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Novel Methods to Evaluate Symptoms in Parkinson's Disease – Rigidity and Finger Tapping

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1. Introduction

Parkinsonian symptoms such as tremor, rigidity, akinesia, and postural instability are perceived subjectively, and therefore understanding the degree of the symptoms varies depending on the neurologist. Sensing technologies and computer science have advanced and can now detect neurological symptoms and the detected data can be analyzed by software and described in a similar manner to how neurologists perceive those symptoms. This chapter discusses two popular neurological examinations in Parkinson's disease (PD); one is rigidity, which is representative of passive movement, and the other is finger tapping, which is representative of active movement.

Rigidity, a well known symptom of PD, is defined as increased muscle tone that is elicited when an examiner moves the patient's limbs, neck, or trunk, and this increased resistance to passive movement is equal in all directions (Fahn & Przedborski 2005). Many researchers have analyzed rigidity by applying biomedical engineering principles and electrophysiological techniques (Fung et al. 2000, Prochazka et al. 1997, Teravainen et al. 1989). However, we do not know exactly what we feel in muscle tone in PD.

Finger tapping, one of The Unified Parkinson's Disease Rating Scale (UPDRS) items, is commonly used in daily neurological examinations. Its evaluation includes velocity, amplitude, and rhythm. However, observation of these is subjective.

To evaluate rigidity and finger tapping, it is necessary to sense muscle tone and finger movement. We have previously developed novel methods to evaluate rigidity and finger tapping (Endo et al. 2009, Kandori et al., 2004). In this chapter, we showed the usefulness of these systems as objective markers of treatment.

2. Evaluating the effects of deep brain stimulation on rigidity and finger tapping

We evaluated the effects of deep brain stimulation (DBS) of the subthalamic nucleus (STN) on rigidity and finger tapping using our measuring materials. The preceded study of the

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effects of STN-DBS revealed that rigidity responded immediately upon tuning DBS, while improvement of finger tapping needed longer time to manifest after tuning DBS. Thus, we analyzed Parkinsonian rigidity by comparing the DBS on state to the DBS off state and finger tapping by comparing pre-operation DBS to post-operation DBS in this study.

2.1 Subjects

Five patients in whom PD was diagnosed according to British Brain Bank clinical criteria (Gibb & Lees 1988) and who received STN-DBS were included in this study. Clinical details of patients with PD who participated in rigidity analysis are shown in Table 1, and those in finger tapping are shown in Table 2. Prior to measurement, patients with PD were assessed using the UPDRS Part III. In this examination, rigidity was scored using a five-point scale (0 = no rigidity, 1 = slight or detectable only when activated, 2 = mild to moderate, 3 = marked, and 4 = severe), and finger-tapping was also scored using the five-point scale (0 = normal; 1 = mild slowing and/or reduction in amplitude; 2 = moderately impaired, definite and early fatiguing, may have occasional arrests in movement; 3 = severely impaired, frequent hesitation in initiating movements or arrests in ongoing movement; and 4 = can barely perform the task). This study was approved by the Institutional Review Board of Osaka University Hospital and written informed consent was obtained from all subjects.

	Age (y)	Sex	Disease duration (y)	Duration after DBS	UPDRS score		
					Part III (*on)	Rigidity (Right)	Rigidity (Left)
pd1	73	M	5	One month	28	1/1(*on/off)	1/1(*on/off)
pd2	70	F	13	One month	8	1/2	1/1
pd3	60	F	11	One year	59	2/3	2/2
pd4	63	F	18	6 years	40	1/2	1/1
pd5	72	F	29	5 years	29	1/1	1/1

Table 1. Clinical details of patients who participated in rigidity analysis. * on/off; DBS-on/off

	Age (y)	Sex	Handed	Initially affected site	Evaluation interval between pre and post (month)	UPDRS PartIII		UPDRS PartIII Finger-tapping score	
						Pre	Post	Pre (L/R)	Post (L/R)
PD1	67	M	Right	Left	3	49	29	3/2	2/1
PD2	69	F	Right	Right	1	26	8	1/2	1/1
PD3	69	M	Right	Right	2	24	17	1/2	1/1
PD4	62	F	Right	Right	1	40	20	2/2	1/1
PD5	73	F	Right	Left	1	34	29	2/1	1/1

Table 2. Clinical details of patients who participated in finger tapping analysis

2.2 Sensing methods
2.2.1 Muscle tonus measurement device

Figure 1 shows a schematic diagram of the muscle tonus measurement system. Details of the device were described in a previous report (Endo et al. 2009). Briefly, elbow joint torque was estimated using the force along the Z-axis and the longitudinal length of the forearm. The elbow joint angle was calculated from the signal generated by the gyroscope. The EMG activity was recorded from surface electrodes attached to the *biceps brachii* and *triceps brachii*.
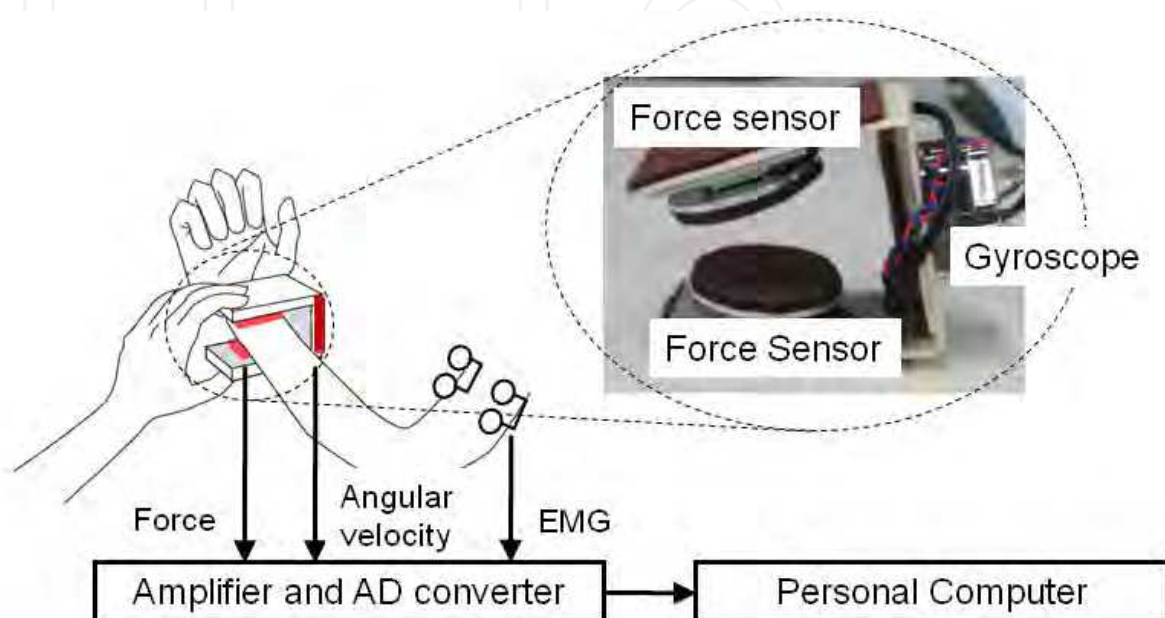
Fig. 1. Schematic diagram of the muscle tonus measurement system

2.2.2 Finger tapping measurement system

The basic method for sensing finger tap movement has been described previously (Kandori et al. 2003, Shima et al. 2008). The finger-tapping measurement system used in this study is shown in Figure 2. A magnetic sensor consisting of two coils is used to measure finger-tapping movement. The coil voltage depending on the distance between the two coils enables estimation of the distance between two fingertips. We calculated the rhythm, amplitude, and velocity of the finger-tapping movement.

