.

In Chapter 2, I present the proposed quantitative evaluation system. Pronation and supination are evaluated by a pediatrician who notes the outcome measure, such as the rotational speed, the elbow excursion, the associated movements, the bimanual symmetry and the compliance. These outcome measures were quantified using data from the three-dimensional acceleration and angular velocity sensors placed on the dorsal aspects of both hands and elbows. I conducted two experiment to evaluate internal validity and construct validity of these outcome measures as quantitative indices for pronation and supination using data of TD children. In first experiment, 39 TD children

aged 9 years (male: 19, female: 20) participated. We obtained the average in each proposed outcome measure using data from all participants and evaluated the internal validity in the average value of each proposed outcome measure using the Bootstrap method. From the result of analysis, the sample average obtained from the original data was within the 95 % confidence interval. This indicates that these parameters of outcome measures were not affected by variability attributable to individual differences. In second experiment, 26 TD children aged 7–12 years (12 boys, 14 girls) participated. Pronation and supination were evaluated on a four-point scale as excellent (4), good (3), pass (2), or fail (1) by five pediatricians who watched the video recordings of the task. To allow comparison with our quantitative parameters of outcome measures for pronation and supination, we normalized all quantitative parameters of outcome measures. The results showed that our proposed quantitative score increased as the pediatrician visual assessment score increased. A significant positive correlation was observed between both scores. The results also showed that our proposed quantitative score reflects the visual assessment of pediatricians with several years of experience.

In Chapter 3, I report pronation and supination in typically developing (TD) children aged from 4 to 12 years quantified using the parameters validated in Chapter 2. The aim of Chapter 3 is to establish criteria for our proposed outcome measures of pronation and supination, to act as a reference for comparison of children with suspected ADHD. Two hundred and twenty-three TD children aged 4–12 years (107 boys, 116 girls) participated in this experiment. The results indicated that the performance of pronation and supination improved with age in TD children. These results are consistent with the result of previous studies and provide more detail of the developmental changes than the conventional criteria for evaluating children suspected ADHD. These results indicate that it may be possible to use our system as quantitative criteria for evaluating development of neurological function. We were able to successfully quantify SNS during pronation and supination.

In Chapter 4, I report pronation and supination in children with ADHD quantified using the parameters validated in Chapter 2. We were able to obtain the developmental change of TD children for pronation and supination using our proposed evaluation system in Chapter 3. Our aim in this chapter is to establish a quantitative evaluation system for children with ADHD. In this chapter, we focused on quantifying the development changes for pronation and supination in children with ADHD to compare the performance of TD children by age. Thirty eight children with ADHD aged 7-11 years (32 males, 6 females) participated in our experiment. Our results suggested that the development of children with ADHD were lower than that of TD children, and had a tendency to lag behind that of TD children by several years.

Moreover, children with ADHD were split into two groups: ADHD only and comorbid ADHD and autism spectrum disorder (ASD) to compare pronation and supination between ADHD and other developmental disorders. These two groups were then also compared with the TD children reported in Chapter 3 to establish the external validity of our proposed system for ADHD. In addition to the outcome measures validated

in Chapter 2, we quantified several novel outcome measures: rotational size, postural stability and temporal change according visual inspection by pediatricians who watched the video recordings of the pronation and supination. From our results, we found a significant difference in several measure outcomes (especially measurement outcomes of non-dominant hand and temporal change). The radar charts showed that the balance among these outcome measures improved with age. The size of the radar chart in children with ADHD was smaller than that in TD children of the same age. These results indicated a tendency for pronation and supination to develop later in children with ADHD, compared to their TD counterparts. Indeed, pronation and supination movement in children with ADHD was comparable to that of younger TD children.

Keywords: Acceleration and angular velocity sensors; Motion analysis; Soft neurological signs; Pronation; Supination; Attention deficit hyperactivity disorder

Contents

Chapter 1. Introduction

In this chapter, I review the current knowledge of one specific developmental disorder, attention deficit hyperactivity disorder (ADHD). I also review soft neurological signs (SNS) and discuss how they are used to help diagnose ADHD, before focusing on one particular SNS, pronation and supination. I then describe previous studies that have quantified pronation and supination and the issues surrounding this topic.

1.1ADHD

ADHD is a neurodevelopmental disorder that is not associated with intellectual retardation. It is difficult for children with ADHD to control their behavior and concentrate on a particular task. The principle symptoms of ADHD are inattention, hyperactivity, and impulsivity.

Children with symptoms of inattention cannot concentrate on one thing and are easily distracted by external stimuli, such as the noise outside a window or the voice of a classmate sitting next to them. However, if they really like a task, they can become absorbed in it without difficulties or problems. The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) lists the following examples of inattention symptoms:

- Often fails to give close attention to details or makes careless mistakes in schoolwork, at work, or with other activities.
- Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (*e.g.*, loses focus, side-tracked).
- Often avoids, dislikes, or is reluctant to do tasks that require mental effort over a long period of time (such as schoolwork or homework).
- Is often easily distracted.

Children with hyperactivity-impulsivity, a symptom of ADHD, cannot sit still during class and often act without thought. The DSM-5 lists the following examples of hyperactivity-impulsivity symptoms:

- Often runs about or climbs in situations where it is not appropriate (adolescents or adults may be limited to feeling restless).
- Is often “on the go” acting as if “driven by a motor”.
- Often has trouble waiting his/her turn.
- Often interrupts or intrudes on others.

The DSM-5 lists nine symptoms for both inattention and hyperactivity-impulsivity as described above (American Psychiatric Association, 2013). If six or more of the nine symptoms apply to a child, the child is suspected of having ADHD. The DSM-5 defines ADHD as symptoms that have continued for at least 6 months at two or more places, such as home and school, and that were present before the child was 12 years old. There are three presentations of ADHD: predominantly inattentive, predominantly hyperactive-impulsive, and combined. The DSM is used as the guideline for the diagnosis of ADHD, but there is no specific diagnostic test.

However, it can be argued that most individuals display these symptoms to some extent during childhood. Therefore, it is difficult to identify children with ADHD. This is compounded by the fact that children with ADHD have normal intelligence. If early signs of ADHD are missed and appropriate action is not taken early, there is a risk of secondary psychological problems or behavioral problems. Therefore, identifying markers of behavioral problems is important to enable early and accurate diagnosis of ADHD.

Current diagnostic methods include interviews with the child and his/her parent, the child's behavioral rating scale score by his/her parent or teacher, pre- and perinatal history, developmental history, family history, and physical and neurological examination. The physical and neurological examination is an important assessment in which pediatricians observe the child's behavior directly in a clinical setting.

1.2 SNS

SNS are minor abnormalities or developmental deviations of the central nervous system, and are used to help diagnose ADHD. There are many specific SNS in childhood, and there are several assessments techniques for SNS, including The Zurich Neuromotor Assessment (ZNA; Largo et al., 2001a, 2001b; Schmidhauser et al., 2006; Rousson et al, 2008), the neurological examination for subtle signs, and the examination of minor neurological dysfunction (the Groningen Assessment; Touwen & Prechtl, 1970). These assessments can be used to indicate cranial nerve function and sensory function by evaluating factors such as posture in various positions, range of motion, coordination, and fine manipulative abilities and associated movements. These assessments are helpful in the diagnosis of ADHD, which is characterized by difficulties in behavior and coordination. Examples of specific tests for SNS are the pronation and supination test, finger-to-nose test, finger opposition test, visual pursuit movements test, and heel-to-toe walking test. If development of the central nervous system is impaired or delayed, SNS appear in various forms and are evident in the results of these tests.

To test pronation and supination, the patient bends their elbows to 90 degrees, and then quickly pronates and supinates their hands. This test is used to assess children aged 4 years and above. Performance is qualitatively evaluated by a pediatrician who notes the rotational speed, the elbow excursion, the pauses of hand at extreme positions of pronation and supination, and associated movements, which are involuntary movements of one hand that occur simultaneously with voluntary movements of the target hand (Hadders-Algra, 2010; Touwen & Prechtl, 1970). Pronation and supination are difficult for patients with a cerebellar lesion, and functional magnetic resonance imaging studies have revealed that pronation and supination typically involves activation of the ipsilateral cerebellum (Wessel & Nitschke, 1997; Tracy et al., 2001). The cerebellum has been associated with attention deficits (Hoppenbrouwers et al., 2008). From these previous studies, we think that the difficulty with pronation and supination can be a characteristic of ADHD. Therefore, we focus on the SNS of pronation and supination in this thesis.

Currently, most tests for SNS involve visual inspection by pediatricians. These tests for SNS are not quantitative. It is desirable to establish quantitative tests for SNS, as this will enable quantification of the progress of and the effect of treatment on ADHD symptoms.

1.3 Quantitative Evaluation of Pronation and Supination

Several methods have been proposed for quantifying pronation and supination. These include three-dimensional video analysis (Kreulen et al., 2004), a microcomputer-based device (Okada & Okada, 1983), and an ultrasonic device that calculates the three-dimensional spatial positions of markers placed on the hands and forearms (Hermsdörfer & Goldenberg, 2002; Hermsdörfer et al., 1999). Kreulen et al. (2004) measured pronation and supination in patients with cerebral palsy pre- and post-operatively to quantify the therapeutic effect of the intervention. Okada & Okada (1983) established quantitative evaluation features of pronation and supination, such as rapidity and regularity, in patients with methylmercury poisoning. Hermsdörfer et al. (2002) quantified pronation and supination in patients with left and right brain damage and control subjects and showed that the temporal and spatial variability of movement cycles was lower in subjects with brain damage than in control subjects.

These studies all contribute to establishing a quantitative evaluation of pronation and supination. However, the methods used all require subjects to be stationary except for the movement of the forearm and hand, and they are therefore difficult to implement in children with suspected ADHD, who may find it difficult to stay still during an examination. In addition, there are no quantitative reports of age-appropriate developmental changes in pronation and supination throughout childhood. To enable measurement of pronation and supination in children with ADHD, it is desirable to establish a quantitative evaluation method that is portable and can be easily used in children. The aim of this thesis was to develop a portable, quantitative evaluation method for pronation and supination that can be used in children with ADHD. We focused on achieving this through the use of acceleration and angular velocity sensors, as this equipment will permit measurement in children with ADHD without being limited to a particular examination location.

1.4 Thesis Overview

In Chapter 2, I present the proposed quantitative evaluation system and the parameters derived from three-dimensional acceleration and angular velocity sensors. The parameters are rotational speed and associated movement and elbow excursion in a maximal effort pronation and supination task, and bimanual symmetry and compliance of the subject's movement with the target movement in an imitative pronation and supination task. An evaluation score created by combining the scores for all proposed parameters is compared with evaluation scores that were assigned by five pediatricians after visual observation, which is a conventional method of evaluating pronation and supination in children with suspected ADHD. This chapter is based on the study by Iramina et al. (2011).

In Chapter 3, I report pronation and supination in typically developing (TD) children aged from 4 to 12 years quantified using the parameters validated in Chapter 2. The aim of Chapter 3 is to establish criteria for our proposed outcome measures of pronation and supination that can act as a reference for comparison of children with suspected ADHD. To test the validity of our proposed system, the score calculated by our proposed parameters is compared to previous studies and the conventional visual assessment criteria (Touwen & Prechtl, 1970; Hadders-Algra, 2010). This chapter is based on the study by Kaneko et al. (2015).

In Chapter 4, I report pronation and supination in children with ADHD quantified using the parameters validated in Chapter 2. These data are compared to the data collected from TD children reported in Chapter 3 to evaluate the potential of the proposed system for use as a tool in the diagnosis of ADHD. Moreover I compare three groups: TD group, group with ADHD only and group with comorbid ADHD and autism spectrum disorder (ASD) to consider the external validity in our proposed system for ADHD. This chapter is based on the study by Kaneko et al. (2016).

Chapter 2. Proposed Quantitative Evaluation System

2.1 Abstract

Pronation and supination are evaluated by a pediatrician who notes the outcome measure, such as the rotational speed, the elbow excursion, associated movements, bimanual symmetry and compliance. These outcome measures were quantified using data from the three-dimensional acceleration and angular velocity sensors placed on the dorsal aspects of both hands and elbows.

We conducted two experiment to evaluate internal validity and construct validity of these outcome measures as quantitative outcome measures for pronation and supination using data of TD children. In first experiment, 39 TD children aged 9 years (male: 19, female: 20) participated. We obtained the average in each proposed outcome measure using data from all participants and evaluated the internal validity in the average value of each proposed outcome measure using the Bootstrap method. From the results of analysis, the sample average obtained from the original data was within the 95 % confidence interval. This indicates that these parameters of outcome measures were not affected by variability attributable to individual differences. In second experiment, 26 TD children aged 7–12 years (12 boys, 14 girls) participated. Pronation and supination were evaluated on a four-point scale as excellent (4), good (3), pass (2), or fail (1) by five

pediatricians who watched the video recordings of the task. To allow comparison with our quantitative parameters of outcome measures for pronation and supination, we normalized all quantitative parameters of outcome measures. The results showed that our proposed quantitative score increased as the pediatrician visual assessment score increased. A significant positive correlation was observed between both scores. The results indicated that our proposed quantitative score reflects the visual assessment of pediatricians with several years of experience.

2.2 Configuration of the Proposed Quantitative Evaluation System

Figure 2-1 shows our proposed evaluation system for pronation and supination. The system comprises four wearable sensors (WAA-006, WAA-010, ATR-Promotions), a guide monitor (CLAiR SK-DTV 133JW2, Sknet), a Bluetooth USB adapter (Princenton PTM-UBT5), a HDMI cable (Sanwa Supply KM-HD20-30K), and a notebook PC (Vaio VGN-NW91FS, Sony). The notebook PC and the guide monitor were connected by the HDMI cable. The system signals were transmitted by Bluetooth to the notebook PC.

Each sensor includes a three-dimensional acceleration sensor and a three-dimensional angular velocity sensor, and wirelessly sends data obtained by these sensors via Bluetooth. The sensors were attached to the participant, with one sensor on each hand and one sensor on each elbow. The axis directions of the sensors are illustrated in Figure 2-2. Figure 2-3 shows waveforms from the three-dimensional acceleration and angular velocity sensors during pronation and supination. The size of sensors is 39 mm × 44 mm × 12 mm. The weight of the sensors is 20 g. The guaranteed operating range of the sensors is shown in Table 2-1. Data were collected at 100 Hz and a 6-Hz low-pass filter was applied prior to analysis.

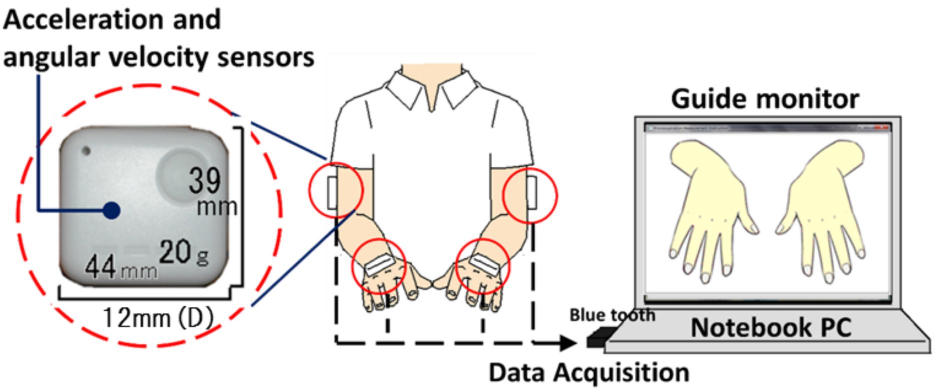

Figure 2-1. Configuration of the proposed quantitative evaluation system.

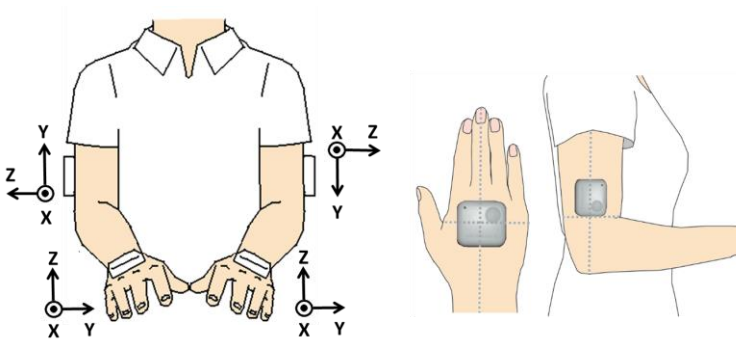

Figure 2-2. The axis directions of the sensors and the position of the sensors.

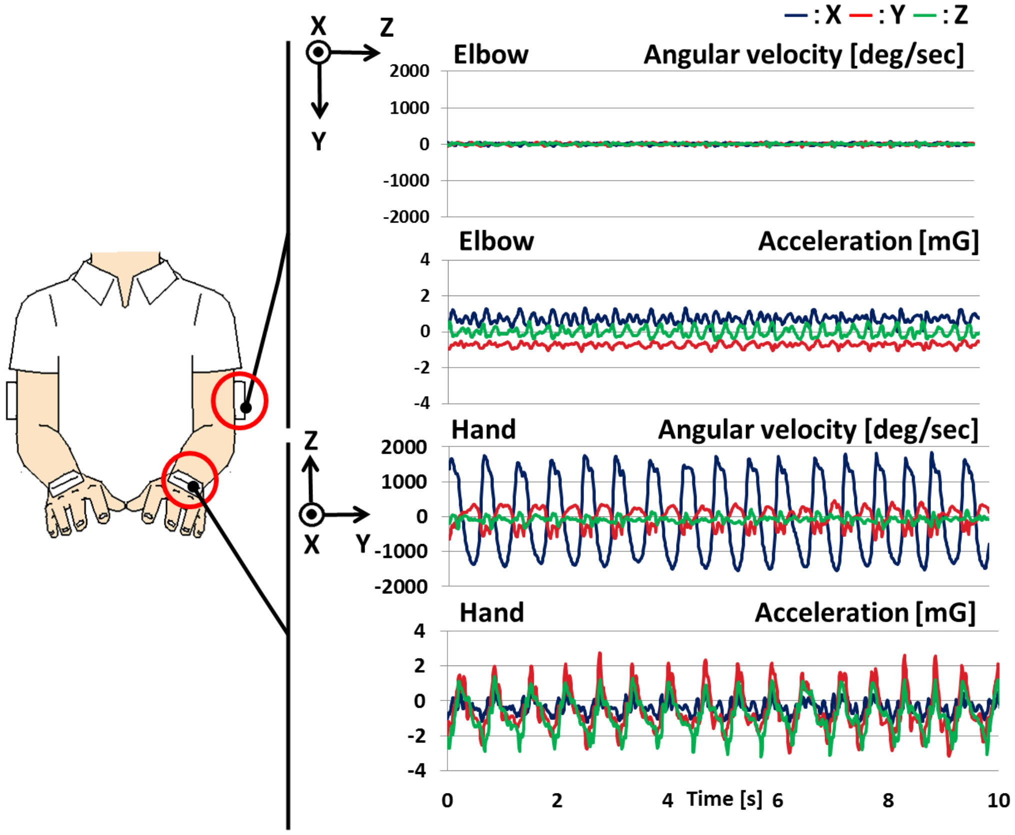

Figure 2-3. Example waveforms from the sensors in each of the three axes during pronation and supination of the hand.

Table 2-1 Guaranteed operating range of the sensors

		Guaranteed operating range	
		WAA-006	WAA-010
Acceleration		±4G	±16G
Angular velocity	X and Y axis	±500deg/s	±2000deg/s
	Z axis	±500deg/s	

2.3 Pronation and Supination Motor Tasks

Before starting the experiment, all participants received an explanation of the motor tasks. They were required to bend their elbows to 90 degrees and to maintain this basic posture throughout the tasks. Three tasks were performed: a maximal effort motor task performed with only the dominant hand, a maximal effort motor task performed with only the non-dominant hand, and an imitative motor task.

For the maximal effort motor task, the participant pronated and supinated the hand as fast as possible. This task was performed with only one hand and participants were instructed to maintain the basic posture with the other (non-rotating) hand. For the imitative motor task, the participant stood in front of a guide monitor and imitated the motions of the demonstration guide shown on the monitor. The demonstration guide showed a motion in which both hands were pronated and supinated 80 times per minute. Each task was performed for 10 s.

2.4 Outcome Measures

All outcome measures were quantified using data from the acceleration and angular velocity sensors placed on the dorsal aspects of both hands and elbows. The waveforms of the three-axis gyroscope and a three-axis accelerometer, along with the axis direction of pronation and supination, are illustrated in Figure 2-2.

2.4.1 Outcome measures in the maximal effort motor task

The following conventional outcome measures for pronation and supination were quantified during the maximal effort motor task: rotational speed, associated movement, and elbow excursion.

Rotational speed reflects the speed of pronation and supination. Rotational speed was calculated using the peak frequency of the continuous fast Fourier transform of acceleration in the Z axis.

Associated movement reflects the involuntary movement of the contralateral hand that occurs during voluntary movement of the target hand (Cox, 2012; Hadders-Algra, 2010). Associated movement was calculated using the absolute value of the total sum of acceleration along the X axis.

Elbow excursion reflects movement of the elbows away from the side of the body. Elbow excursion was calculated using the absolute value of the total sum of acceleration along the Z axis.

If participants moved their hands or elbows while pronating and supinating their forearms, the value indicating associated movement or elbow excursion increased, as shown in Figure 2-4.

2.4.2 Outcome measures in the imitative motor task

The following novel outcome measures for pronation and supination were quantified during the imitative motor task: bimanual symmetry, compliance.

Bimanual symmetry reflects the precision of symmetrical movement between the left hand and the right hand and was quantified using the time delay in acceleration in the Z axis between the right hand and left hand, as shown in Figure 2-5. If the phase between the right hand waveform and the left hand waveform increased, time delay increased.

Compliance reflects the correlation between the participants' motion speed and motion speed of the demonstration guide and was calculated using the time delay between the participant's hands being in the basic position and the guidance hands being in the basic position. A value of zero for angular velocity in the X axis was used to indicate the participant's hands being in the basic position, as shown in Figure 2-6.

2.4.3 Analysis

Each task was performed for about 10 s. This was divided into seven phases of about 2.5 s duration, with about 1.25 s overlap between consecutive phases, to allow analysis of temporal change in outcome measures (Figure 2-7). The value of each outcome measure was mean value across the seven phases.

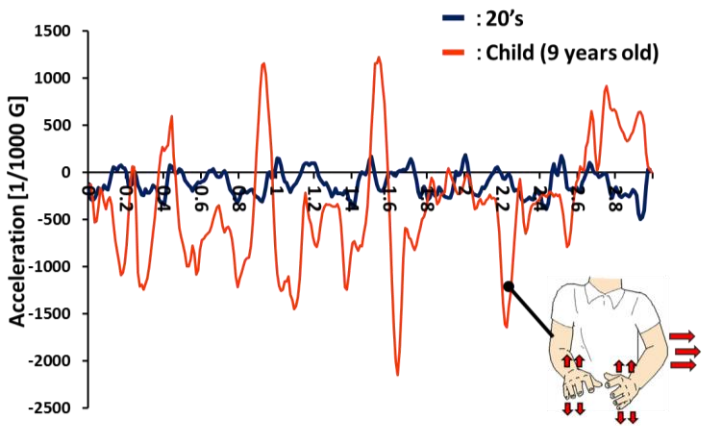

Figure 2-4. Waveforms of hand acceleration in the X axis. The blue line shows the acceleration when the participant (age 20 years) did not move the hand. The red line shows the acceleration when the participant (age 9 years) moved the arms and hands up and down. If the participant moved their arms and hands while pronating and supinating their hands, the magnitude of hand acceleration in the X axis increased.

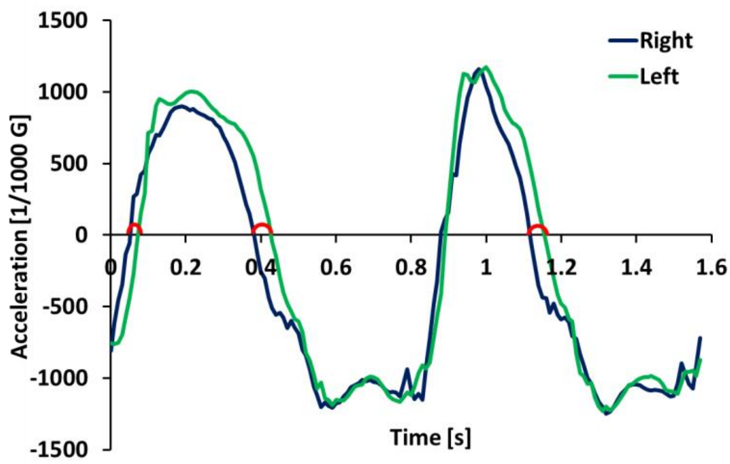

Figure 2-5. Asynchronous time of acceleration in the Z axis between the right hand and the left hand. Red lines show the asynchronous time between the left hand and the right hand.

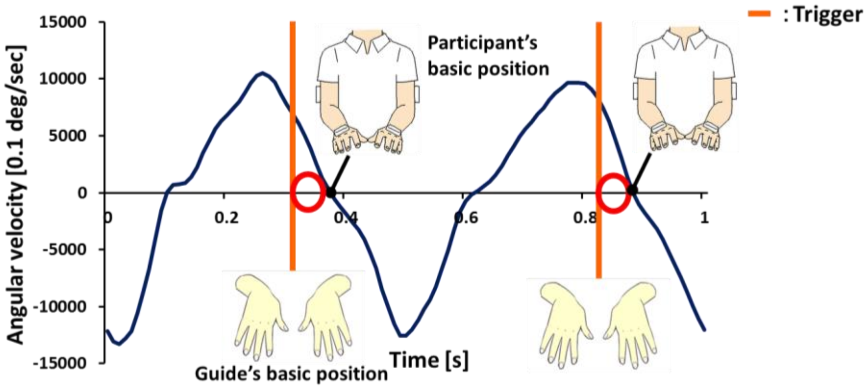

Figure 2-6. The difference in time between the angular velocity in the X axis and a trigger, indicated by the vertical orange line.

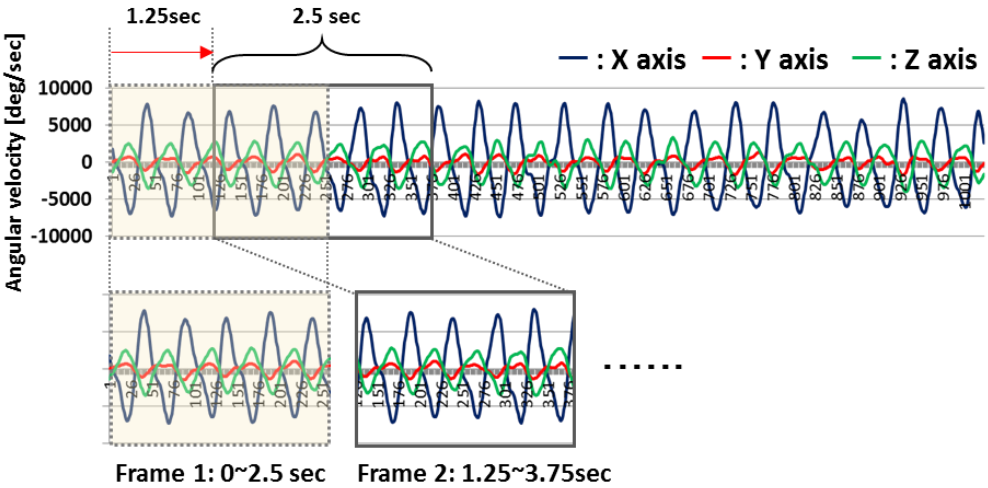

Figure 2-7. Data processing. The waveform recorded during each task was divided into seven phases of 2.5 s duration, with 1.25 s overlap between consecutive phases.

2.5 Internal Validity

The appropriateness of these outcome measures as quantitative indices of pronation and supination was evaluated using data from 39 TD children aged 9 years (male: 19, female: 20).

2.5.1 Participants and procedure

39 TD children aged 9 years (male: 19, female: 20) participated in this experiment. Hand dominance was evaluated by asking the participant to throw a ball with their preferred hand. All were right-hand dominant. Participants were recruited from Fukuoka Municipal Elementary School and had never previously participated in our experiment. Before starting the experiment, all participants and their parents received an explanation about the aim, procedures, and hazards of the experiment. All participants agreed to participate. The study was approved by the Kyushu University Ethics Committee. We obtained the average in each proposed outcome measure using data from all participants and evaluated the internal validity in the average value of each proposed outcome measure using the Bootstrap method.

2.5.2 Results and Dissection

The Bootstrap method was used to evaluate the internal validity in the average value of each proposed outcome measure. The data from all participants were resampled with replacement. The resample size is the same size of the original data. We calculated the bootstrap average from the resample data and repeated this process 1000 times to get the histogram of bootstrap average and confidence interval.

Figure 2-8 to 2-12 show the histogram of bootstrap average in the proposed outcome measurements. Left figure shows the parameter of outcome measure during pronation and supination with non-dominant hand. Right figure shows for dominant hand. In all figures, the horizontal axis show the bootstrap average in each proposed outcome measures. The dotted lines show the lower and upper of the 95 % confidence interval. The blue dotted line show the average obtained from the original data.

As shown in figures, the sample average obtained from the original data is within the 95 % confidence interval. This indicates that these parameters of outcome measures were not affected by variability attributable to individual differences.

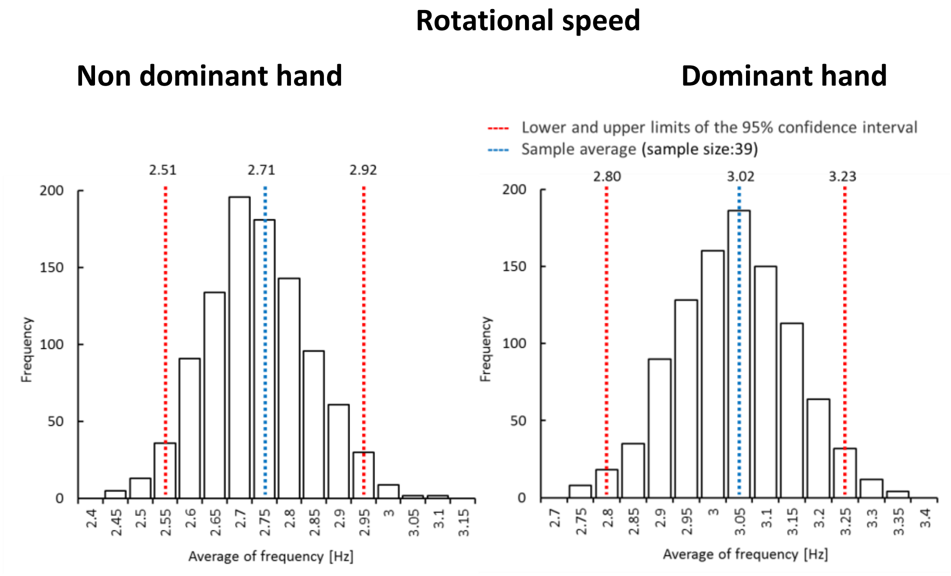

Figure 2-8. Histogram of bootstrap average (1000 bootstrap samples). Left figure shows parameter of rotational speed during pronation and supination with non-dominant hand (95% Confidence interval: 2.51; 2.92, Sample average: 2.71). Right figure shows for dominant hand (95% Confidence interval: 2.80; 3.23, Sample average: 3.02).

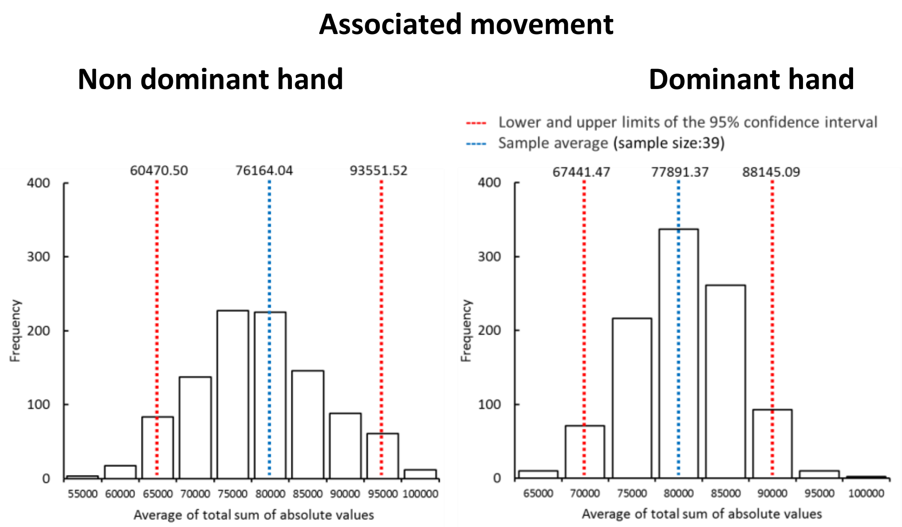

Figure 2-9. Histogram of bootstrap average (1000 bootstrap samples). Left figure shows parameter of associated movement during pronation and supination with non-dominant hand (95% Confidence interval: 60470.5; 93551.52, Sample average: 76164.04). Right figure shows for dominant hand (95% Confidence interval: 67441.47; 88145.09, Sample average: 77891.37).

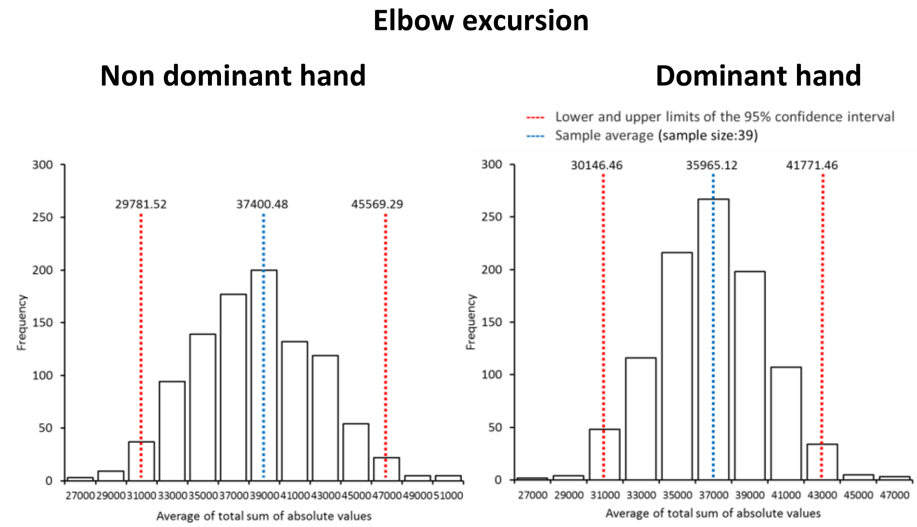

Figure 2-10. Histogram of bootstrap average (1000 bootstrap samples). Left figure shows parameter of elbow excursion during pronation and supination with non-dominant hand (95% Confidence interval: 29781.52; 45569.29, Sample average: 37400.48). Right figure shows for dominant hand (95% Confidence interval: 30146.46; 41771.46, Sample average: 35965.12).

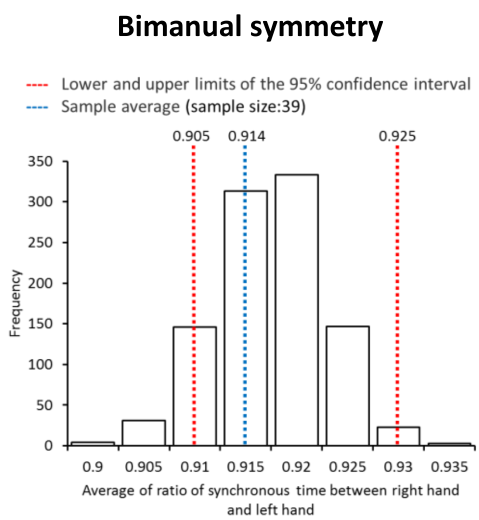

Figure 2-11. Histogram of bootstrap average of bimanual symmetry (1000 bootstrap samples). 95% Confidence interval: 0.905; 0.925, Sample average: 0.914.