2.3 Protocols
2.3.1 Protocols for measuring rigidity

Each subject with DBS-on state or DBS-off state was instructed to relax in a sitting position; the examiner applied the measuring device to the wrist joint of the subject and practiced passive flexion and extension movements at the elbow joint. The measurement of DBS-off state started at 1 min after DBS was turned off. The measurement was made by repeating the four phases of movement as described in a previous report (Endo et al. 2009): (1) holding the elbow at maximum extension for at least 3 s (Fig. 3A), (2) passive flexion for 2 s, (3) holding the elbow at maximum flexion for at least 3 s (Fig. 3B), and (4) passive extension for 2 s (ramp-and-hold). This measurement was repeated twice for each of the left and right upper limbs and the resulting values were averaged on each side independently. Two measurements each for left and right upper limbs were obtained per subject.
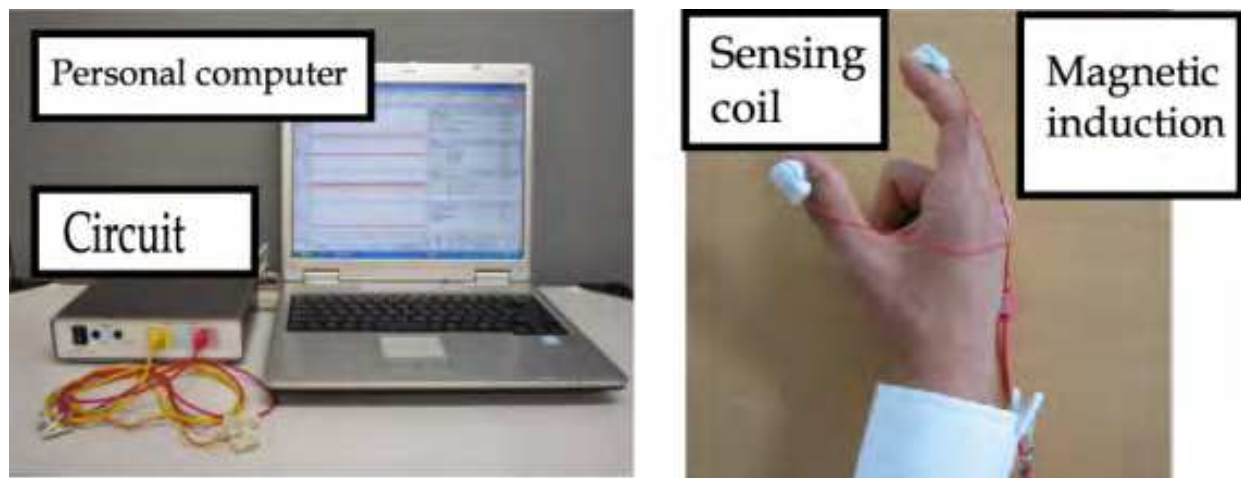
Fig. 2. Finger-tapping measurement system

Figure 4A and Figure 5A shows the typical longitudinal data extracted from the right upper limb of patient pd3 in Table 1 with a UPDRS rigidity score of 2/3 (DBS-on/off). Figure 4A represents the DBS-off state and Figure 5A represents the DBS-on state. Torque-angle characteristics in passive flexion and passive extension are also shown in Figure 4B (DBS-off state) and Figure 5B (DBS-on state).

2.3.2 Protocols for measuring finger tapping
Five patients with PD were evaluated 1 week before and 3 to 5 months after surgery. The magnetic sensors were worn on the subject's index finger and thumb. The subject practiced the finger tapping movement for about 10 s. The subject was asked to execute the finger tapping movements as quickly and widely as possible for 15 s. The finger-tapping wave of patient PD1 before and after intervention is shown in Figure 6.

2.4 Data analysis
2.4.1 Data analysis for rigidity
The resulting data were analyzed by extracting features from elbow joint torque-angle characteristics during passive flexion and extension as shown in Figure 7. The features used here were elastic coefficients in extension and flexion and the sum of the differences of averaged torque values. These were calculated as follows: for the elastic coefficients, the slopes of the regression lines for both flexion and extension were estimated based on the torque-angle data. The data from the start point to the last maximal extension phase were used to calculate the elastic coefficient, which included four to five cycles. At this time, torque values were adjusted for gravity using the mass of the forearms and hands as estimated from the subject's body weight (de Leva 1996). For the sum of the differences of averaged torque values, first we averaged the flexion torque values across four trials at a certain joint angle and also averaged the extension torque values similarly. Then, the differences of the averaged torque values at 30°, 60°, and 90° were calculated and the resulting values were summed.