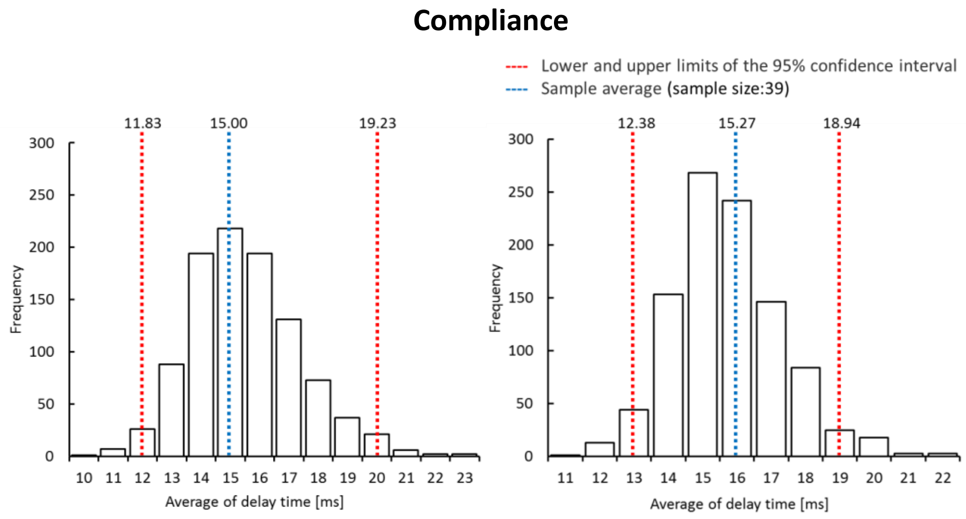

Figure 2-12. Histogram of bootstrap average (1000 bootstrap samples). Left figure shows a parameter of compliance during pronation and supination with non-dominant hand (95% Confidence interval: 11.83; 19.23, Sample average: 15.00). Right figure shows for dominant hand (95% Confidence interval: 12.38; 18.94, Sample average: 15.27).

2.6 Construct Validity

Conventionally, pronation and supination are assessed qualitatively by pediatricians. Therefore, the construct validity of the proposed outcome measures as quantitative measures of pronation and supination was evaluated by comparison to a visual assessment score assigned by pediatricians.

2.6.1 Participants and procedure

Twenty six TD children aged 7–12 years (12 boys, 14 girls) participated in this experiment (Table 2-2). Hand dominance was evaluated by asking the participant to throw a ball with their preferred hand. All participants were right-hand dominant. Participants were recruited from Fukuoka Municipal Elementary School and had never previously participated in our experiment. Pronation and supination motor tasks were performed as described above and were recorded by CCD camera in addition to the wearable sensors. Pronation and supination were evaluated on a four-point scale as excellent (4), good (3), pass (2), or fail (1) by five pediatricians who watched the video recordings of the task. For each participant, each pediatrician provided a single score that incorporated rotational speed, bimanual symmetry between the left and right hands, postural stability of the hand, and so on. The pediatricians had varying lengths of experience diagnosing children with suspected ADHD (25, 25, 15, 10, and 5 years experience). For each participant, each pediatrician provided a single score that incorporated rotational speed, bimanual symmetry between the left and right hands, postural stability of the elbow, and so on. They were allowed to watch each performance several times before providing their rating.

Table 2-2. Number of study participants.

Age (years)	**Male**	**Female**	**Total**
7	2	2	4
8	2	3	5
9	3	1	4
10	3	2	5
11	2	1	3
12	0	5	5
Total	12	14	26

2.6.2 Analysis

Each pediatrician provided a score for each participant, and these were averaged across the five pediatricians to obtain a single score for each participant. To allow comparison with our quantitative parameters of outcome measures for pronation and supination, we combined all quantitative outcome measures into a single value to provide a single quantitative score for each participant. The first step in this process was to normalize the score for each outcome measure using the following formula:

$$y_h = 50 + \frac{20}{\sigma_a}(-x_h + \mu_a)$$

This is based on the formula for calculating T-scores. x_h is the non-normalized score, and μ_a and σ_a are the mean and standard deviation of the outcome measure across all participants. As shown in the formula, the mean value of all participants was set to 50 points and the score range for all participants was set 0–100 points. A normalized score was calculated for each outcome measure and the normalized scores were averaged across all outcome measures to create a single score for each participant.

2.6.3 Results and Discussion

The assumption of normality was tested for all data using the Shapiro-Wilk test. Pearson's correlation was used for normally distributed data, and Spearman's correlation was used when the data were not normally distributed. Figure 2-13 shows the comparison between the single quantitative score and the average visual assessment score assigned by the five pediatricians. A significant positive correlation ($p < 0.01$, $R^2 = 0.344$) was observed between both scores, with regression equation $y = 8.91x+26.7$. As the pediatrician visual assessment score increased, the quantitative score increased.

Figure 2-14 shows the comparison between the single quantitative score and the visual assessment score given by each pediatrician. For pediatricians 1 to 4 (25, 25, 15 and 10 years experience), the quantitative score increased as the visual assessment score increased, and there was a significant positive correlation between the two scores ($p <0.01$, $R^2 = 0.352$, $R^2 = 0.176$, $R^2 = 0.328$, $R^2 = 0.309$, respectively). However the correlation coefficient was low for the pediatrician 5 (5 years experience), and there was no significant correlation between both scores (p = NS, R^2=0.08). These results indicate that our proposed quantitative score reflects the visual assessment of pediatricians with several years experience.

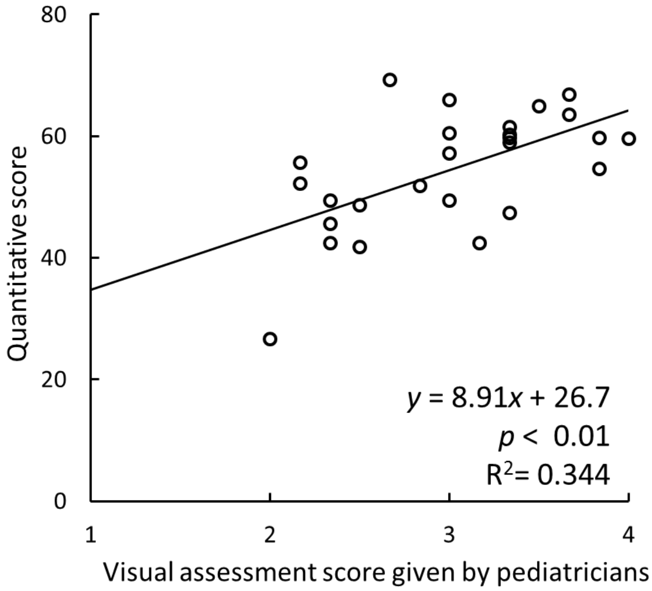

Figure 2-13. Correlation between proposed quantitative score and visual assessment score assigned by pediatricians. The visual assessment score assigned by pediatricians was excellent (4), good (3), pass (2), or fail (1). A significant positive correlation ($p < 0.01$, $R^2 = 0.344$) was observed between both scores, with regression equation y = 8.91x+26.7.

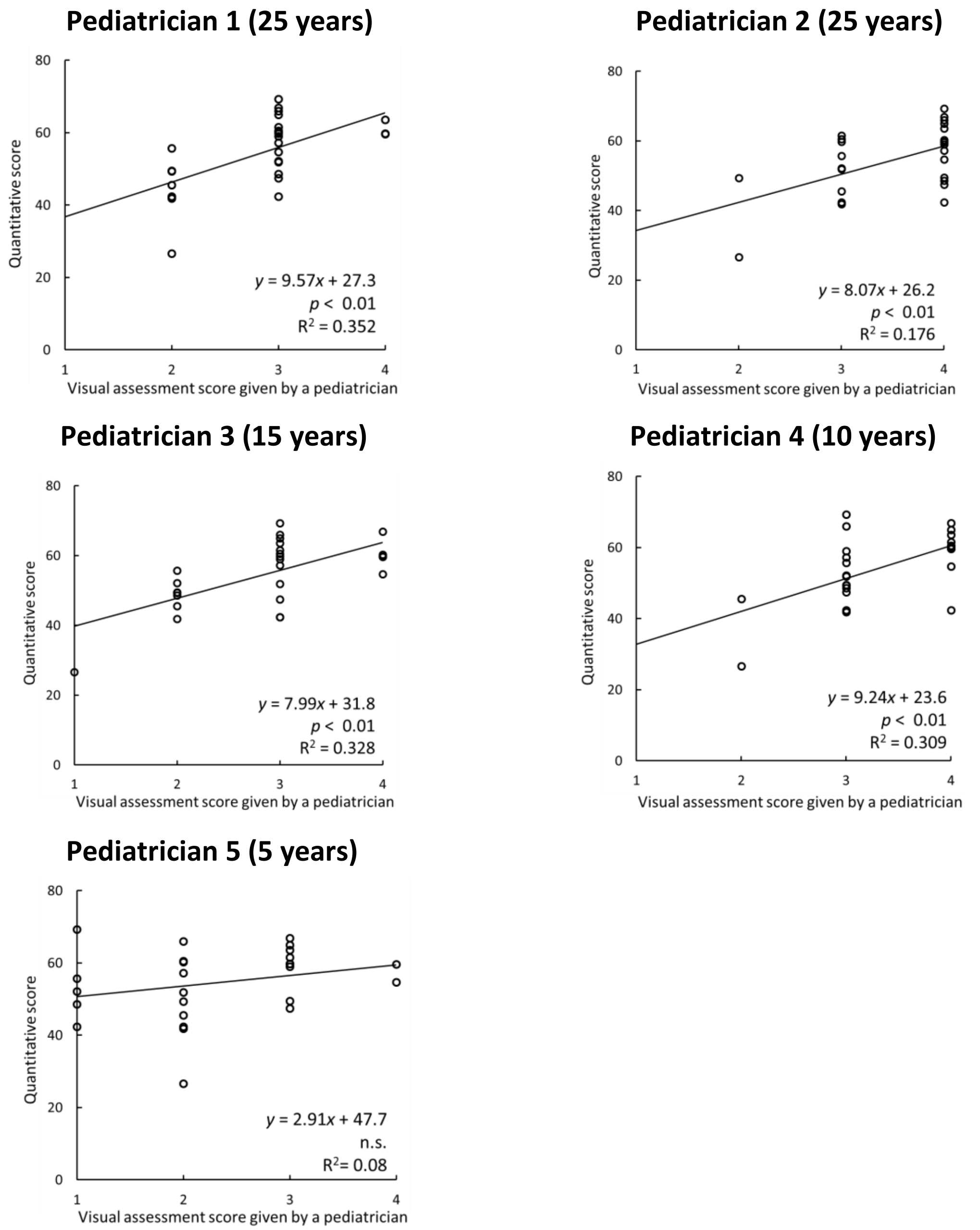

Figure 2-14. Correlation between proposed quantitative score and visual assessment score assigned by each pediatrician. The numbers within brackets indicate the number of years of experience of the pediatrician. For pediatricians 1 to 4, the quantitative score increased as the visual assessment score increased, and there was a significant positive correlation between the two scores (p < 0.01, R^2 = 0.352, 0.176, 0.328, and 0.309, respectively). For pediatrician 5, there was no significant correlation between the two scores.

Chapter 3. Pronation and Supination Developmental Changes in Typically Developing Children

3.1 Abstract

The aim of Chapter 3 is to establish criteria for our proposed outcome measures that can act as a reference for comparison of children with suspected ADHD. Two hundred and twenty-three TD children aged 4–12 years (107 boys, 116 girls) participated in this experiment. We established the parameters of outcome measures: rotational speed, associated movement, elbow excursion, bimanual symmetry and compliance of pronation and supination.

The results indicated that the performance of pronation and supination improved with age in TD children. These results are consistent with the result of previous studies and provide more detail of the developmental changes than the conventional criteria for evaluating children suspected ADHD. These results indicate that it may be possible to use our system as quantitative criteria for evaluating SNS during pronation and supination. We were able to successfully quantify SNS during pronation and supination.

3.2 Procedure and Participants

The experimental procedure and analysis were as described in Chapter 2. Two hundred and twenty-three TD children aged 4–12 years (107 boys, 116 girls) participated in this experiment (Table 3-1). All participants were right-hand dominant. Hand dominance was evaluated by asking the participant to throw a ball with their preferred hand. Participants were recruited from Fukuoka Municipal Elementary School and a kindergarten associated with the Hyogo University of Teacher Education and had never previously participated in our experiment. Before starting the experiment, all participants and their parents received an explanation about the aim, procedures, and hazards of the experiment. All participants agreed to participate. The study was approved by the Kyushu University Ethics Committee.

3.3 Result

Figures 3-1 to 3-5 show the development changes of TD children for pronation and supination quantified using our proposed evaluation system. In these figures, the vertical axis shows the quantified variable and the horizontal axis shows the age of the participants. The upper panels of these figures show the data divided into several age groups according developmental stage of conventional assessment criteria. The lower panels of these figures show the development changes.

Tukey’s Honest Significant Difference test was used to evaluate age-related differences in pronation and supination. This test can be used when there are a different number of samples in each group and has been used in previous research that has reported growth patterns in children (Hermsdörfer & Goldenberg, 2002; Hermsdörfer et al., 1999).

Table 3-1. Number of study participants.

Age (years)	**Male**	**Female**	**Total**
4	6	3	9
5	9	5	14
6	4	7	11
7	13	19	32
8	22	14	36
9	19	21	40
10	17	20	37
11	8	18	26
12	9	9	18
Total	107	116	223

3.3.1 Maximal effort motor task

The result for the maximal-effort motor task performed with one hand are shown in Figures 3-1 to 3-3. The right column shows the development changes for the task performed with the dominant (right) hand and the left column shows the development changes for the task performed with the non-dominant (left) hand.

The upper panels of Figure 3-1 show the data divided into three age groups according developmental stage of conventional assessment criteria for rotational speed: 4- and 5-year olds, 6-, 7-, 8-, 9-, and 10-year olds, and 11- and 12-year olds (Hadders-Algra, 2010). There were significant differences in rotational speed across the three developmental stages ($p < 0.05$). The lower panels of Figure 3-1 show the developmental change for rotational speed. For rotational speed of the dominant hand, there were significant differences between 4-year olds and 7-, 8-, 9-, 10-, 11-, and 12-year olds, between 5-year olds and 9-, 10-, 11-, and 12-year olds, and between 6-year olds and 7-, 8-, 9-, 10-, 11-, and 12-year olds, between 7-year olds and 10-, 11-, and 12-year olds, between 8-year olds and 11-, 12-year olds ($p < 0.05$). For rotational speed of the non-dominant hand, there were significant difference between 4-year olds and 6-, 7-, 8-, 9-, 10-, 11-, and 12-year olds, between 5-year olds and 9-, 10-, 11-, and 12-year olds, and between 6-, 7- and 8-year olds and 11- and 12-year olds.

The upper panels of Figure 3-2 show the data divided into three age groups according developmental stage of conventional assessment criteria for associated movement: 4-, 5- and 6-year olds, 7-, 8-, 9-, 10-, and 11-year olds, and 12-year olds (Touwen & Prechtl, 1970; Largo et al., 2001b; Hadders-Algra, 2010). For associated movement of dominant hand, there were significant differences in associated movement across the three developmental stages ($p < 0.05$). For associated movement of non-dominant hand, there were significant differences in associated movement between 4-, 5- and 6-year olds and 7-, 8-, 9-, 10-, and 11-year olds, between 4-, 5- and 6-year olds and 12-year olds ($p < 0.05$). The lower panels of Figure 3-2 show the developmental changes for associated movement. When the non-dominant hand was rotating, there were significant differences in associated movement of the dominant hand between 4-year olds and 5-, 6-, 7-, 8-, 9-, 10-, 11-, and 12-year olds, between 5-, 6-year olds and 7-, 8-, 9-, 10-, 11-, and 12- year olds ($p < 0.05$). When the dominant hand was rotating, there were significant differences in associated movement of the non-dominant hand between 4-year olds and 6-, 7-, 8-, 9-, 10-, 11-, and 12-year olds ($p < 0.05$).

The upper panels of Figure 3-3 show the data divided into three age groups according developmental stage of conventional assessment criteria for elbow excursion: 4- and 5-year olds, 6- and 7-year olds, and 8-, 9-, 10-, 11-, and 12-year olds (Hadders-Algra, 2010). The elbow excursion of the dominant hand had a tendency to decrease with age, but there was no significant main effect of age. There were significant differences in the elbow excursion of the non-dominant hand between the first developmental stage and the second developmental stage, between the first developmental stage and the third developmental stage ($p < 0.05$; see Figure 3-3, upper panels). The lower panels of Figure

3-3 show the developmental changes for elbow excursion. There were significant differences in elbow excursion between 4-, 5- and 6-year olds and 7-, 9-, 10-, and 12-year olds in developmental change ($p < 0.05$).

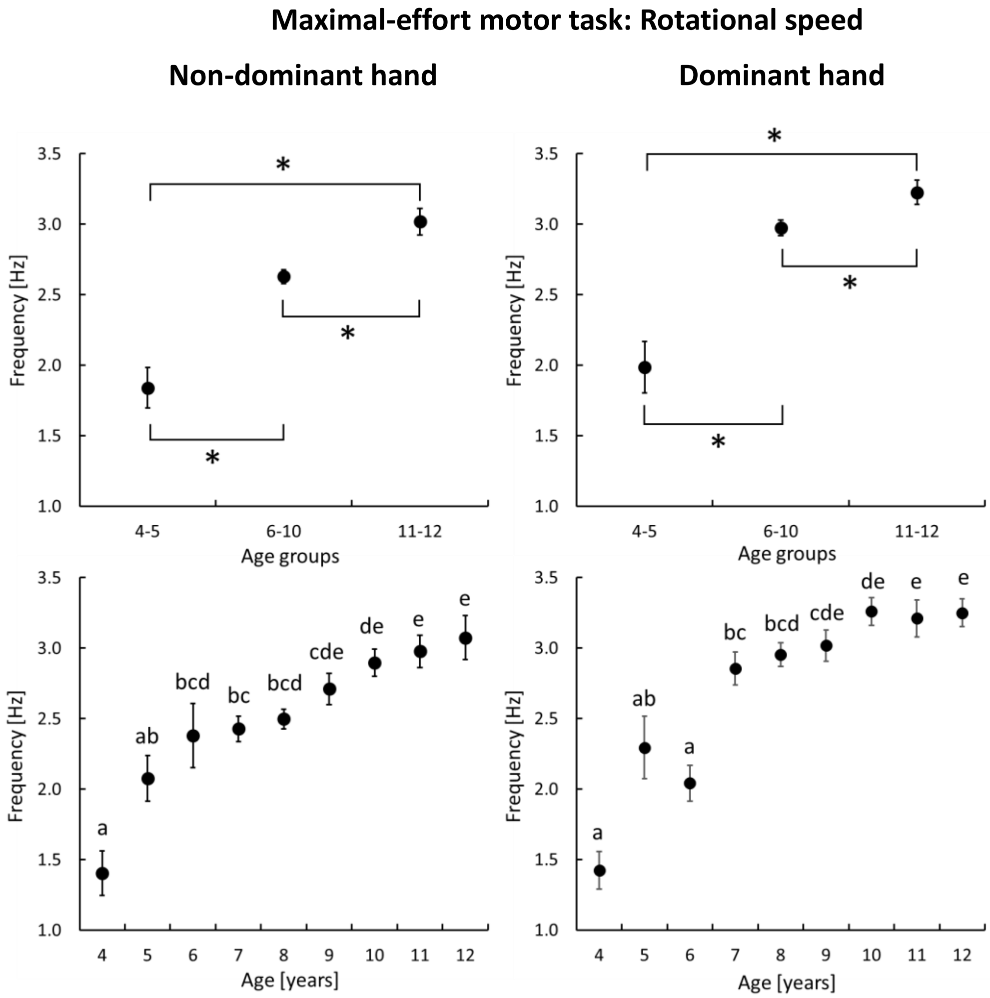

Figure 3-1. Average and standard error of rotational speed in TD children. The black dots show the average of rotational speed by age group for TD children. The left column shows the rotational speed for the task performed with the non-dominant hand and the right column shows the rotational speed for the task performed with the dominant hand. In the top row, the asterisk indicates $p < 0.05$ and the double asterisk indicates $p < 0.01$. In bottom row, there is a significant difference between age groups that do not include the same letter ($p < 0.05$).

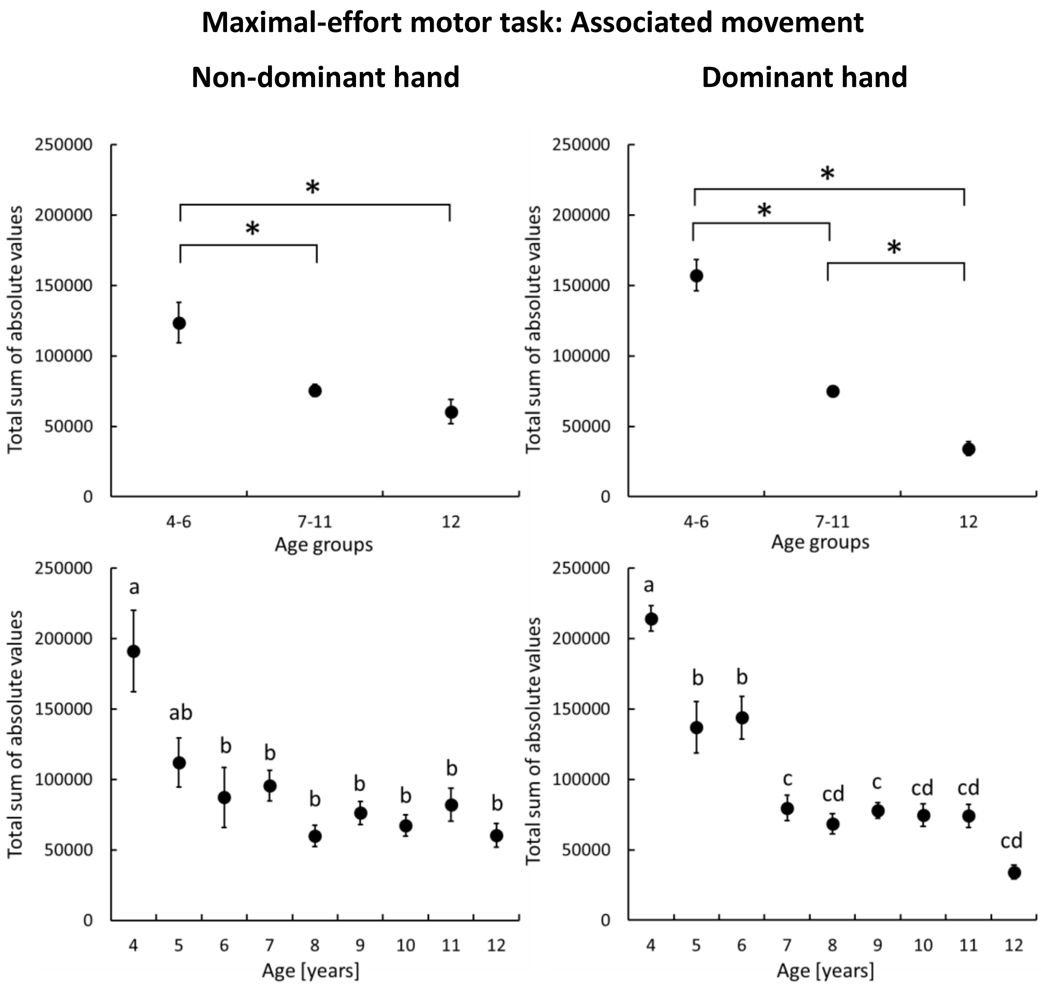

Figure 3-2. Average and standard error of associated movement in TD children. The black dots show the average of associated movement by age group for TD children. The left column shows the associated movement for the task performed with the dominant (right) hand and the right column shows the associated movement for the task performed with the non-dominant (left) hand. In the top row, the asterisk indicates $p < 0.05$ and the double asterisk indicates $p < 0.01$. In bottom row, there is a significant difference between age groups that do not include the same letter ($p < 0.05$).

3.2.2. Imitative motor task

The result for the imitative motor task are shown in Figures 3-4 and 3-5. The right-hand column of Figure 3-5 shows the development changes for the task performed with the dominant (right) hand and the left-hand column shows the development changes for the task performed with the non-dominant (left) hand.

The upper panel of Figure 3-4 shows the data divided into two age groups according developmental stage of conventional assessment criteria for bimanual symmetry (the synchronous time between the right and left hands): 4- and 5-year olds, 6-, 7-, 8-, 9-, 10-, 11-, and 12-year olds (Van Mier, 2006; Hadders-Algra, 2010). There was significant difference between two developmental stages ($p < 0.05$). The lower panel of Figure 3-4 shows the developmental change for bimanual symmetry. There were significant differences in bimanual symmetry between 4- and 6- year olds and 8-, 9-, 10-, 11-, and 12-year olds, between 5-and 7- year olds and 10-year olds ($p < 0.05$).

The upper panels of Figure 3-5 show the data divided into two age groups according developmental stage of conventional assessment criteria for compliance: 4- and 5-year olds, 6-, 7-, 8-, 9-, 10-, 11- and 12-year olds (Hadders-Algra, 2010). There were significant differences in compliance between two age groups ($p < 0.05$). The lower panels of Figure 3-5 show the developmental changes for compliance. In the dominant hand, there were significant differences in compliance between 4- and 5- year olds and 7-, 8-, 9-, 10-, 11-, and 12-year olds, between 6-year olds and 7-, 8-, 9-, 11-, and 12-year olds. In the non-dominant hand, there were significant differences in compliance between 4-, 5- and 6-year olds and 8-, 9-, 10-, 11- and 12-year olds, and between 7-year olds and 9-, 11-, and 12-year olds.

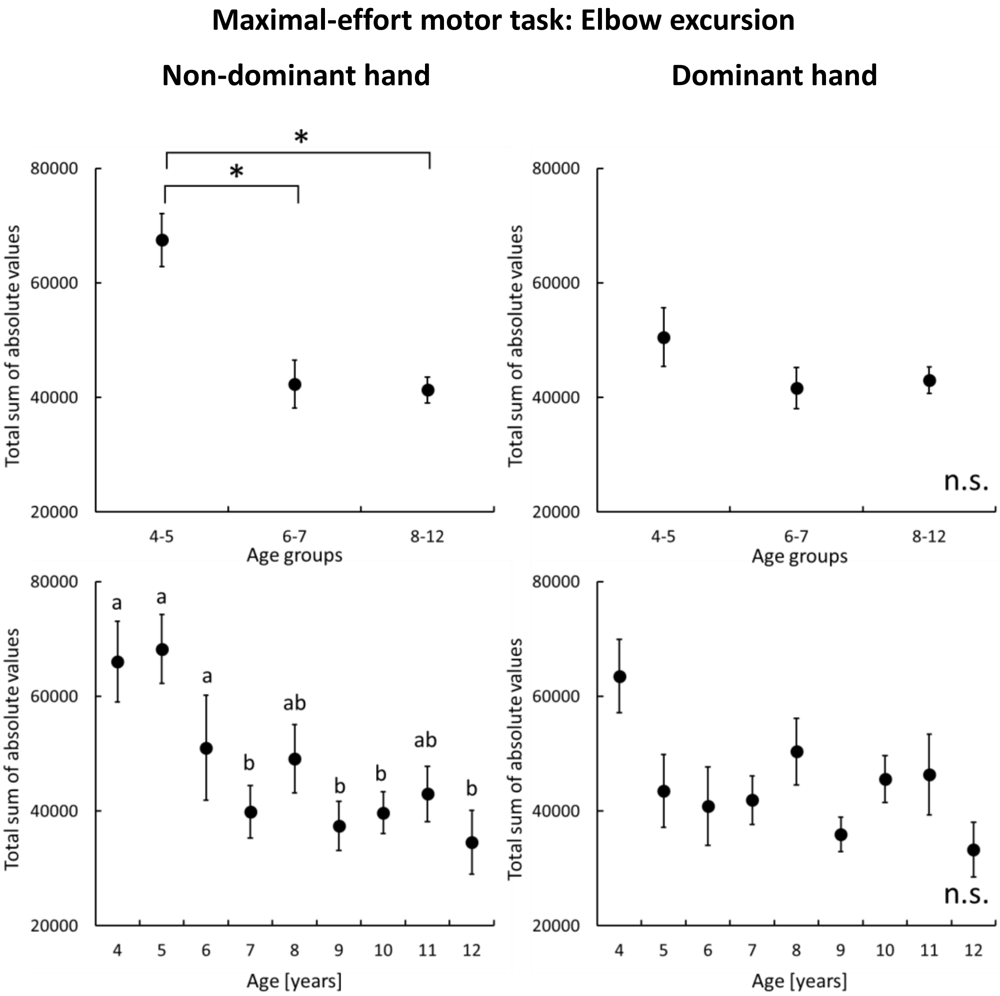

Figure 3-3. Average and standard error of elbow excursion in TD children. The black dots show the average of elbow excursion by age group for TD children. In the top row, the asterisk indicates $p < 0.05$. In bottom row, there is a significant difference between age groups that do not include the same letter ($p < 0.05$).

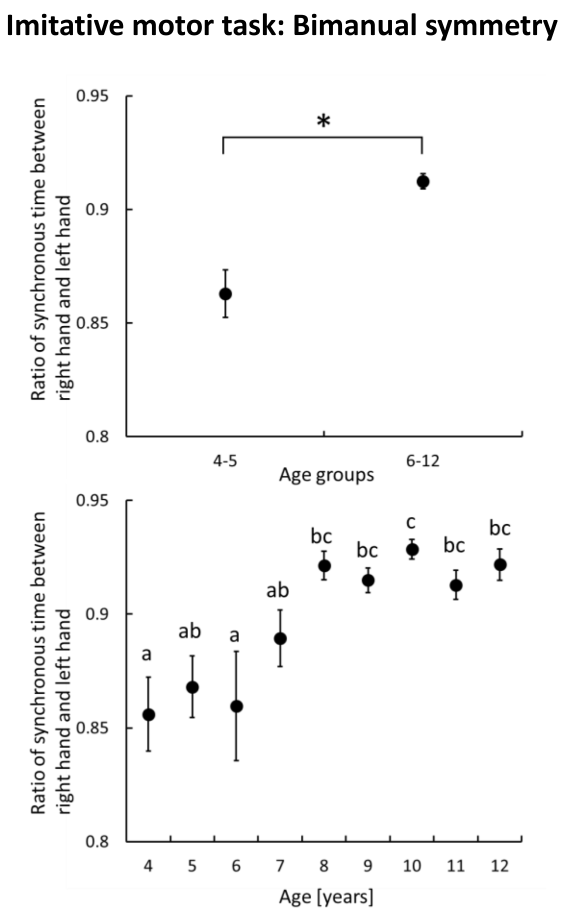

Figure 3-4. Average and standard error of bimanual symmetry in TD children. The black dots show the average of bimanual symmetry by age group for TD children. In the top row, the asterisk indicates $p < 0.05$. In bottom row, there is a significant difference between age groups that do not include the same letter ($p < 0.05$).

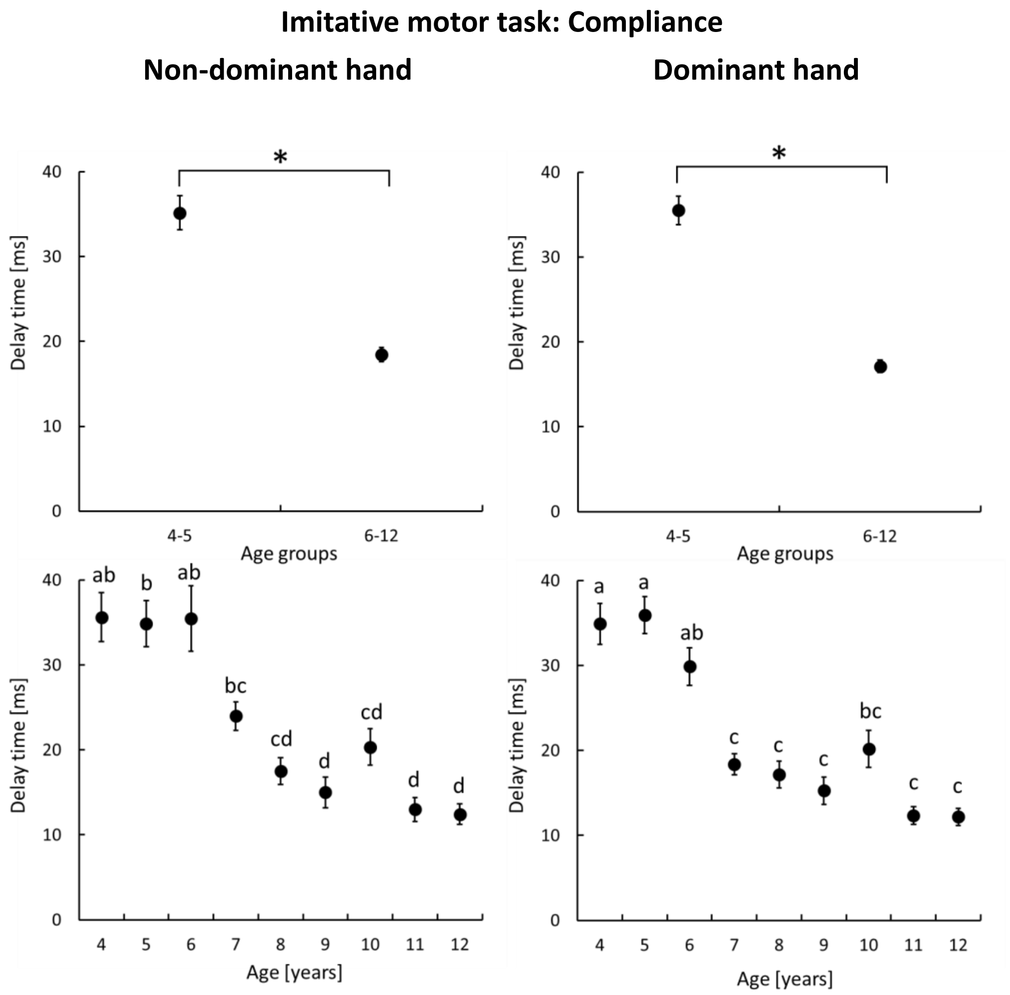

Figure 3-5. Average and standard error of compliance in TD children. The black dots show the average of compliance by age group for TD children. In the top row, the asterisk indicates $p < 0.05$. In bottom row, there is a significant difference between age groups that do not include the same letter ($p < 0.05$).

3.4 Discussion

3.4.1 Developmental changes in TD children

In this chapter, we measured pronation and supination in TD children using our proposed quantitative evaluation method to establish typical development. This information can be used to identify criteria for diagnosis of ADHD.

There are several SNS that can be tested, including sensory function, coordination, abnormal or associated movements, repetitive movements, motor speed, accuracy of limb movements, axial movements, balance, maintenance, and dysrhythmias (Fellick et al., 2001; Iannetti et al., 2005; Martins et al., 2013; Patankar et al., 2012; Peters et al., 2008). Several studies have reported developmental changes in SNS in TD children (Largo et al., 2003; Fellick et al., 2001; Gabbard et al., 2011; Kakebeeke et al., 2013; Kar et al., 2011; Martins et al., 2008; Rueckriegel et al., 2008). In the conventional examination of pronation and supination, subjects quickly pronate and supinate one hand while the elbows are bent to 90 degrees (Hadders-Algra, 2010; Largo et al., 2001a, 2001b). Several outcome measures have been used to evaluate pronation and supination, including associated movement, excursion of the elbows, dysrhythmias, motor speed, and mirror movement (Hadders-Algra, 2010; Largo et al., 2001a, 2001b; Touwen & Prechtl, 1970). We quantified rotational speed, associated movement and elbow excursion in the maximal effort motor task and bimanual symmetry and compliance in the imitative motor task.