These three features, that is, the elastic coefficients in extension and flexion and the sum of the differences of averaged torque values, were normalized using the mass of the subject's body weight, because these are dependent on the subject's muscle mass.
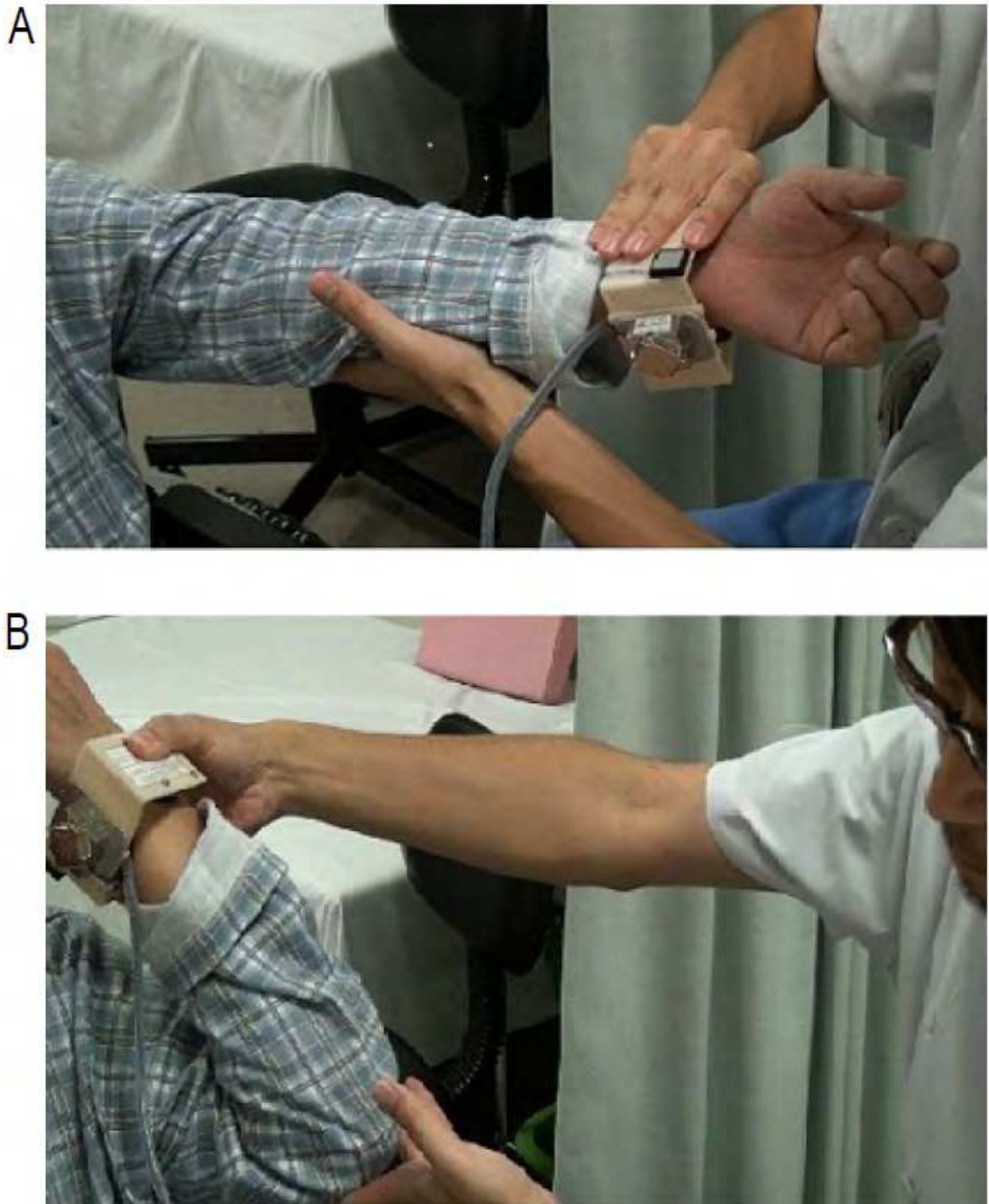
Fig. 3. Measuring protocol. A: holding the elbow at maximum extension. B: holding the elbow at maximum flexion
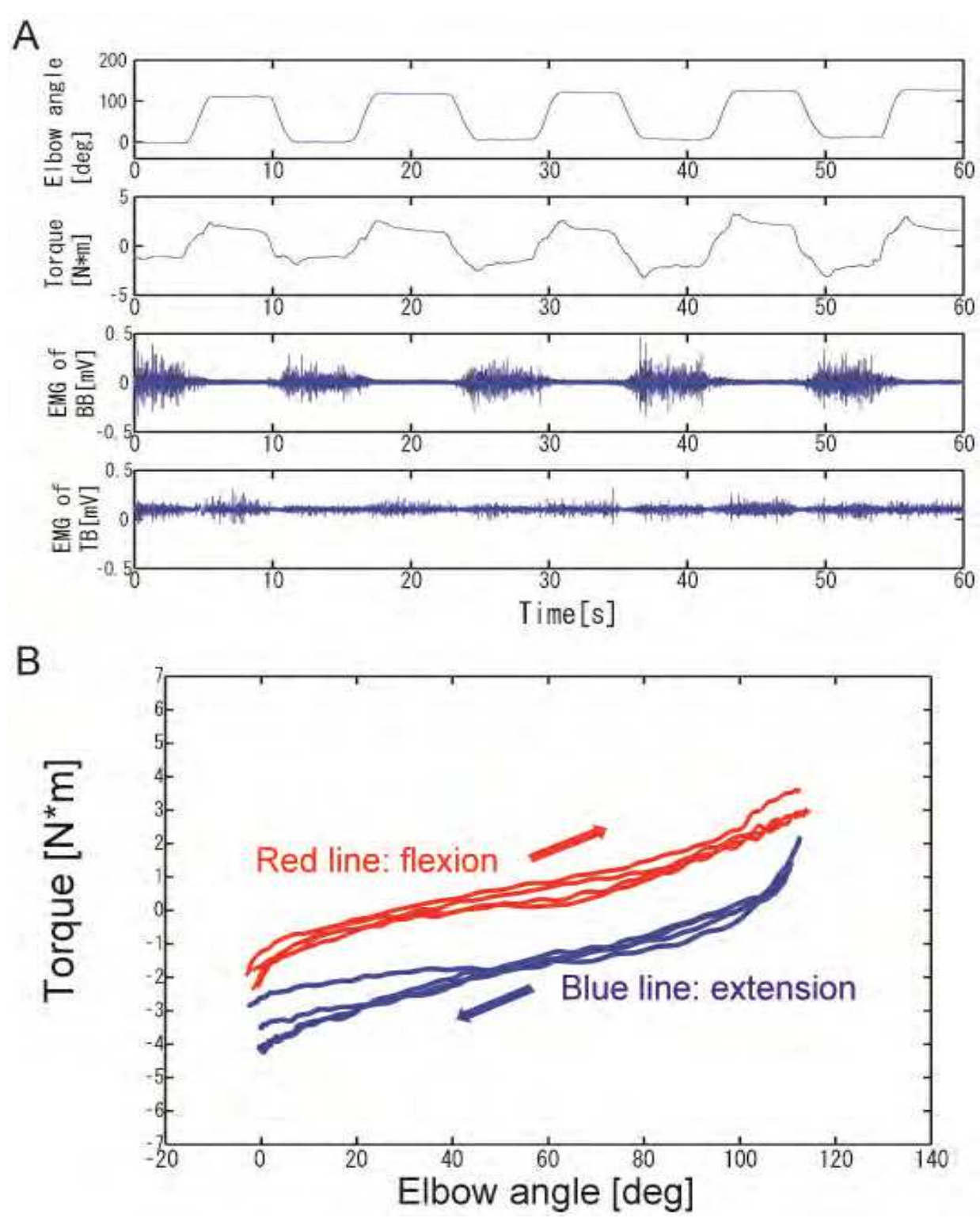
Fig. 4. Typical longitudinal data (A) and torque-angle characteristics (B) in passive flexion and passive extension (DBS-off state) obtained from the right upper limb of patient pd3 with UPDRS rigidity score 3.
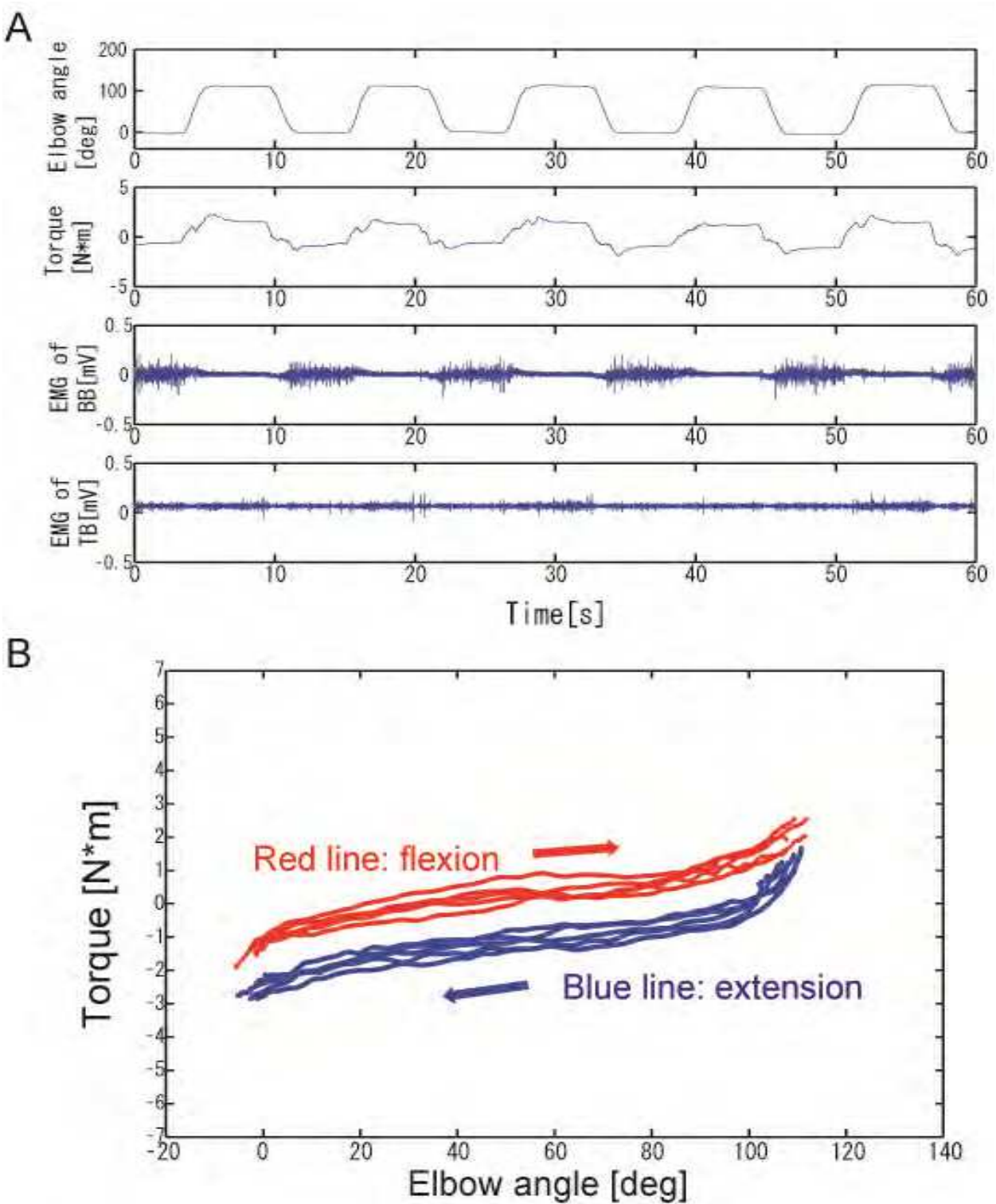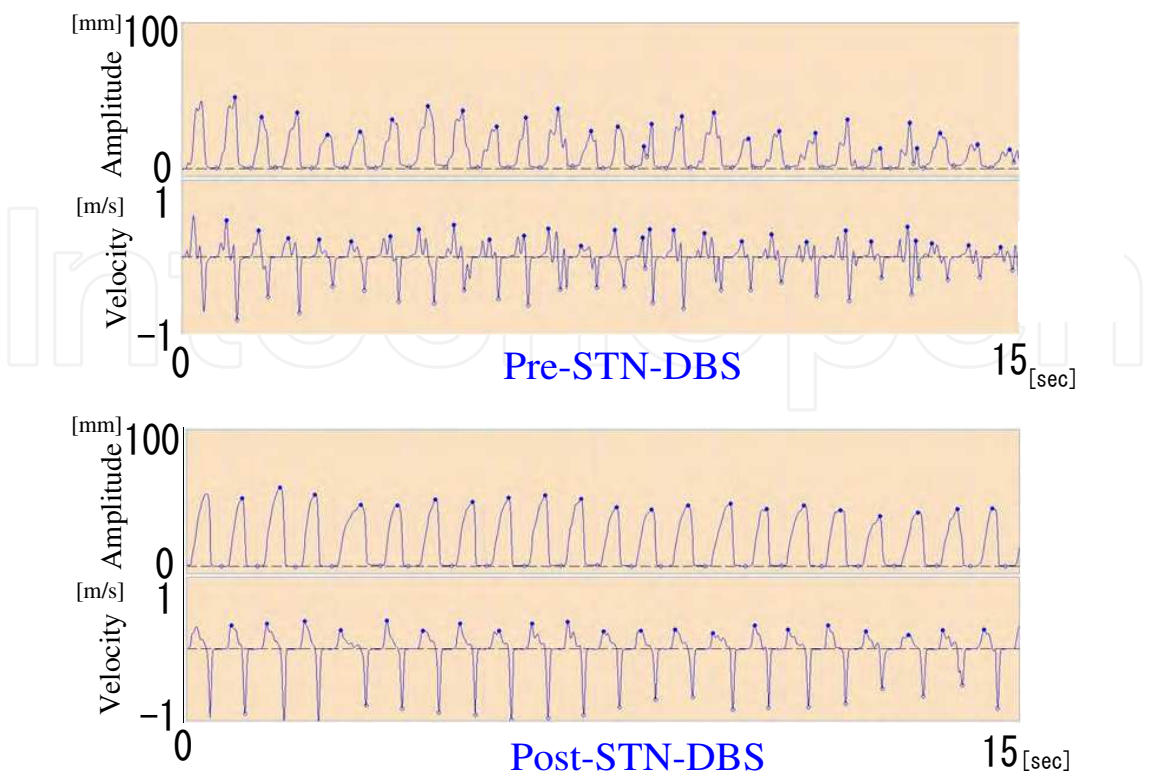
Fig. 5. Typical longitudinal data (A) and torque-angle characteristics (B) in passive flexion and passive extension (DBS-on state) obtained from the right upper limb of patient pd3 with UPDRS rigidity score 2.