Conventional assessment of rotational speed by visual observation categorizes the movement as slow (1–2 Hz), medium (2–3 Hz), or fast (3–4 Hz). Developments in motor speed occur as children become older, with children in the slow group aged 4–5 years, children in the medium group aged 6–10 years, and children in the fast group aged over 10 years (Hadders-Algra, 2010). We found that the average rotational speed was 1.5–2 Hz at the first stage of development (age 4–5 years), about 2.5–3 Hz at the second stage of development (age 6–10 years), and reached 3–3.5 Hz at the third stage of development (Figure 3-1, upper panels). The rotational speed therefore increased as children grew older. Moreover we found significant differences in rotational speed across the three stages of development. Previous studies have reported progressive improvement of motor speed between the age of 5 to 10 years in TD children (Gasser et al., 2007; Gasser et al., 2010). We found that rotational speed in both hands increased from 5 to 10 years of age, supporting the results of this previous study (Figure 3-1, lower panels). These results are consistent with previous studies and the conventional assessment criteria for rotational speed. We also found that the rotational speed rapidly increased between 4 and 7 years of age, and then gradually increased after 7 years of age. We proposed that our system can evaluate more detailed developmental changes in rotational speed from the first stage to the second stage, from the second stage to the third stage than the conventional criteria for visual assessment.

The magnitude of associated movement was large, indicating that the non-rotating hand moved and did not maintain the basic position during the pronation and supination task. Several studies have reported developmental changes in associated movement of the hand evaluated using visual assessment (Gasser et al., 2007; Gasser et al., 2010). The associated movement gradually decreased with age (Patankar et al., 2012; Connolly and Stratton, 1968; Lazarus and Todor, 1987; Gasser, 2007; Gasser, 2010). With conventional assessment, associated movement became evident between the ages of 4 and 6 years, decreased between the ages of 7 and 11 years, and was generally not observed after the age of 12 years (Touwen, 1970; Largo et al., 2001b). The largest inter-individual differences were found in children of kindergarten age and in the early school years (Largo et al., 2003; Hadders-Algra, 2010). We found that associated movement decreased as age increased, supporting the results of these previous studies. We also found significant differences among the three developmental stages (4–6 years, 7–11 years, and 12 years). Moreover, the developmental curve indicates that associated movement rapidly decreased from the age of 4 to 6 years and then more gradually decreased until the age of 12 years (Figure 3-2, lower panels). These results are consistent with previous developmental studies and the conventional assessment criteria. We were able to obtain more detailed data on developmental change of associated movement than can be obtained using the conventional visual assessment criteria. Largo et al. (2001b) reported that associated movement decreased with age and didn't occur after 12 years of age. Moreover, previous studies reported that girls showed less associated movement than boys (Connolly and Stratton, 1968; Gasser et al, 2007, 2010). We only studied TD children aged up to 12 years; a study of older children is required to confirm the findings of previous studies. In order to propose more detailed criteria for pronation and supination as an SNS, we need to study more subjects, including children aged over 12 years, so that we can better quantify the relation between sex, age and outcome measure of pronation and supination.

Previous studies using conventional criteria have reported that the elbow excursion decreased between the ages of 4–7 years. At 4–5 years of age, excursion was over 15 cm; at 6–7 years of age, excursion was 5–15 cm; and after 8 years of age, excursion was under 5 cm (Hadders-Algra, 2010). When the data were analyzed with participants split into three groups according to conventional criteria for elbow excursion (age 4–5 years, age 6–7 years, and age >8 years), we found a tendency for elbow excursion to decrease as age increased, and there was a significant difference between the age groups when the task was performed with the non-dominant hand. Our results are consistent with previous developmental studies and conventional assessment criteria. However, there was no significant difference with age for the elbow excursion of the dominant hand. This may be due to inter-individual differences in the magnitude of associated movement of the elbow, which were large in children of kindergarten age and in the early school years (Largo et al., 2003; Hadders-Algra, 2010).

In the imitative motor task, we quantified bimanual symmetry as a measure of coordination between the right and left hands. Developmental changes in bimanual symmetry during drawing and circle performance have been reported between the ages of 4 and 12 years, and the bimanual symmetry of 4- and 5-year olds was inferior to that of children aged 6 years and older (Van Mier, 2006; Hadders-Algra, 2010). We found a significant difference between the two developmental stages (Figure 3-4, upper panel). We also found that bimanual symmetry did not change between 4 and 6 years of age, rapidly increased between 6 and 7 years of age, and then became stable after 8 years of age. Our results are consistent with previous developmental studies and provide more detail of the developmental changes that occur after the age of 6 years.

In a follow-a-finger test in which compliance was quantified by visual observation, performance of 4- and 5-year olds was especially low in comparison to performance of children aged 6 years and older (Hadders-Algra, 2010). We found that a significant difference between the two stage. We also found that compliance improved between the ages of 4 and 7 years and stabilized after the age of 7 years (Figure 3-5, lower panels). Our results are therefore consistent with previous developmental studies and provide more detail of the developmental changes that occur after the age of 6 years. However, previous studies reported that girls showed high skill of compliance than boys (Flatters et al, 2014). In order to propose more detailed criteria for pronation and supination as an SNS, we need to quantify the relation between sex and outcome measure of pronation and supination.

3.4.2 Differences between the dominant and non-dominant hands

All participants in this study were right-hand dominant. In the maximal effort motor task, we measured the pronation and supination of the dominant and the non-dominant hand. The development of the dominant hand was better than that of the non-dominant hand in the maximal effort motor task. Rotational speed of the dominant hand was greater than that of the non-dominant hand from the age of 7 years (Figure 3-1, lower panel). The development of the dominant hand was greater than that of the non-dominant hand from the age of 7 or 8 years. The dominant hand can change up until the age of 8 years (Ames, 1947); therefore, our result indicated that developmental difference of dominant hand and non-dominant hand in rotational speed after dominant hand was decided. The associated movement and the elbow excursion were greater when the task was performed with the non-dominant hand than when the task was performed with the dominant hand across the three age groups (Figure 3-2 and 3-3, upper panels). It is generally assumed that the associated movement of the dominant hand when the participant performs the maximal effort motor with non-dominant hand is larger than that of the non-dominant hand when the participant performs the maximal effort motor with dominant hand (Touwen & Prechtl, 1970; Hadders-Algra, 2010). Our results are consistent with the result of previous studies.

3.5 Conclusion

In this chapter, we quantified developmental changes in pronation and supination using our novel system. Results obtained using our system showed developmental changes that were consistent with previous developmental studies and conventional assessment criteria for pronation and supination. This indicates that it may be possible to use our system as a quantitative assessment criteria for developmental disorders. In the next chapter we compare the performance of children with ADHD to the development changes quantified in this chapter.

Chapter 4. Pronation and Supination in Children with ADHD Evaluated Using Our Proposed System

4.1 Abstract

We were able to obtain the developmental change of TD children for pronation and supination using our proposed evaluation system in previous chapter. Our aim in this chapter is to establish a quantitative evaluation method for the differential diagnosis of ADHD. In this chapter, we focused on quantifying the development changes for pronation and supination in children with ADHD to compare the performance of TD children by age. Thirty eight children with ADHD aged 7-11 years (32 males, 6 females) participated in our experiment. Our results suggested that the development of children with ADHD were lower than that of TD children, and had a tendency to lag behind that of TD children by several years.

Moreover, children with ADHD were split into two groups: ADHD only and comorbid ADHD and autism spectrum disorder (ASD) to compare pronation and supination between ADHD and other developmental disorders. These two groups were then also compared with the TD children reported in Chapter 3 to establish the external validity of our proposed system for ADHD. In addition to the above outcome measures:

rotational speed, associated movement, elbow excursion, bimanual symmetry, and compliance, we quantified several novel outcome measures: rotational size, postural stability and temporal change according visual inspection by pediatricians who watched the video recordings of the pronation and supination. From our results, we found a significant difference in several measure outcomes (especially measurement outcomes of non-dominant hand and temporal change). The radar charts showed that the balance among these outcome measures improved with age. The size of the radar chart in children with ADHD was smaller than that in TD children of the same age. These results indicated a tendency for pronation and supination to develop later in children with ADHD, compared to their TD counterparts. Indeed, pronation and supination movement in children with ADHD was comparable to that of younger TD children.

4.2 Comparison of children between ADHD and TD children

4.2.1 Procedure and Participants

The experimental procedure and analysis were as described in Chapter 2. Thirty-eight children with ADHD aged 7–11 years (32 males, six females) participated in this experiment (Table 4-1). All participants were right-hand dominant. Hand dominance was evaluated by asking the participant to throw a ball with their preferred hand. Participants were recruited from Kurume University Hospital. They were diagnosed with ADHD according to The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-4) and had an intelligence quotient of more than 70 as defined by the Wechsler Intelligence Scale for Children, third edition. Before starting the experiment, all participants and their parents received an explanation about the aim, procedures, and hazards of the experiment. All participants agreed to participate. The study was approved by the Kyushu University Ethics Committee.

Table 4-1. Study participants.

TD group			ADHD group			
Age (years)	Male / Female	Total	Age (years)	Male/ Female	Total	IQ
4	6 / 3	9				
5	9 / 5	14				
6	4 / 7	11				
7	13 / 19	32	7	5 / 2	7	110.8 (10.9)
8	22 / 14	36	8	3 / 1	4	101.8 (20.7)
9	19 / 21	40	9	7 / 2	9	94.0 (9.0)
10	17 / 20	37	10	9 / 1	10	99.4 (6.2)
11	8 / 18	26	11	8 / 0	8	103.9 (10.4)
12	9 / 9	18				
Total	107 / 116	223	Total	32 / 6	38	101.3 (12.9)

SD in parentheses. IQ: Intelligence quotient. IQ was assessed using the Wechsler Intelligence Scale for Children, Third Edition.

4.2.2 Results

The performance of children with ADHD was compared to that of the TD children of the same age reported in Chapter 4 using a Mann-Whitney U test and a Student's t-test. The assumption of normality was tested for all data using the Shapiro-Wilk test. Student's t-test was used for normally distributed data, and Mann-Whitney U test was used when the data were not normally distributed. Figures 4-1 to 4-5 show the outcomes for children with ADHD and TD children. In these figures, the vertical axis shows the quantified variable and the horizontal axis shows the age of the participants. The upper panels of these figures show the data divided into several age groups according developmental stage reported in Chapter 3. The development changes are shown in the lower panels of these figures. The right column shows the development changes for the task performed with the dominant (right) hand and the left column shows the development changes for the task performed with the non-dominant (left) hand.

Figure 4-1 shows the rotational speed in the maximal effort motor task. The upper panels of Figure 4-1 show the data of children with ADHD divided into two age groups according developmental stage of conventional assessment criteria for rotational speed. The rotational speed of the dominant hand was lower in children with ADHD than in TD children. There were significant differences between TD children and children with ADHD group for the dominant hands ($p < 0.05$), but there were no significant differences between TD children and children with ADHD for the non-dominant hand.

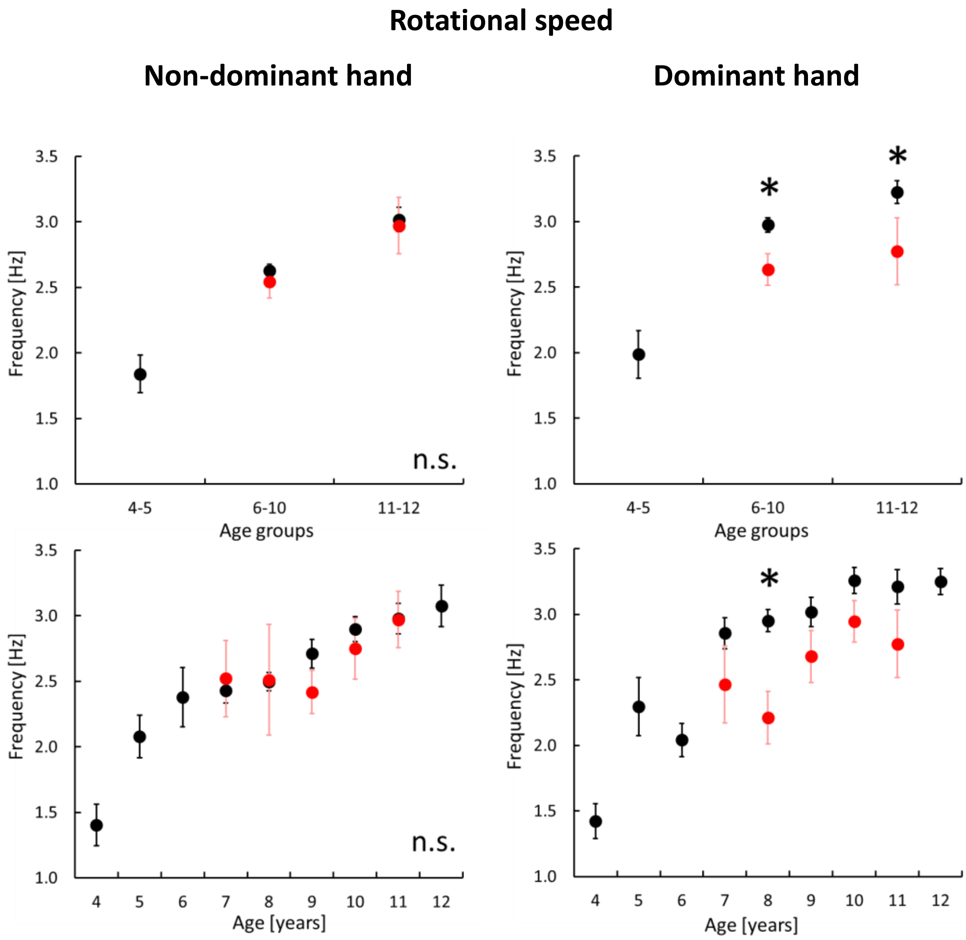

Figure 4-1. Rotational speed in TD children and children with ADHD. The left column shows the rotational speed when the task was performed with the non-dominant hand and the right column shows the rotational speed when the task was performed with the dominant hand. The black dots show the average score of TD children and the red dots show the average score of children with ADHD. Upper figures show the comparison for age groups based on conventional criteria for visual observation. Lower figures show the comparison for each age from 4 to 12 years old (*: $p < 0.05$, **: $p < 0.01$).

Figure 4-2 shows the associated movement in the maximal effort motor task. There were significant differences between TD children and children with ADHD group. For both hands, the associated movement was larger in children with ADHD than in TD children. For the developmental changes, there were significant differences between children with ADHD and TD children for 7- year olds ($p < 0.05$) when the task was performed with the dominant hand and for 8- and 9- year olds ($p < 0.05$ and $p < 0.01$, respectively) when the task was performed with the non-dominant hand. For the age group, there was a significant difference between TD children and children with ADHD aged 7–11 years.

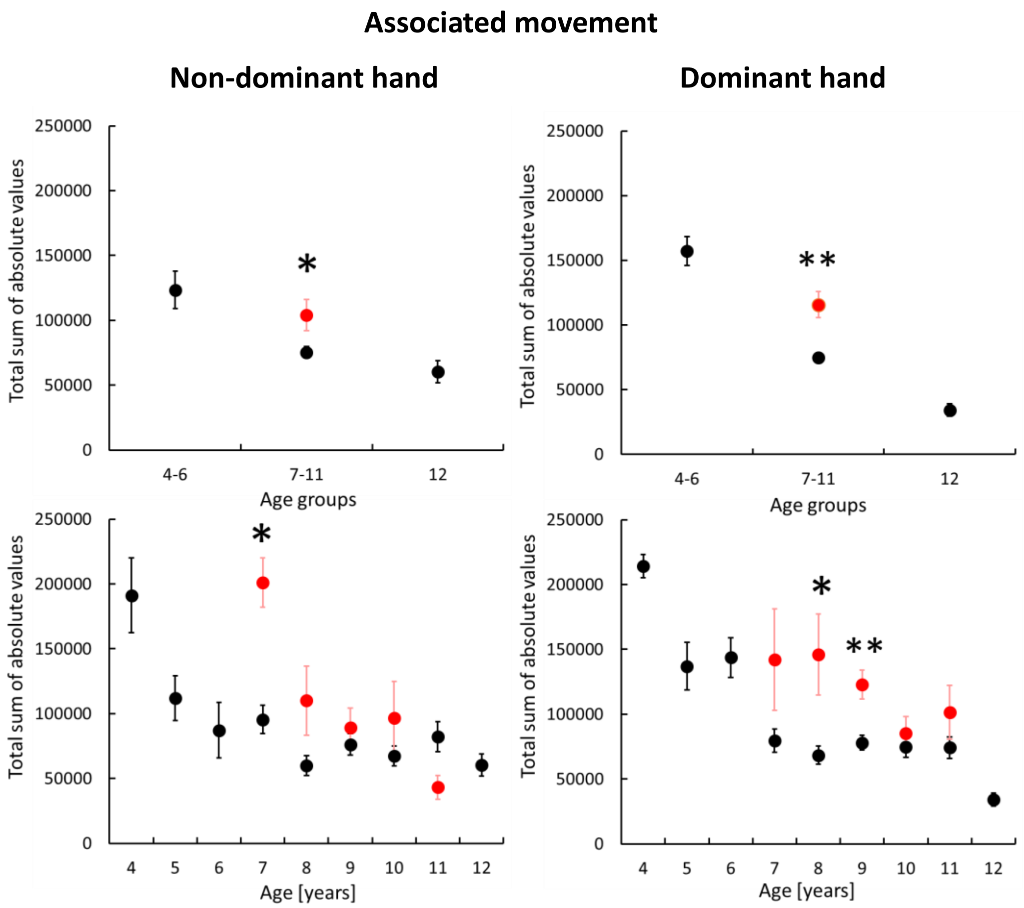

Figure 4-2. Associated movement in TD children and children with ADHD. The left column shows the associated movement when the task was performed with the dominant hand and the right column shows the associated movement when the task was performed with the non-dominant hand. The black dots show the average score of TD children and the red dots show the average score of children with ADHD. (*: $p < 0.05$, **: $p < 0.01$).

Figure 4-3 shows the elbow excursion. For the age groups of the dominant hand, there was a significant difference between children with ADHD and TD for 8–11 years. For the developmental changes, there was no significant differences between children with ADHD and TD children at any age.

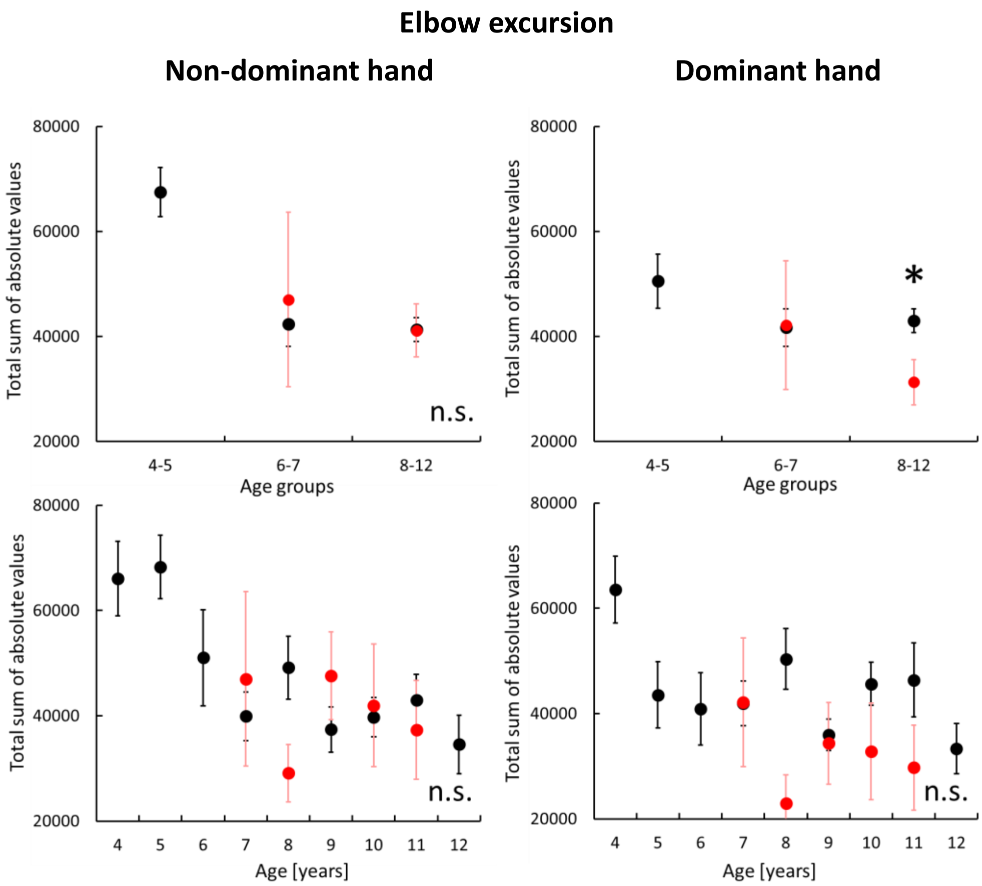

Figure 4-3. Elbow excursion in TD children and children with ADHD. The black dots show the average score of TD children and the red dots show the average score of children with ADHD. Upper figures show the comparison for age groups based on conventional criteria for visual observation. Lower figures show the comparison for each age from 4 to 12 years old (*: $p < 0.05$, **: $p < 0.01$).

Figure 4-4 shows the bimanual symmetry in the imitative motor task. There were significant differences between TD children and children with ADHD group ($p < 0.05$). Bimanual symmetry was lower in children with ADHD than in TD children. There was a significant difference between children with ADHD and TD children for 7-, 8-, and 10-year olds in developmental change ($p < 0.05$).

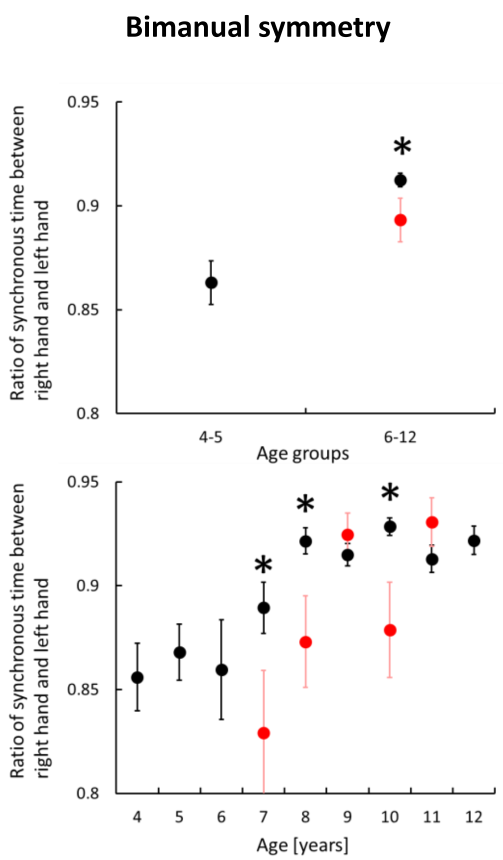

Figure 4-4. Bimanual symmetry in TD children and children with ADHD. The black dots show the average score of TD children and the red dots show the average score of children with ADHD. Upper figures show the comparison for age groups based on conventional criteria for visual observation. Lower figures show the comparison for each age from 4 to 12 years old (*: $p < 0.05$, **: $p < 0.01$).

Figure 4-5 shows the compliance in the imitative motor task. Compliance was greater in children with ADHD than in TD children. There were significant differences between children with ADHD and TD children for all age groups.

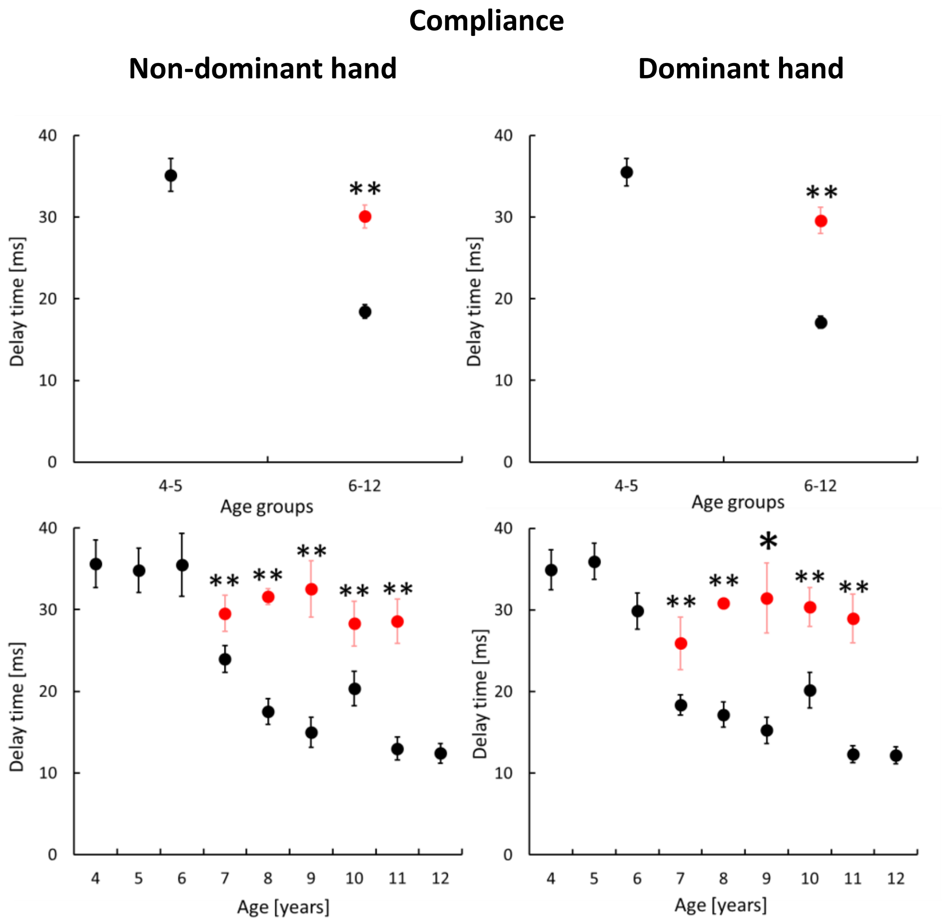

Figure 4-5. Compliance in TD children and children with ADHD. The black dots show the average score of TD children and the red dots show the average score of children with ADHD. Upper figures show the comparison for age groups based on conventional criteria for visual observation. Lower figures show the comparison for each age from 4 to 12 years old (*: $p < 0.05$, **: $p < 0.01$).

4.3 Comparison among children with ADHD, children with ADHD and comorbid ASD, and TD children

4.3.1 Procedure and Participants

The experimental procedure and analysis were as described in Chapter 2. Children with ADHD were split into two groups: ADHD only and comorbid ADHD and autism spectrum disorder (ASD). These two groups were then also compared with the TD children reported in Chapter 3 to establish the external validity of our proposed system for ADHD (Table 4-2).

Table 4-2. Number of study participants for ADHD and ASD analysis.

Age	Control	ADHD	ADHD+ASD
7	32 (13 / 19)	2 (1 / 1)	1 (1 / 0)
8	36 (22 / 14)	0 (0 / 0)	1 (0 / 1)
9	40 (19 / 21)	7 (7 / 0)	1 (0 / 1)
10	37 (17 / 20)	3 (3 / 0)	0 (0 / 0)
11	26 (8 / 18)	5 (4 / 1)	4 (4 / 0)
Total	171 (79 / 92)	17 (15 / 2)	7 (5 / 2)

4.3.2 Outcome measures for ADHD

In addition to the above outcome measures: rotational speed, associated movement, elbow excursion, bimanual symmetry, and compliance, we quantified several novel outcome measures: rotational size, postural stability and temporal change according visual inspection by pediatricians who watched the video recordings of the pronation and supination.

Rotational size reflects whether or not the participant moved through the full 180° range, i.e., moved the hand until it was horizontal. This was quantified from the continuous fast Fourier transform of acceleration in the Z axis and quantified as the frequency of the peak power. Postural stability of the hands reflects the up-and-down movement of the hands. Postural stability was calculated using the absolute value of the total sum of acceleration along the X axis. Each task was performed for about 10 s. This was divided into seven phases of about 2.5 s duration, with about 1.25 s overlap between consecutive phases, to allow analysis of temporal change in outcome measures as described in Chapter 2 (Figure 2-7). Temporal change was quantified as the standard deviation of each outcome measure across the seven phases.

4.3.3 Results

Figures 4-6 to 4-12 show the comparison of performance among children with ADHD only, children with ADHD and ASD, and TD children. The upper panels of these figures show the mean values of each outcome measure. The lower panels of these figures show the standard deviation of each outcome measure. Tukey’s Honest Significant

Difference test was used to evaluate age-related differences in pronation and supination. This test can be used when there are a different number of samples in each group.

4.3.3.1 Maximal effort motor task

Rotational speed in the maximal effort motor task was significantly different between ADHD and TD groups, and between ADHD with ASD and TD groups for the dominant hand ($p < 0.05$ and $p < 0.01$, respectively; see Figure 4-6, upper panel). When the task was performed with the non-dominant hand, associated movement of the dominant hand was significantly different between ADHD and TD groups, and between ADHD with ASD and TD groups for the dominant hand ($p < 0.05$; see Figure 4-7, upper panel) and excursion of the dominant elbow was significantly different between ADHD, and TD groups ($p < 0.05$; see Figure 4-8, upper panel).

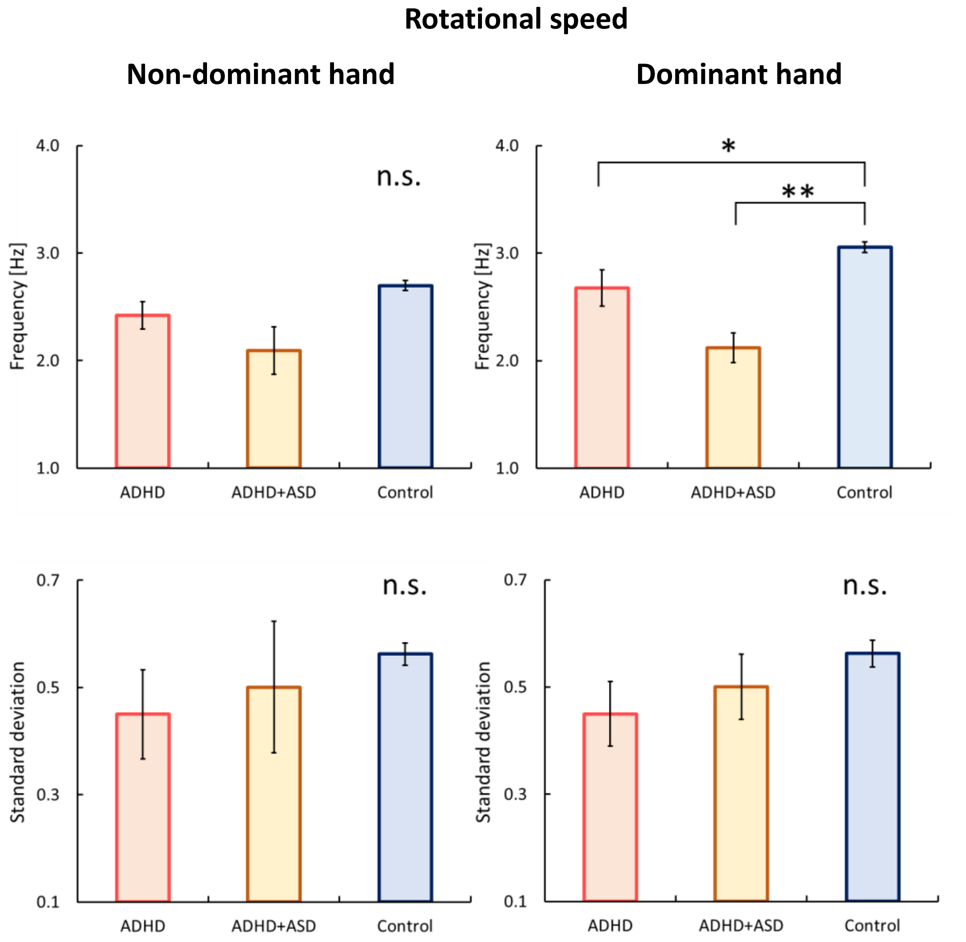

Figure 4-6. Rotational speed for children with ADHD only, children with ADHD and ASD, and TD children (control). The left column shows the results for the task performed with the non-dominant hand and the right column shows the results for the task performed with the dominant hand. The participants in all groups are 7 to 11 years old. The upper figures show the average of rotational speed in each group. The lower figures show the variance of rotational speed in each group. (*: $p < 0.05$, **: $p < 0.01$)

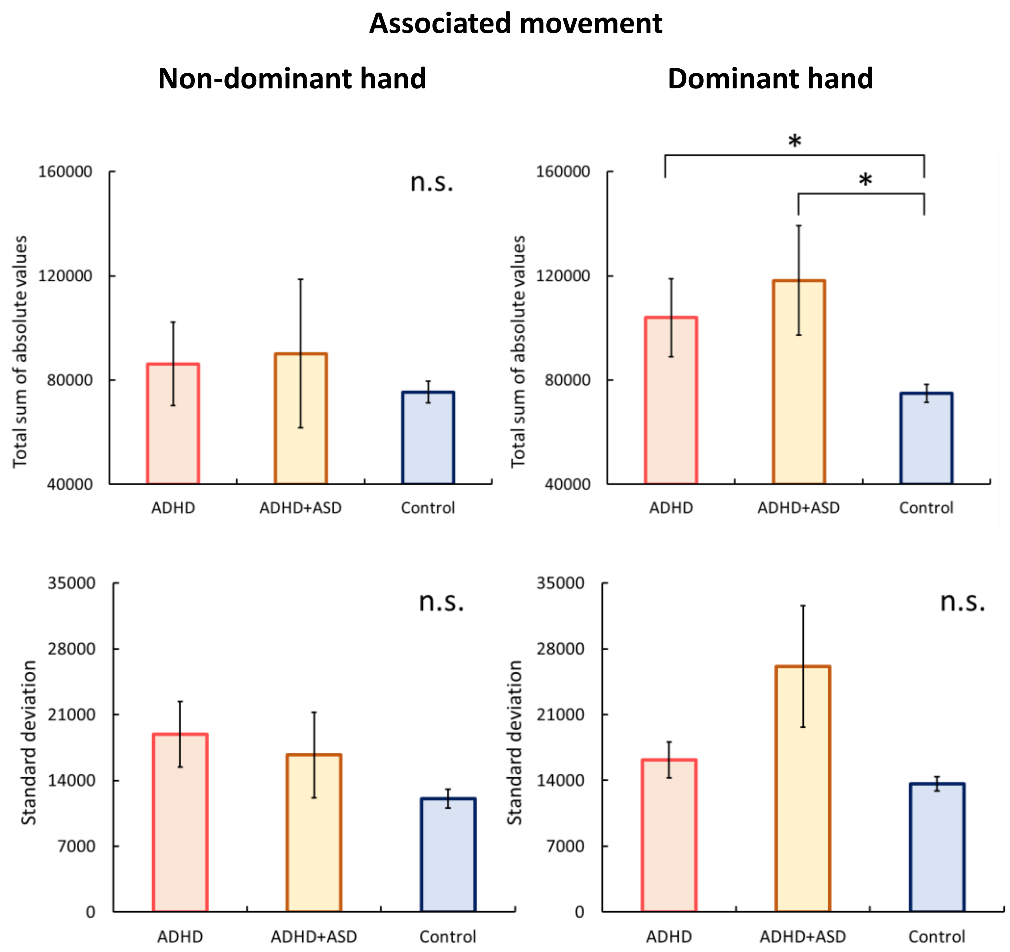

Figure 4-7. Associated movement for children with ADHD only, children with ADHD and ASD, and TD children (control). The left column shows the results for the task performed with the dominant hand and the right column shows the results for the task performed with the non-dominant hand. The participants in all groups are 7 to 11 years old. The upper figures show the average of associated movement in each group. The lower figures show the variance of associated movement in each group. (*: $p < 0.05$)