Fig. 6. The finger-tapping wave of patient PD1 before and after intervention
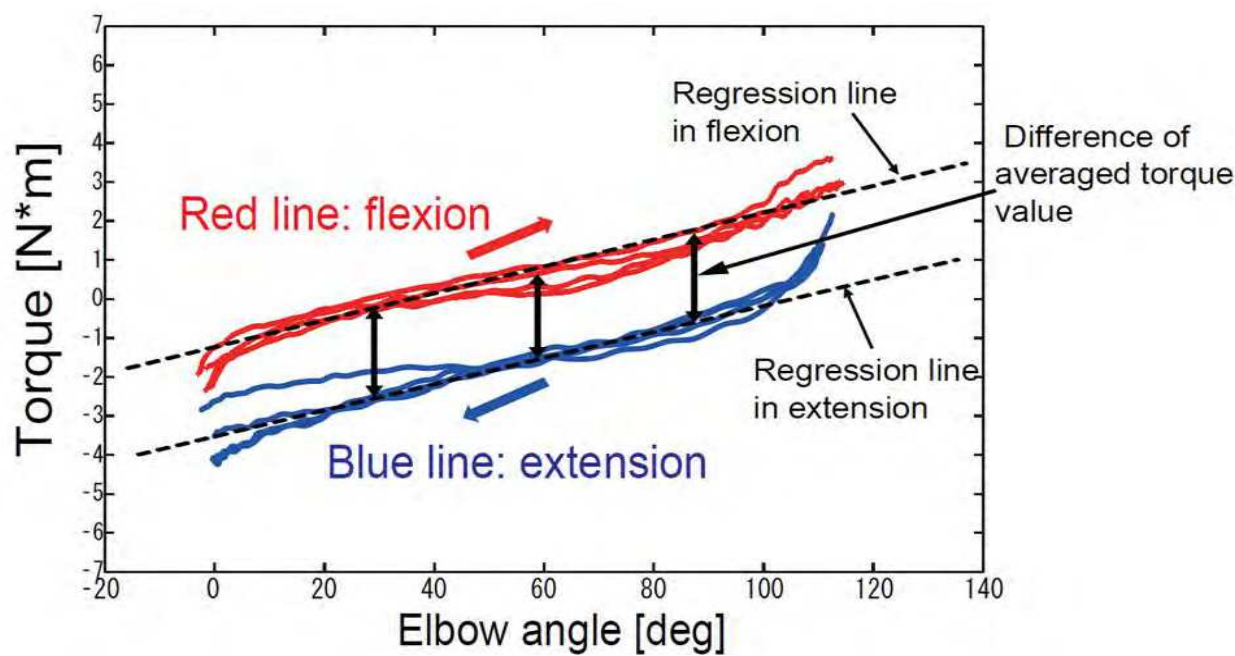
Fig. 7. Extracting features from torque-angle characteristics. Elastic coefficients in flexion and extension were calculated by estimating the slopes of the regression lines for both phases. Differences in the averaged torque values were calculated at 30°, 60°, and 90°.