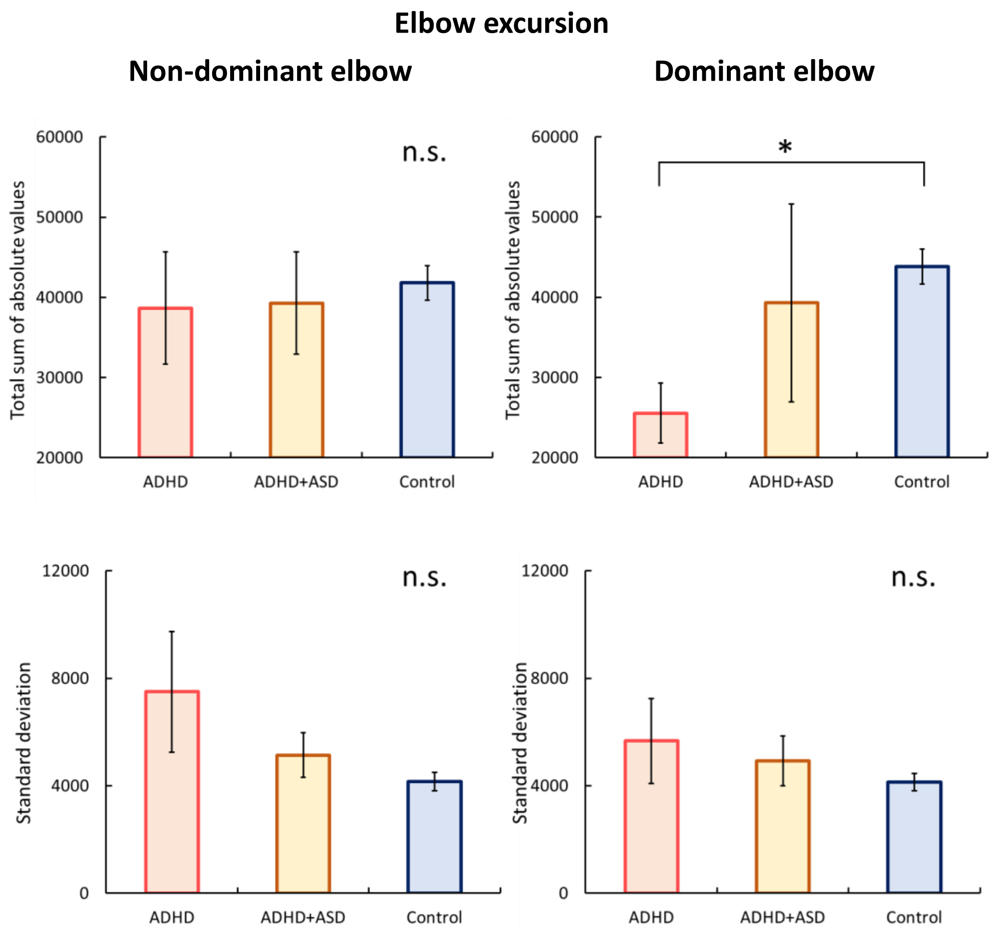

Figure 4-8. Elbow excursion for children with ADHD only, children with ADHD and ASD, and TD children (control). The participants in all groups are 7 to 11 years old. The upper figures show the average of elbow excursion in each group. The lower figures show the variance of elbow excursion in each group. (*: $p < 0.05$)

4.3.3.2 Imitative motor task

The bimanual symmetry of ADHD and ADHD with ASD groups had a tendency to be lower than that of the TD groups, but there was no significant differences across the three groups (Figure 4-9, left panel). There were significant differences between ADHD

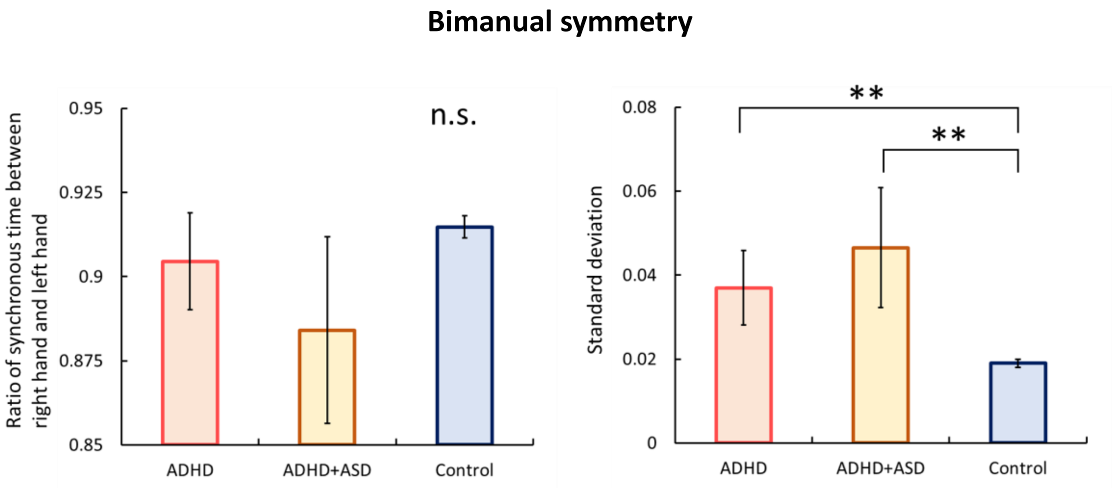

Figure 4-9. Bimanual symmetry for children with ADHD only, children with ADHD and ASD, and TD children (control). The left figure shows the average of bimanual symmetry in each group. The right figure shows the variance of elbow excursion in each group. (**: $p < 0.01$)

and TD groups, and between ADHD with ASD and TD groups for the temporal change of bimanual symmetry ($p < 0.01$; see Figure 4-9, right panel). There were significant differences in the compliance and the temporal change of compliance for the non-dominant hand between ADHD and TD groups, and between ADHD with ASD and TD groups ($p < 0.01$ and $p < 0.05$, respectively; see Figure 4-10, left-hand column). The compliance and the temporal change of compliance significantly differed between ADHD and TD groups in the dominant (Figure 4-10, right-hand column). In non-dominant hand, there was a significant difference in the rotational size between ADHD with ASD and TD groups ($p < 0.05$; see Figure 4-11, upper panel). The temporal change of rotational size significantly differed between ADHD and TD groups, and ADHD with ASD and TD groups ($p < 0.05$ and $p < 0.01$, respectively; see Figure 4-11, lower panel). For the postural stability of the non-dominant hand, there were significant differences between ADHD and TD groups, and between ADHD with ASD and TD groups ($p < 0.05$; see Figure 4-12, upper panel). For the postural stability of the dominant hand, there was a significant difference between ADHD and TD groups ($p < 0.01$; see Figure 4-12, upper panel). The temporal change of postural stability significantly differed between ADHD, ADHD with ASD and TD groups in the both hands.

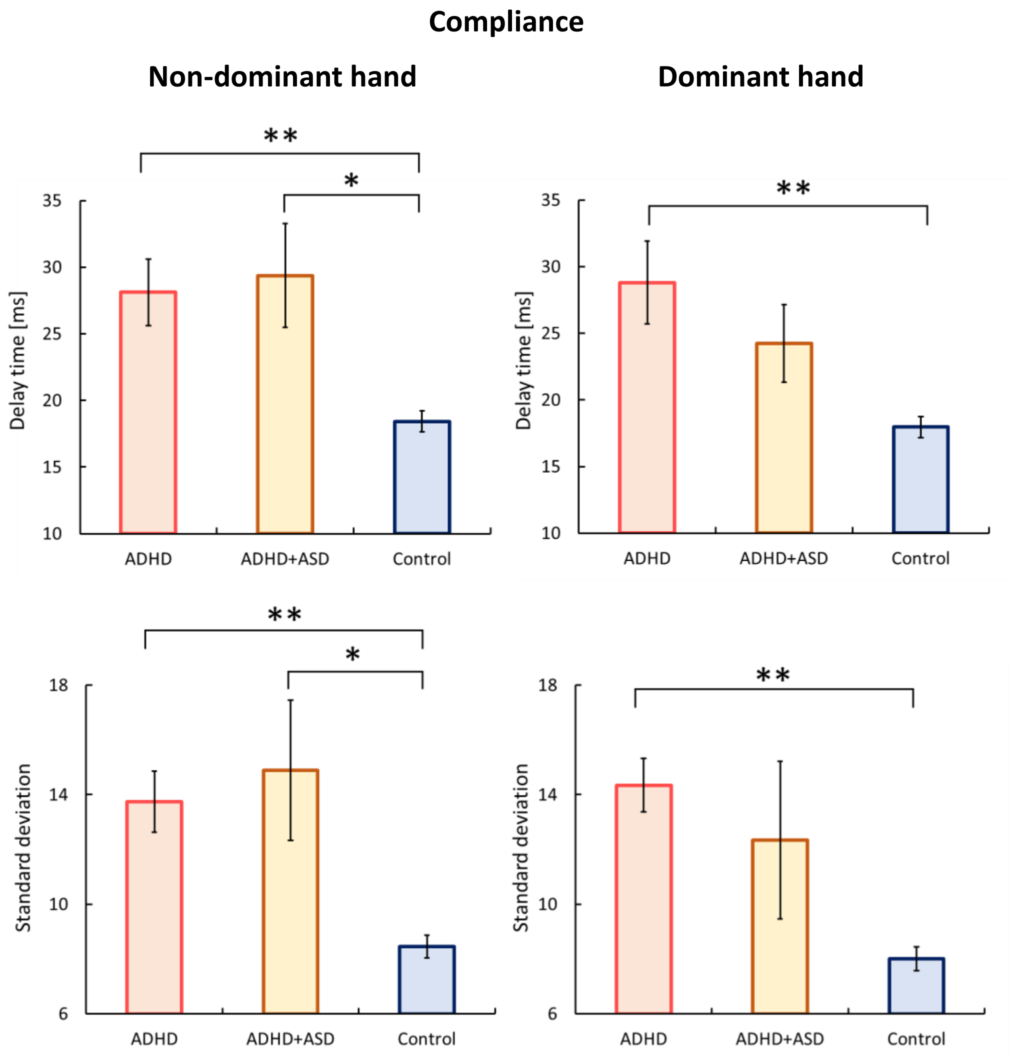

Figure 4-10. Compliance for children with ADHD only, children with ADHD and ASD, and TD children (control). The participants in all groups are 7 to 11 years old. The upper figures show the average of compliance in each group. The lower figures show the variance of compliance in each group. (*: $p < 0.05$, **: $p < 0.01$)

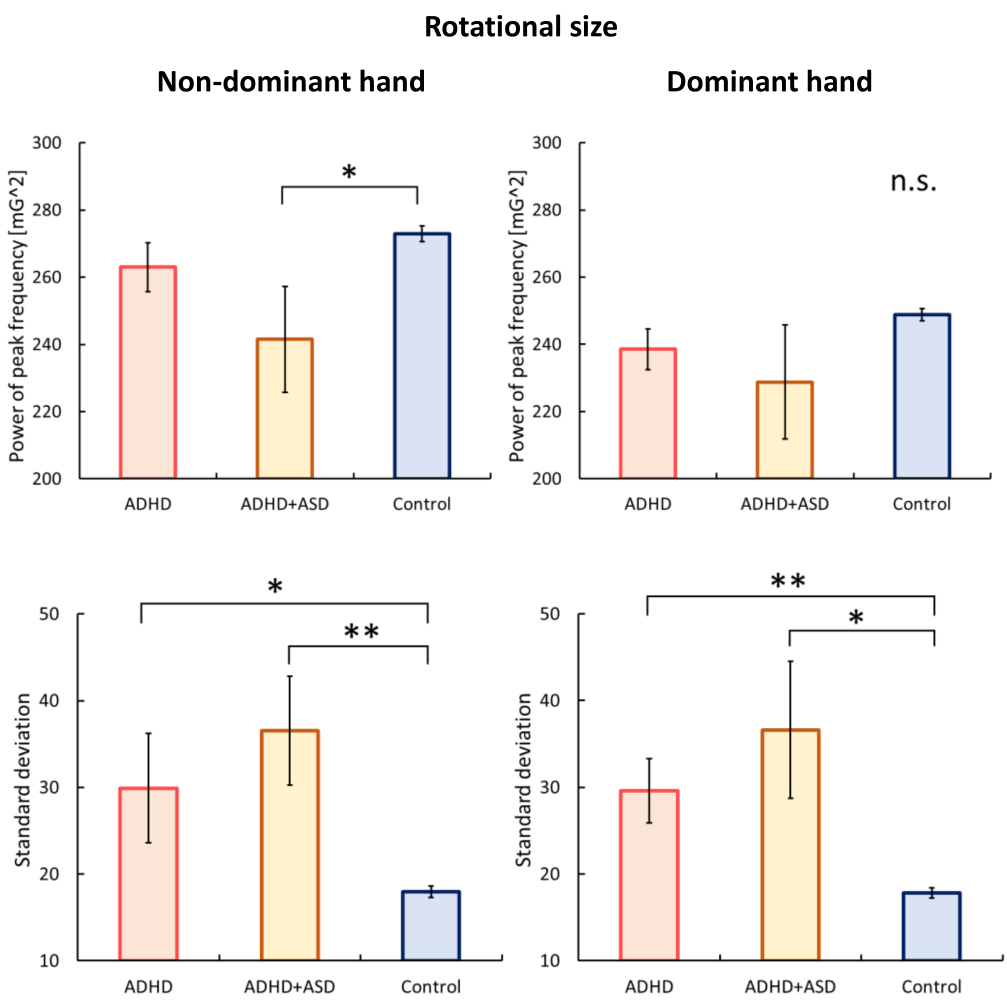

Figure 4-11. Rotational size for children with ADHD only, children with ADHD and ASD, and TD children (control). The participants in all groups are 7 to 11 years old. The upper figures show the average of rotational size in each group. The lower figures show the variance of rotational size in each group. (*: $p < 0.05$, **: $p < 0.01$)

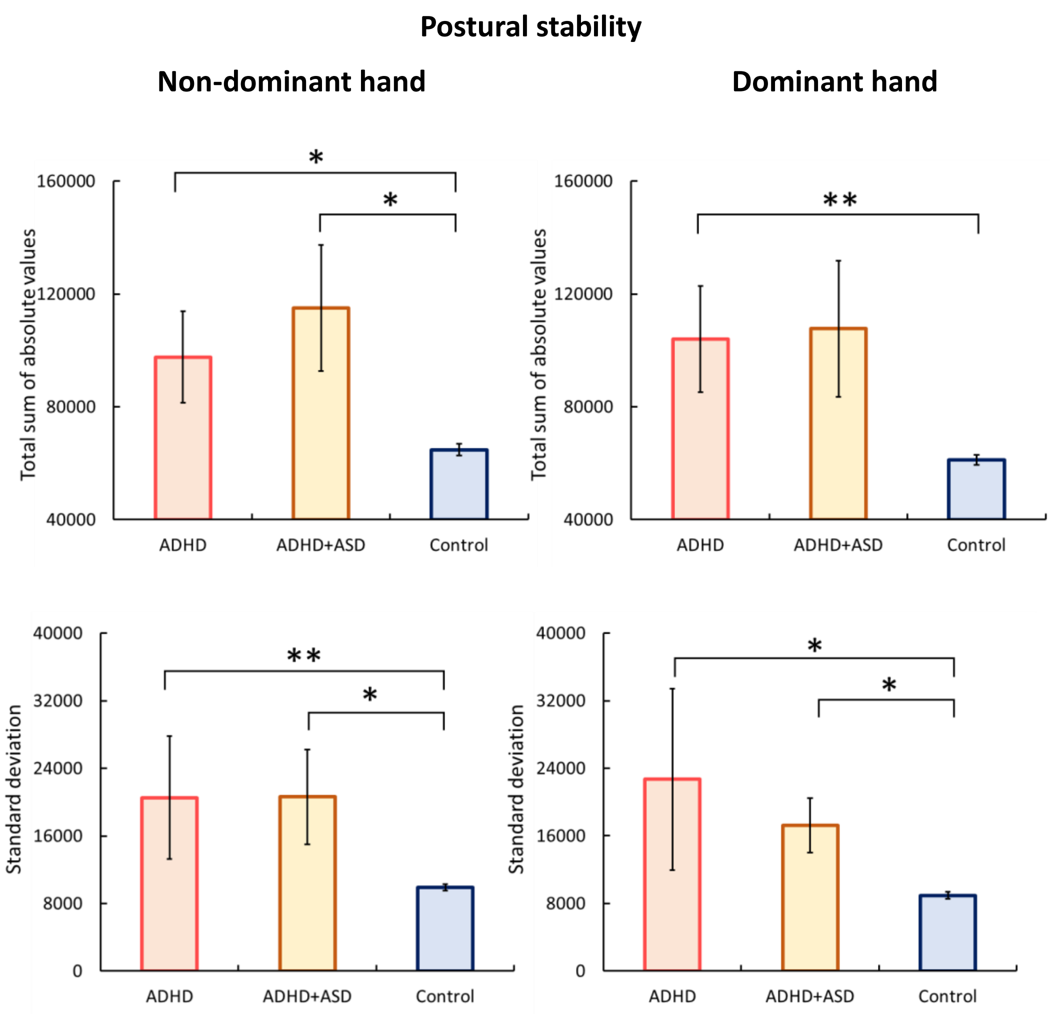

Figure 4-12. Postural stability for children with ADHD only, children with ADHD and ASD, and TD children (control). The participants in all groups are 7 to 11 years old. The upper figures show the average of postural stability in each group. The lower figures show the variance of postural stability in each group. (*: $p < 0.05$, **: $p < 0.01$)

4.3.3.3 Radar chart

We could obtain several outcome measures that significantly differed between ADHD and TD groups, and between ADHD with ASD and TD groups: rotational speed in the dominant hand, associated movement when the task was performed with the non-dominant hand, temporal change of bimanual symmetry, temporal change of rotational size of the dominant hand and non-dominant hand, postural stability of the non-dominant hand, temporal change of postural stability of the non-dominant hand and dominant hand, compliance of the non-dominant hand, temporal change of compliance of non-dominant hand. To allow comparison with the characteristic of these outcome measure for pronation and supination across the three groups: TD, ADHD, ADHD with ASD groups, we normalized the outcome measures using the following formula:

$$y_h = 50 + \frac{20}{\sigma_a}(-x_h + \mu_a)$$

This is based on the formula for calculating T-scores. x_h is the non-normalized score, and μ_a and σ_a are the mean and standard deviation of the outcome measure across all participants. As shown in the formula, the mean value of all participants was set to 50 points and the score range for all participants was set 0–100 points. A normalized score was calculated for each outcome measure and the normalized scores were averaged across all outcome measures to create a single score for each participant.