2.4.2 Data analysis for finger tapping

We statistically analyzed five parameters of repetitive index finger-to-thumb oppositions for 15 seconds (Fig. 8). A single finger-tapping interval (FTI) was defined as the interval between the onset of a finger tap and the onset of the next finger tap. We measured the following: the maximum opening velocity (MoV) in a single finger-tapping movement; the maximum closing velocity (McV) in a single finger-tapping movement; the maximum amplitude (MA) during a single finger-tapping movement; and the standard deviation (SD) of FTI, the index of rhythm as the variation of finger-tapping coordination. The mean MA, MoV, and McV for 15 s were calculated. The frequency was the number of finger taps in 15 s (NFT).
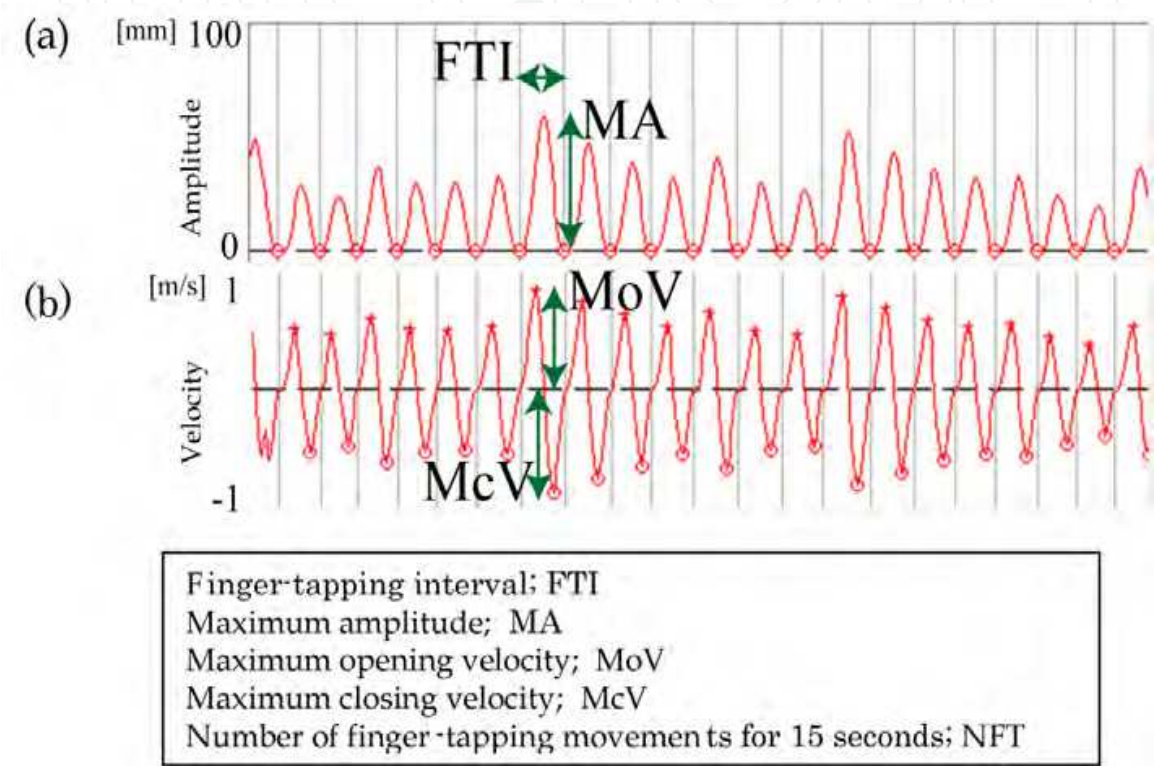
Fig. 8. Measured amplitude and calculated velocity in finger-tapping movement. (a) Measured amplitude, (b) Calculated velocity.

2.5 Results

Rigidity

Using the data obtained from both left and right upper limbs of five patients with PD, 10 data sets on muscle tonus were available for final analysis. The effects of STN-DBS on three parameters are shown in Figures 9, 10, and 11. Age-matched normal values of elastic coefficients in extension and flexion and the sum of the differences of averaged torque values from 20 control subjects were 1.0[N*m/rad*kg], 1.0[N*m/rad*kg], and 1.0[N*m/kg], respectively.

In the arms with a UPDRS rigidity score 2 or 3 in the DBS-off state, DBS-on improved their scores. Figures of elastic coefficients in extension and flexion and the sum of the differences of averaged torque values in this muscle tonus system supported UPDRS rigidity score improvement. In addition, these three parameters also showed improvement even in arms where the UPDRS rigidity scores did not improve in the DBS-on state. This result indicates

that this muscle tonus measuring system is sensitive, objective, and precise. On the other hand, in arms with a UPDRS rigidity score of 1, which is a subtle change in muscle tonus, apparent improvement was not detected using this system. The difference of averaged torque values is the most sensitive among the three parameters.
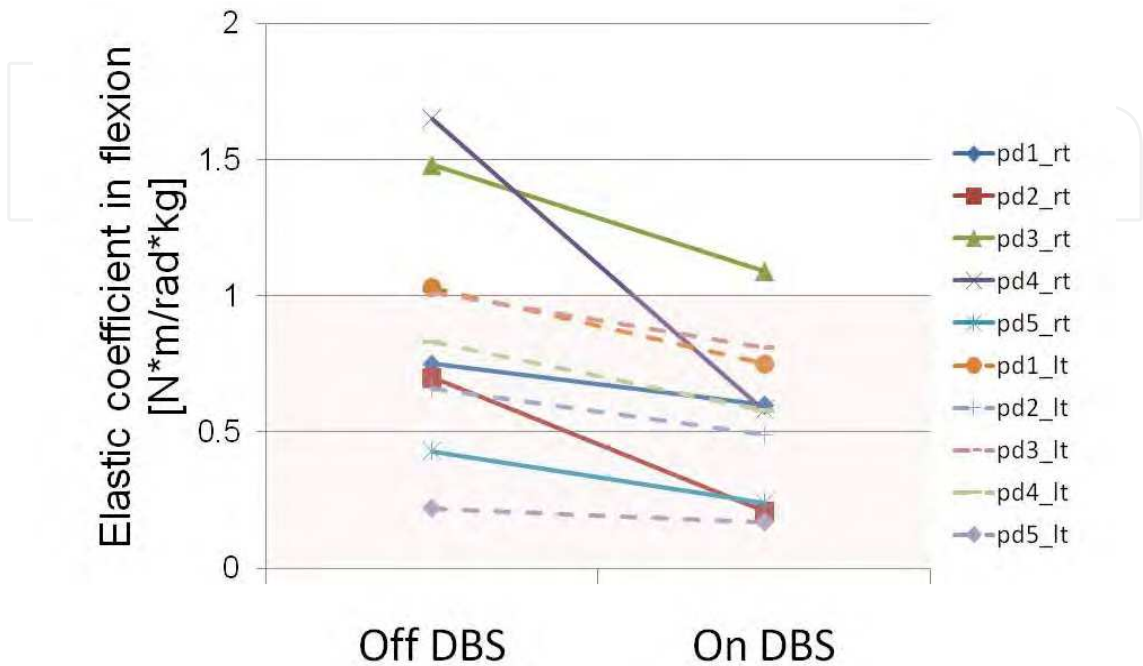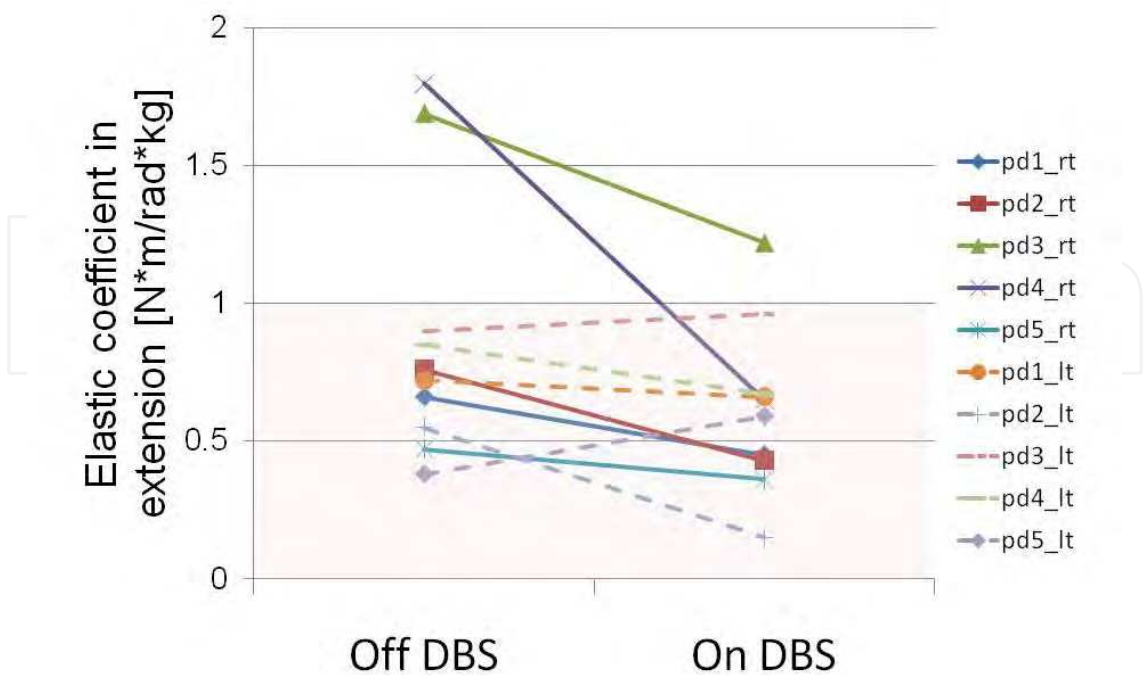

Fig. 9. Effects of deep brain stimulation on the elastic coefficient in flexion. The filled area (less than 1.0[N*m/rad*kg]) represents the normal region.
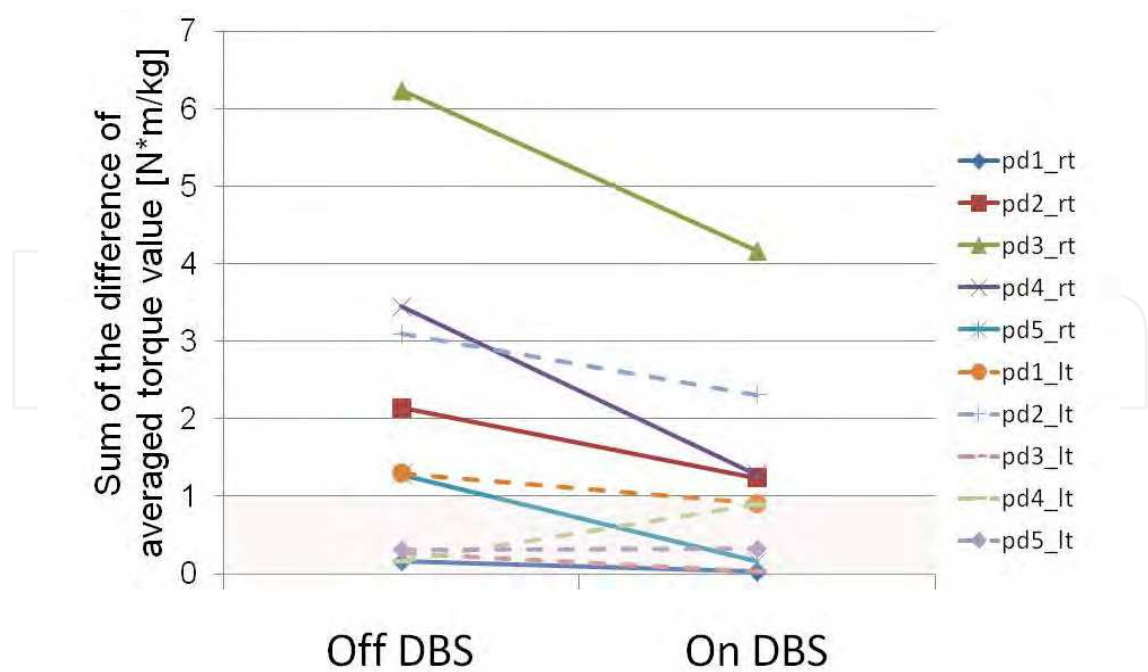

Fig. 10. Effects of deep brain stimulation on the elastic coefficient in extension. The filled area (less than 1.0[N*m/rad*kg]) represents the normal region.

Fig. 11. Effects of deep brain stimulation on the sum of the differences of averaged torque values. The filled area (less than 1.0[N*m/kg]) represents the normal region.

Finger tapping

As shown in Table 2, improvement in UPDRS finger-tapping score after DBS was observed in PD1, PD2, and PD4. The finger-tapping wave of PD1 before and after intervention is shown in Figure 6. Irregular and disordered finger tapping changed to a smooth and correct performance after DBS. This system allows examiners to understand improvement at first sight. In the parameter analysis of finger-tapping movement, all patients with PD showed significant improvement after DBS in three parameters: mean of MoV, mean of McV, and mean of MA. However, it was not necessarily the case that STN-DBS improved the SD of FTI (Fig. 12). In summary, MoV, McV, and MA in PD1, PD2, and PD4 apparently improved, suggesting these are possible treatment markers.

3. Conclusion

We succeeded in showing the effects of DBS on rigidity and finger-tapping movement quantitatively using these instruments. The severity of symptoms obtained by these systems would not show much difference among examiners. Because neurologists could grasp subtle changes after not only DBS but also an increase in drug dose such as dopamine receptor agonists, these instruments would indicate treatment efficacy to neurologists before patients realized the improvement in their symptoms.