Radar charts for pronation and supination of TD, ADHD, and ADHD with ASD groups are shown in Figure 4-13. The size of the radar chart in children with ADHD was smaller than that of same-age TD children. The radar chart of children with ADHD was also unbalanced than that of same-age TD children.

Radar charts for pronation and supination of TD children aged 4 to 11 years old, children with ADHD aged 7 to 11 years old are shown in the left and right panels of Figure 4-14, respectively. Children are categorized by age: 4 to 6 years old (upper), 7 to 9 years old (middle), 10 and 11 years old (lower). In TD children, the balance of the quantitative score for each outcome measure improved with age. The size of the radar chart in children with ADHD was smaller than that of same-age TD children. These results indicate a tendency for pronation and supination movement to develop later in children with ADHD, compared to their TD counterparts. Indeed, pronation and supination movement in children with ADHD was comparable to that of younger TD children.

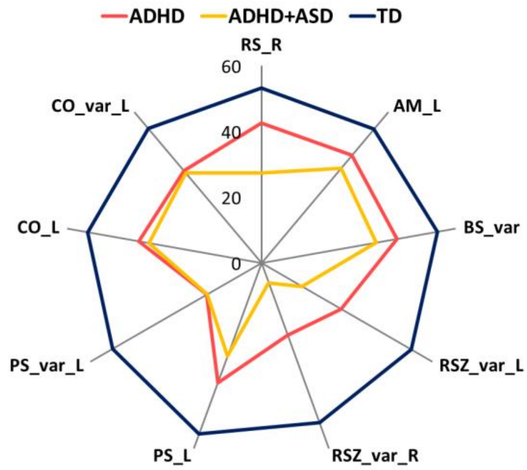

Figure 4-13. A radar chart summarizing all pronation and supination outcome measures in TD children (blue), children with ADHD only (red), and children with ADHD and ASD (yellow). RS: Rotational speed, AM: associated movement, BS: bimanual symmetry, RSZ: rotational size, CO: compliance, PS: postural stability. “var” means variance of the parameter . “L” and “R” indicate left (non-dominant) hand and right (dominant) hand, respectively. There are significant difference in all parameters between TD children and children with ADHD.

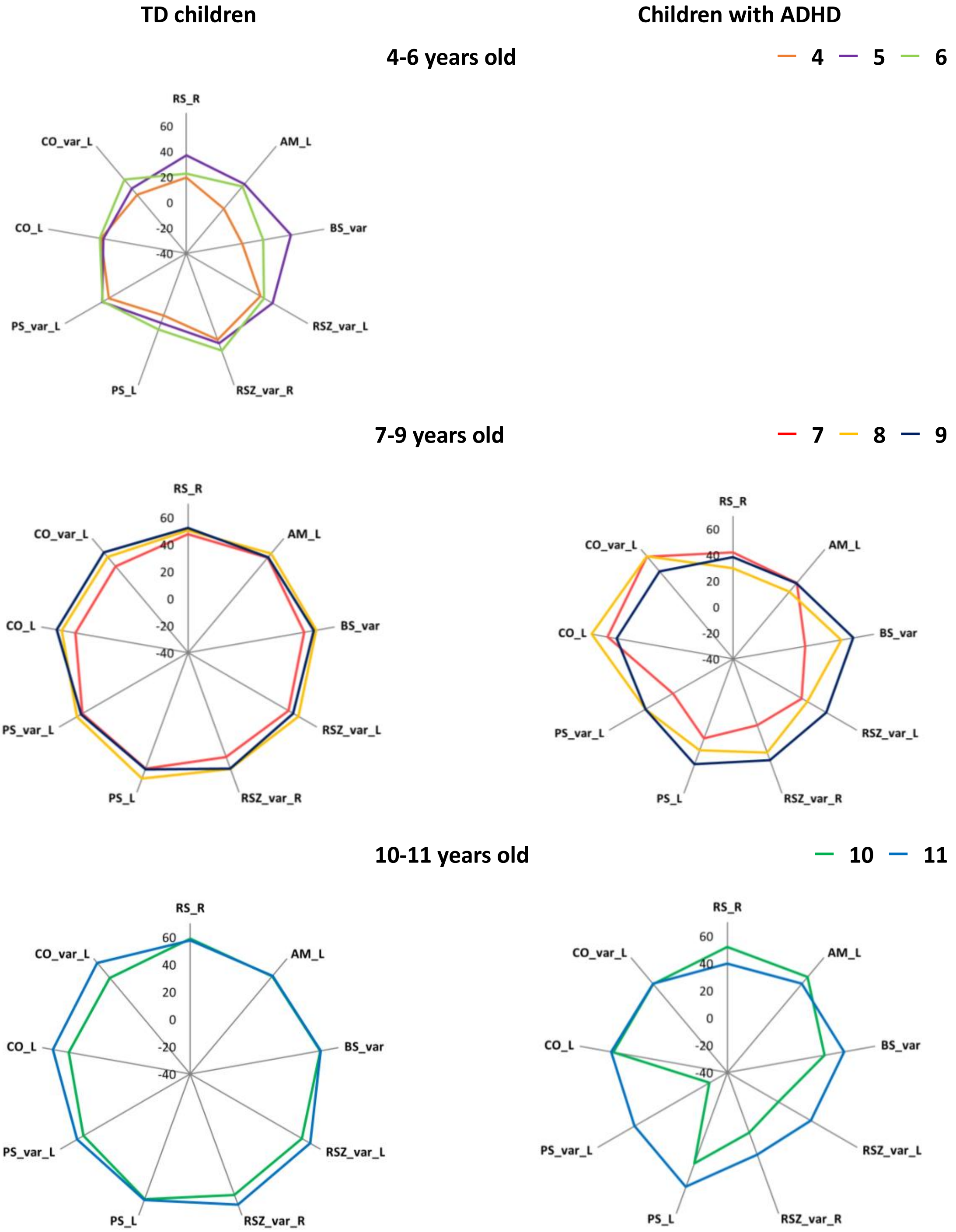

Figure 4-14. Radar charts summarizing all pronation and supination outcome measures in TD children and children with ADHD grouped by age. Charts on the left are of TD children, and charts on the right are of children with ADHD. Top row shows the radar chart of children aged from 4 to 6 years old, middle row shows the radar charts of children aged from 7 to 9 years old, and bottom row shows the radar charts of children aged 10 to 11 years old.

4.4 Discussion

The results of Chapter 3 indicated that the performance of pronation and supination improved with age in TD children. These results are consistent with the result of previous research and the conventional assessment criteria. In this chapter, we compared the performance of pronation and supination between children with ADHD and TD children.

The rotational speed of children with ADHD became faster as they grew older. For the dominant hand, rotational speed was slower in children with ADHD than in TD children. For the non-dominant hand, there was no difference between children with ADHD and TD children. These results indicate that rotational speed in the dominant hand develops slower in children with ADHD than in TD children.

We found a significant difference in associated movement between children with ADHD and TD children. It is generally assumed that the associated movement of the dominant hand when the participant performs the maximal effort motor with non-dominant hand is larger than that of the non-dominant hand when the participant performs the maximal effort motor with dominant hand (Touwen & Prechtl, 1970; Hadders-Algra, 2010). Our result also indicate that the associated movement of the dominant hand was slightly greater than that of the non-dominant hand. These results are consistent with the result of previous research.

There was no significant difference with age for the elbow excursion. This may be due to inter-individual differences in the magnitude of associated movement of the elbow, which were large in children of kindergarten age and in the early school years (Largo et al., 2003; Hadders-Algra, 2010).

It is difficult for children with a developmental disorder to produce coordinated movements (Gillberg, 1998; Piek et al., 1999). Our results indicated that bimanual symmetry was lower in children with ADHD in the imitative motor task than in TD children and, there was a significant difference between TD children and children with ADHD. In our results, there was significant differences between TD children and children with ADHD in compliance. Our results indicated that compliance in children with ADHD was not smoothly for each outcome measure. It is difficult for children with a developmental disorder to move smoothly (Rinehart et al., 2006). Our results are consistent with the previous study.

For several outcome measures, there was no relation of the outcome measure to age in children with ADHD. It is thought that one of the reasons for this is the fact that we have not tested whether our proposed method can be used to distinguish children with ADHD from children with other developmental disorders in this experiment. Previous studies have reported differences in response times and evaluation scores for pronation and supination between TD children and several developmental disorders, including ADHD (Patankar et al., 2012; Fewell & Deutscher, 2002; Uslu, et al., 2007; Pineda, et al., 1999; Gonga et al, 2015; Kroes, et al., 2002; Williams et al., 2013; Pitcher et al., 2003), learning disorder (Adams et al., 1974), ASD (De Jong et al., 2011; Williams et al., 2006), and developmental coordination disorder (Williams et al., 2013; Wilmut et al, 2006; Freitag et al., 2007; Ghaziuddin et al.,1992; Ghaziuddin et al., 1994; Slater et al., 2010). Moreover, Pitcher et al. reported that a moto ability of children with ADHD and developmental coordination disorder was lower than that of children with ADHD only in fine motor task of SNS (Pitcher et al., 2003). These studies indicate that the performance of pronation and supination may be influenced not only by age but also by comorbid disorders. It is necessary to consider how our measures of pronation and supination are influenced by developmental disorders other than ADHD, because our aim is to establish a quantitative evaluation method for the differential diagnosis of ADHD. To this end, we compared three groups: children with ADHD only, children with ADHD and ASD, and TD children. We found a significant difference in rotational speed in the dominant hand, associated movement when the task was performed with the non-dominant hand, temporal change of bimanual symmetry, temporal change of rotational size of the dominant hand and non-dominant hand, postural stability of the non-dominant hand, temporal change of postural stability of the non-dominant hand and dominant hand, compliance of the non-dominant hand, temporal change of compliance of non-dominant hand. These results indicate that these parameters may be able to differentially diagnose ADHD.

We also examined the function’s balance between these outcome measures. The radar charts showed that the balance among these outcome measures improved with age.

The size of the radar chart in children with ADHD was smaller than that in TD children of the same age, and was similar to that in TD children of a younger age. These results indicated a tendency for pronation and supination to develop later in children with ADHD, compared to their TD counterparts. Indeed, pronation and supination movement in children with ADHD was comparable to that of younger TD children. Previous studies have reported that the cortical development of children with ADHD lags behind that of TD children by several years (Landgren & Gillberg, 2000). Our results are consistent with these reports, and show that our system and proposed outcome measures may be suitable as quantitative criteria to evaluate developmental delays in neurological function in children with ADHD.

In this chapter, we have reported the performance of pronation and supination in children with ADHD. However, the number of participants was not large enough to compare pronation and supination between ADHD and other developmental disorders. Future studies need to include more participants to accomplish this aim. Children with ADHD usually have multiple problems such as motor coordination, learning, and cognition. SNS is one method for evaluating children with ADHD. Therefore we also need to consider the correlation between the function of pronation and supination, and the Developmental Coordination Disorder Questionnaire (Wilson et al., 2000) used for the screening developmental coordination disorders, severity, subtypes of ADHD and so on.

4.5 Conclusion

In this study, we quantified pronation and supination in children with ADHD. A comparison of these participants to the TD children reported in Chapter 3 revealed that the development of pronation and supination by children with ADHD has a tendency to lag behind that by TD children by several years.

Moreover, children with ADHD were split into two groups: ADHD only and comorbid ADHD and autism spectrum disorder (ASD) to establish a quantitative evaluation method for the differential diagnosis of ADHD. We found a significant difference in several measure outcomes (especially measurement outcomes of non-dominant hand and temporal change). The radar charts showed that the balance between these outcome measures improved with age. The size of the radar chart in children with ADHD was smaller than that in TD children of the same age. These results indicated a tendency for pronation and supination to develop later in children with ADHD, compared to their TD counterparts. Indeed, pronation and supination movement in children with ADHD was comparable to that of younger TD children.

In conclusion, our system can be used to evaluate the neurodevelopmental delay of children with ADHD.

Chapter 5. General Discussion

We have proposed a quantitative evaluation system for ADHD that uses acceleration and angular velocity sensors. Several previous studies have proposed quantitative evaluations of pronation and supination, but the proposed systems are difficult to use in children, particularly children with ADHD (Kreulen et al., 2004; Okada & Okada, 1983; Hermsdörfer & Goldenberg, 2002). The system proposed in this thesis is comprised of small wireless sensors and is suitable for use in children.

In Chapter 2, we proposed parameters to quantify pronation and supination: rotational speed, associated movement, elbow excursion, bimanual symmetry, and compliance. These parameters were selected based on the conventional assessment of pronation and supination. Comparison between a combined score from all of these parameters and a visual assessment score assigned by pediatricians revealed a high correlation between our score and the visual assessment score assigned by pediatricians with many years experience.

In Chapter 3, we used our system to quantify pronation and supination in TD children. We found that rotational speed was around 2 Hz in TD children aged 4-5 years old, gradually increased from 2 Hz to 3.5 Hz in TD children aged 6–10 years old, and was stable after the age of 10 years. Previous studies have reported progressive improvement of motor speed between the ages of 5 to 10 years (Gasser et al, 2007; Gasser et al, 2010), and the current evaluation categories for motor speed are slow (1–2 Hz), medium (2–3 Hz), and fast (3–4 Hz). Developments in motor speed occur as children become older, with children in the slow group aged 4–5 years, children in the medium group aged 6–10 years, and children in the fast group aged over 10 years (Hadders-Algra, 2010). Our results for rotational speed are therefore consistent with previous studies and existing evaluation categories and provide more detail of the developmental changes.

The associated movement rapidly decreased from the ages of 4 to 6 years and then gradually decreased until the age of 12 years. Previous studies have also reported that associated movement gradually decreases with age (Patankar et al., 2012; Connolly and Stratton, 1968; Lazarus and Todor, 1987; Gasser, 2007; Gasser, 2010). These studies reported that associated movement became evident between the ages of 4 and 6 years, decreased between the ages of 7 and 11 years, and was generally not observed after the age of 12 years (Touwen & Prechtl, 1970; Largo et al., 2001b). There was a significant difference among the three developmental stages. Our results for associated movement are therefore consistent with previous studies.

Previous studies reported that elbow excursion was over 15 cm at 4–5 years of age; at 6–7 years of age, excursion was 5–15 cm; and after 8 years of age, excursion was under 5 cm (Hadders-Algra, 2010).We found that elbow excursion had a tendency to decrease between the ages of 4 to 7 years and stabilize after the age of 8 years. Our results are consistent with this previous study. However, there was no significant difference with age for the elbow excursion of the dominant hand. This may be due to inter-individual differences in the magnitude of associated movement of the elbow, which were large in children of kindergarten age and in the early school years (Largo et al., 2003; Hadders-Algra, 2010).

For the novel measure of bimanual symmetry in the imitative motor task we reported the developmental change observed in TD children. In our results, bimanual symmetry did not change between the ages of 4 and 6 years, gradually improved between the ages of 6 and 8 years, and stabilized after the age of 8 years. In previous studies, developmental changes in bimanual symmetry during drawing and circle performance have been reported between the ages of 4 and 12 years, and the bimanual symmetry of 4- and 5-year olds during drawing was inferior to that of children aged 6 years and older (Van Mier, 2006; Hadders-Algra, 2010). Our results are consistent with this study and obtained a significant difference between the two developmental stages.

We also reported the developmental change in compliance in the imitative motor task. Compliance improved between the ages of 4 and 7 years and stabilized after the age of 7 years and obtained a significant difference between the two groups. In a previous study of a follow-a-finger test in which compliance was quantified by visual observation, compliance of 4- and 5-year olds was lower than that of children aged 6 years and older (Hadders-Algra, 2010). Our results are therefore consistent with previous developmental studies and provide more detail of the developmental changes that occur after the age of 6 years.

Overall, the results of Chapters 2 and 3 indicate that it may be possible to use our system to obtain quantitative data to evaluate the development of neurological function.

In Chapter 4, we compared the performance of pronation and supination between children with ADHD and TD children. Rotational speed was slower in children with ADHD than in TD children. The dominant hand of TD children develops faster than that of children with ADHD. These results indicate that rotational speed in the dominant hand develops slower in children with ADHD than in TD children. In children with ADHD, associated movement decreased with age, as it did in TD children, but it was greater than in children with ADHD than TD children of the same age in our results. It is generally assumed that the associated movement of the dominant hand when the participant performs the maximal effort motor with non-dominant hand is larger than that of the non-dominant hand when the participant performs the maximal effort motor with dominant hand (Touwen & Prechtl, 1970; Hadders-Algra, 2010). In our results, the associated movement of the dominant hand also became smaller than that of the non-dominant hand as the children. These results are consistent with the result of previous research.

It is difficult for children with a developmental disorder to produce smooth and coordinated movements (Rinehart et al., 2006; Gillberg, 1998; Piek et al., 1999). Our results also indicated that bimanual symmetry and compliance were lower in children with ADHD than in TD children and, there was a significant difference between TD children and children with ADHD.

We compared three groups: children with ADHD only, children with ADHD and

ASD, and TD children to compare pronation and supination between ADHD and other developmental disorders. From our results, we found a significant difference in several outcome measurements (especially measurement outcomes of non-dominant hand and temporal change). The balance of these outcome measures in children with ADHD was smaller than that in TD children of the same age, and was similar to that in TD children of a younger age. These results indicate a tendency for pronation and supination to develop later in children with ADHD, compared to their TD counterparts. Indeed, pronation and supination movement in children with ADHD was comparable to that of younger TD children. Previous studies have reported that the cortical development of children with ADHD lags behind that of TD children by several years (Landgren & Gillberg, 2000). Our results show that our system and proposed outcome measures may be suitable as quantitative criteria to evaluate developmental delays in neurological function in children with ADHD.

We propose that pronation and supination may be associated not only with age, but also with ADHD, and that our quantitative measures of pronation and supination may be useful as an assessment method for ADHD. We found significant differences in rotational speed in the dominant hand, associated movement when the task was performed with the non-dominant hand, temporal change of bimanual symmetry, temporal change of rotational size of the dominant hand and non-dominant hand, postural stability of the non-dominant hand, temporal change of postural stability of the non-dominant hand and dominant hand, compliance of the non-dominant hand, temporal change of compliance of non-dominant hand between children with ADHD, children with ADHD and ASD, and TD children. These results indicate that these outcome measures were sensitive to characteristics of ADHD and these parameters may be able to differentially diagnose ADHD.

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