In the present analysis, rigidity was quantified by "work", in which the average work was done by the torque motor over one cycle (Shapiro et al. 2007). However, the concept of "work" views the flexion and extension movements as a single system, and strictly speaking, it is different from the sum of the differences of averaged torque values that we extracted. If one repeats sinusoidal flexion and extension movements as a measurement protocol, most features could not be properly evaluated at each phase because the stretch reflex has greater impact when the flexion phase is switched to the extension phase.
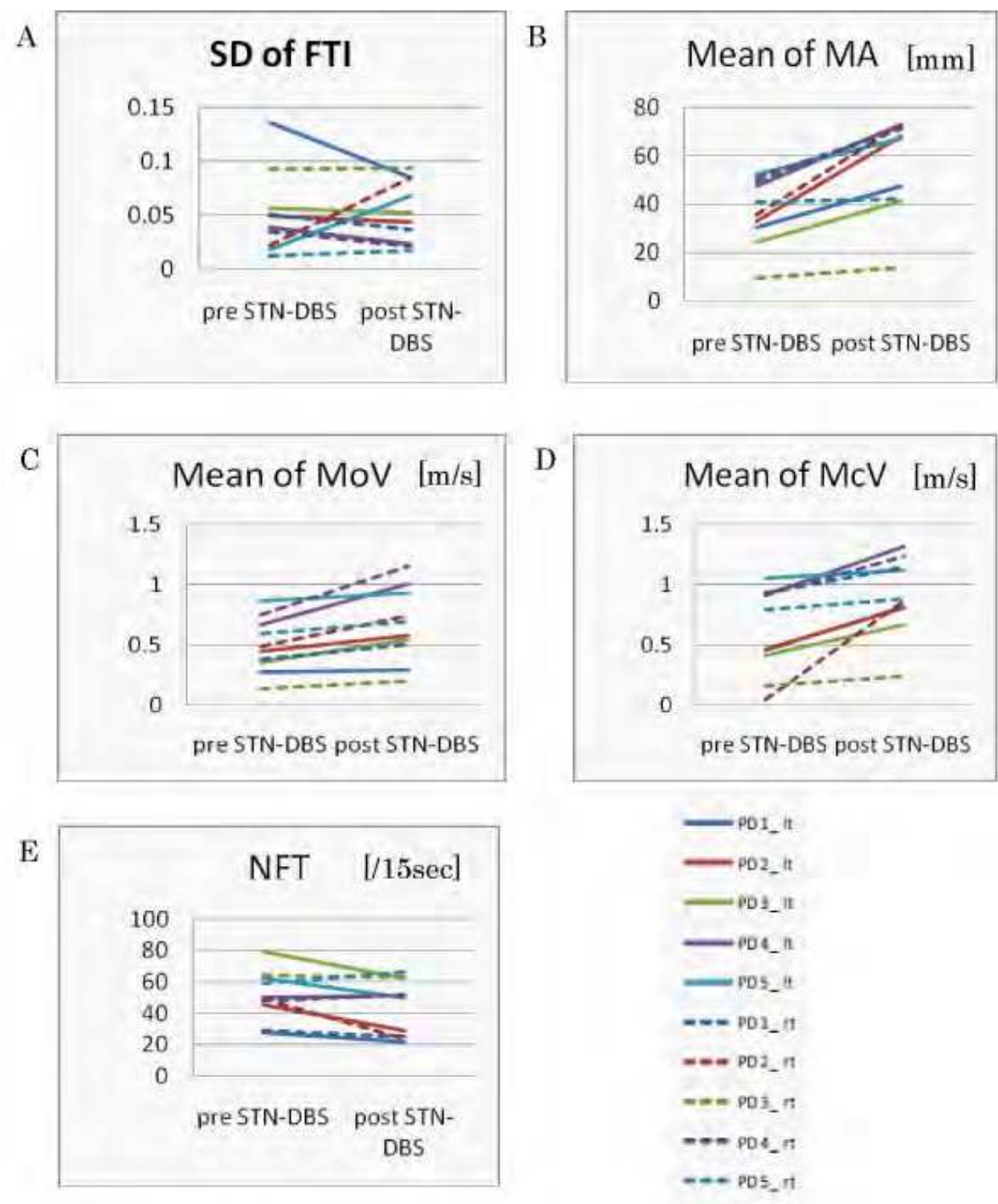
Fig. 12. Differences in five finger tapping parameters between before and after STN-DBS
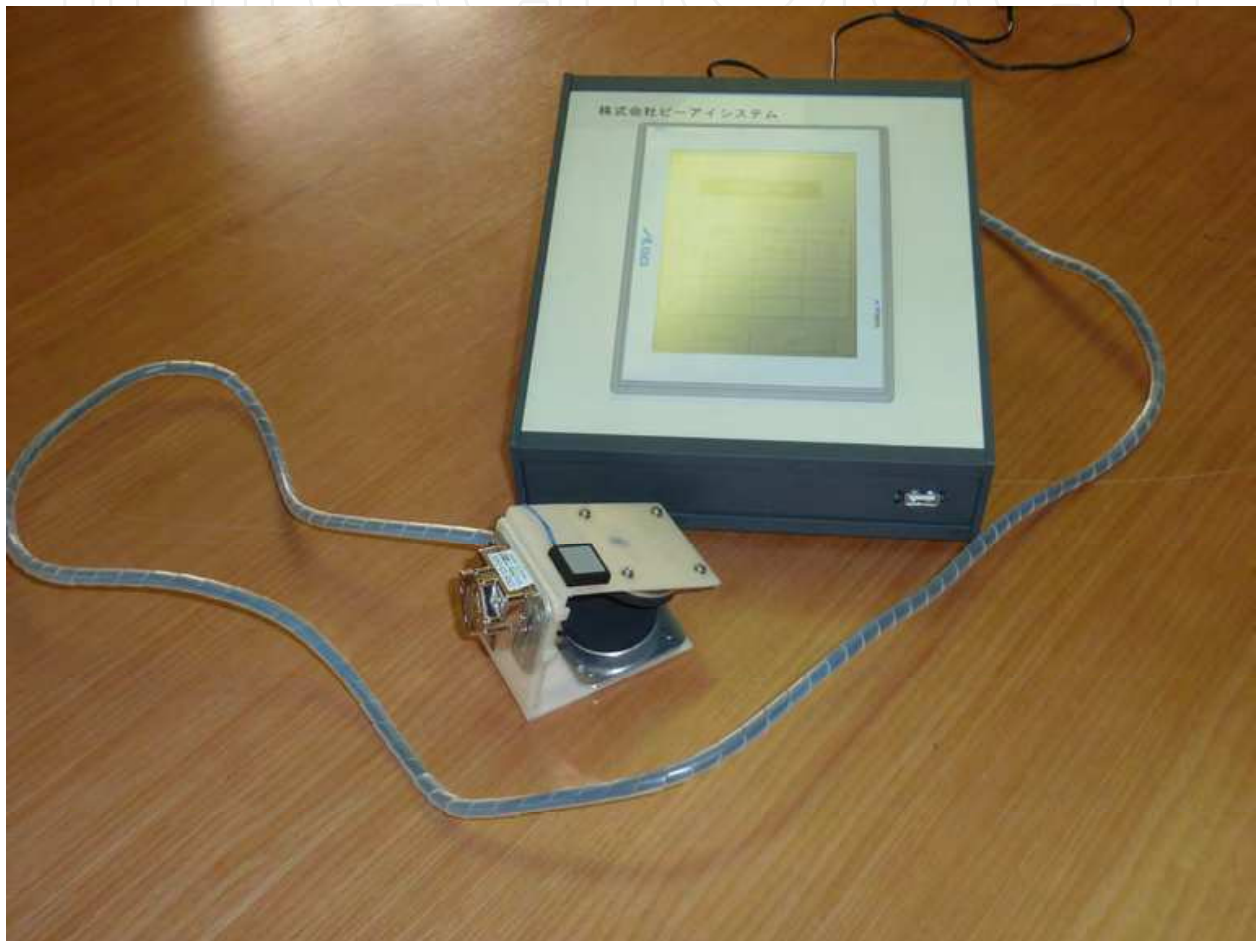(A)SD of FTI (B)Mean of MA (C)Mean of MoV (D)Mean of McV (E)NFT

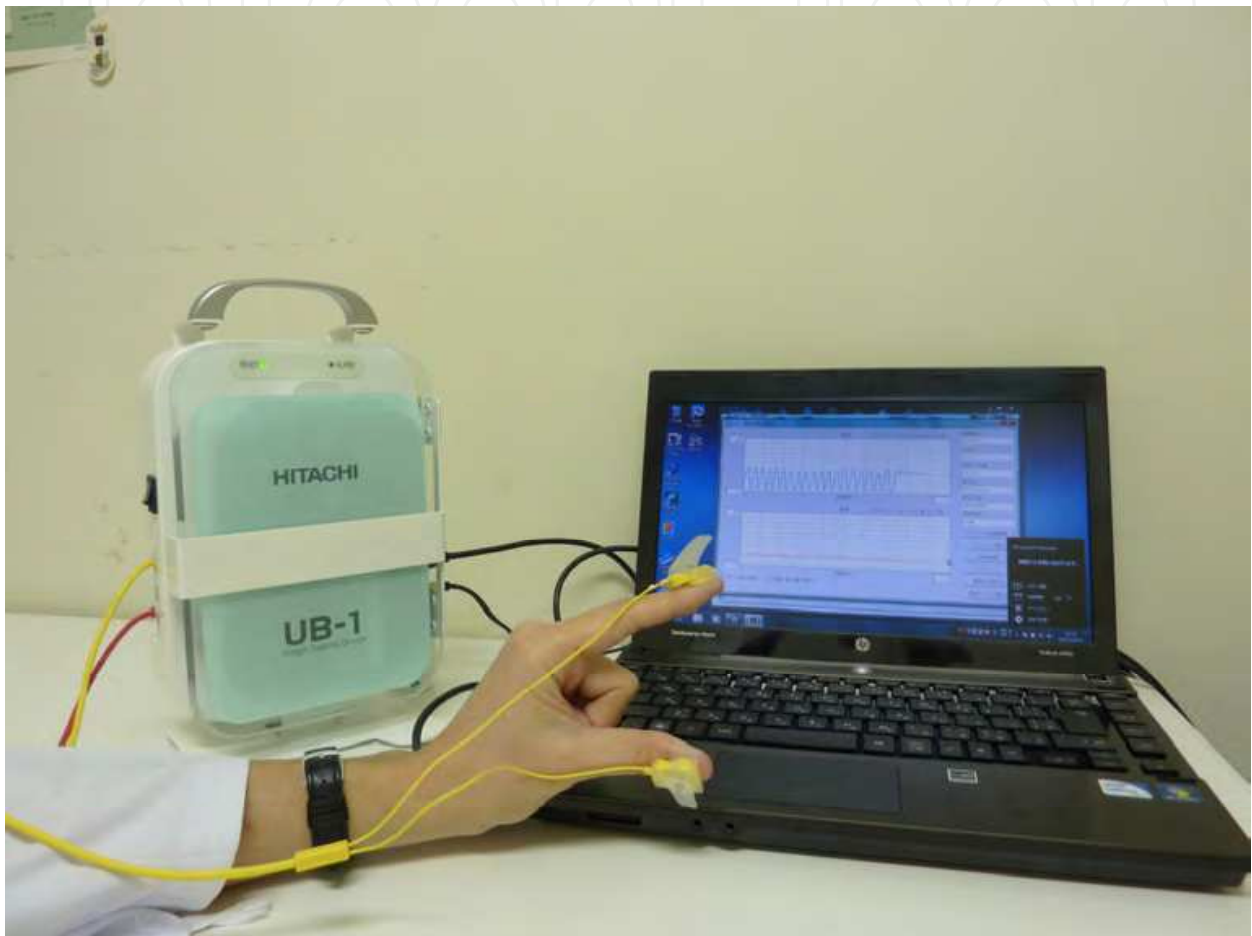Fig. 13. Prototype of compact muscle tonus measurement system

Fig. 14. New finger tapping analysis system by Hitachi Co. Ltd. (Hitachi Computer Peripherals Co. Ltd., Tokyo branch, 1-11-1, Ohmorikita, Ohta-ku, Tokyo, Zip.143-0016, JAPAN, TEL: +81-3-5753-6870, FAX: +81-3-5753-6872)

We previously reported that the muscle activity index in the static phase (EMG index) obtained for *biceps brachii* muscles, elastic coefficients, and sum of the differences of averaged torque values correlated well with the UPDRS score. Recently, we found that the EMG index is a good marker to distinguish a UPDRS rigidity score of 1 from the normal control (unpublished data). Because the elastic coefficients and the sum of the differences of averaged torque values seemed to be simple and better indicators of drug efficacy than the EMG index (unpublished data), we decided to use elastic coefficients and the sum of the differences of averaged torque values in this study. Rigidity is a clinical sign that gets worse immediately after DBS and therefore, this system is suitable for the tuning of DBS.

In finger tapping, we previously reported fourteen parameters of finger-tapping movement and a radar chart showed obvious differences in most of these parameters between normal controls and patients with PD (Yokoe et al. 2009). Principal component analysis showed that these parameters could be classified into three components: (1) mean of both amplitude and velocity, (2) number of finger tappings and mean FTI, and (3) SD of FTI. The first (velocity- and amplitude-related parameters) and third (rhythm-related parameters) components contributed to the discrimination of PD from normal controls. Regarding which component reflects treatment efficacy, parameters in the first component, including mean of MoV, mean of McV, and mean of MA, are good markers. The second component, including the number of finger tappings, does not reflect treatment efficacy. The third component, including the SD of FTI, depends on the patient. The left hand of PD1 showed improvement, although the right hand of PD2 worsened. However, both fingers moved faster and larger after DBS (Fig. 12). These results indicate that DBS works on the first component parameters rather than those of the third component.

These novel systems for testing muscle tonus and finger-tapping, which are compact, simple, and efficient, are very useful for daily neurological examinations. The muscle tonus measurement system was recently established, as shown in Figure 13 (product of PI System Co. Ltd, http://www.pis.co.jp), and the finger-tapping measurement system recently came on the market in Japan from Hitachi Co. Ltd. as shown in Figure 14.

These sensing systems identify rigidity or spasticity and the nature of abnormal finger tapping in PD and show Parkinsonian symptoms as a system error in software of repetitive movement.

4. Acknowledgment

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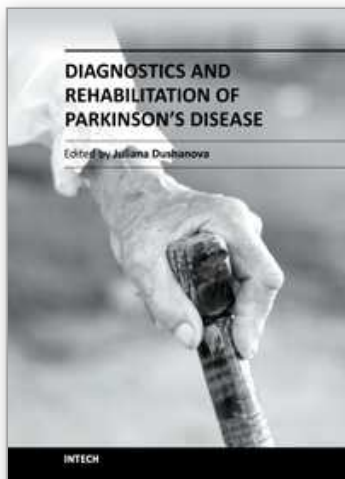
Diagnostics and Rehabilitation of Parkinson's Disease

Edited by Dr. Juliana Dushanova

Diagnostics and Rehabilitation of Parkinson's Disease presents the most current information pertaining to news-making topics relating to this disease, including etiology, early biomarkers for the diagnostics, novel methods to evaluate symptoms, research, multidisciplinary rehabilitation, new applications of brain imaging and invasive methods to the study of Parkinson's disease. Researchers have only recently begun to focus on the non-motor symptoms of Parkinson's disease, which are poorly recognized and inadequately treated by clinicians. The non-motor symptoms of Parkinson's disease have a significant impact on patient quality of life and mortality and include cognitive impairments, autonomic, gastrointestinal, and sensory symptoms. In-depth discussion of the use of imaging tools to study disease mechanisms is also provided, with emphasis on the abnormal network organization in parkinsonism. Deep brain stimulation management is a paradigm-shifting therapy for Parkinson's disease, essential tremor, and dystonia. In the recent years, new approaches of early diagnostics, training programmes and treatments have vastly improved the lives of people with Parkinson's disease, substantially reducing symptoms and significantly delaying disability. Written by leading scientists on movement and neurological disorders, this comprehensive book should appeal to a multidisciplinary audience and help people cope with medical, emotional, and practical challenges.

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