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RESEARCH ARTICLE

Remarkable hand grip steadiness in individuals with complete spinal cord injury

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Abstract

Although no damage occurs in the brains of individuals with spinal cord injury, structural and functional reorganization occurs in the sensorimotor cortex because of the deafferentation of afferent signal input from below the injury level. This brain reorganization that is specific to individuals with spinal cord injury is speculated to contribute to the improvement of the motor function of the remaining upper limbs. However, no study has investigated in detail the motor function above the injury level. To clarify this, we designed an experiment using the handgrip force steadiness task, which is a popular technique for evaluating motor function as the index of the variability of common synaptic input to motoneurons. Fourteen complete spinal cord injury (cSCI) individuals in the chronic phase, fifteen individuals with lower limb disabilities, and twelve healthy controls participated in the study. We clarified that the force steadiness in the cSCI group was significantly higher than that in the control groups, and that sports years were significantly correlated with this steadiness. Furthermore, multiple analyses revealed that force steadiness was significantly predicted by sports years. These results suggest that brain reorganization after spinal cord injury can functionally affect the remaining upper limb motor function. These findings may have implications in the clinical rehabilitation field, such as occupational rehabilitation of the upper limbs. They also indicate that individuals with complete spinal cord injury, based on their enhanced force adjustment skills, would excel at fine motor tasks such as manufacturing and handicrafts.

Keywords Spinal cord injury · Force steadiness · Hand grip · Brain reorganization

Introduction

Complete deafferentation of the spinal cord results in significant reorganization of the cortical regions around the dominant areas of the sensorimotor cortex connected to the area below the lesion level (Freund et al. 2011). In recent years, a growing body of evidence suggests that such functional reorganization in individuals with traumatic complete spinal cord injury (cSCI) involves neurophysiological changes in the brain structure, resting state functional connectivity, diffusion, spectroscopy, and brain metabolism (Solstrand Dahlberg et al. 2018). For example, it has been well established that the gray matter volume in the motor cortex leg area of the primary sensorimotor cortex decreases (Freund et al. 2011; Jurkiewicz et al. 2009), while the upper limb and face area of the primary sensorimotor cortex are medially displaced (Wrigley et al. 2009; Henderson et al. 2011). Some studies have also reported an enhancement of functional connectivity between the left and right hemispheres in motor-related areas (Hou et al. 2016) and an improvement of primary motor cortex activity (Sabre et al. 2016).

It is well known that brain reorganization in healthy individuals, such as cortical expansion and neural efficiency, can contribute to motor function improvement (Callan and Naito 2014). This cortical expansion implies the unmasking of

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pre-existing synaptic connections (Floyer-Lea et al. 2006). Unmasking is well-known as a compensation system in the brain that results from decreased GABA levels. GABA exhibits inhibitory functions and its reduction increases functional connectivity between potential synapses (Floyer-Lea et al. 2006). Such an increased synapse connection is an important factor that improves motor function (Perrey 2013). Regarding individuals with cSCI, as mentioned above, the upper limb area of the primary sensorimotor cortex is expanded. Accordingly, upper limb function in cSCI individuals may be higher than that in healthy ones due to the expansion of the upper limb dominant area in the sensorimotor cortex. However, it has not yet been determined how such brain reorganization in individuals with spinal cord injury contributes to motor function improvement of the remaining body parts, such as the upper limbs. Previous studies on motor function in cSCI individuals have mainly focused on the paralyzed body parts (Capogrosso et al. 2016; Wagner et al. 2018), with only few reporting on the remaining upper limb function (Pernigo et al. 2012; Ionta et al. 2016). However, even though Ionta et al. (2016) focused on the ability of hand recognition in cSCI individuals, it remains to be determined whether there is a change in motor function of the remaining upper limbs in cSCI individuals. Elucidating details on the adaptation of upper limb motor function after brain reorganization may have great implications in the clinical rehabilitation field, such as occupational rehabilitation of the upper limbs.

Reorganization in sensorimotor related areas can result in a higher motor function of the upper limbs in cSCI individuals than in healthy individuals. To quantify this improvement in upper limb motor function, we designed an experiment involving a hand grip force steadiness task. This force steadiness task is a well-known index for evaluating neuro-motor control (Enoka et al. 2003; Saito et al. 2016) and an index of the variance in the common synaptic input received by motor neurons (Negro et al. 2009; Farina et al. 2016; Feeney et al. 2017; Thompson et al. 2018). Therefore, force fluctuation during the force steadiness task has been suggested to reflect the state of the motor unit, such as discharge characteristics, discharge times of individual motor units, and cumulative activity of the recruited motor units (Enoka et al. 2003; Negro et al. 2009; Enoka and Duchateau 2017; Feeney et al. 2017; Thompson et al. 2018). Several factors, such as age, type and intensity of muscle contraction, and the individual's physical activity status can affect the coefficient of force variation in this task (Enoka et al. 2003; Farina et al. 2016). Additionally, in recent years it has been noted that force fluctuation can be affected by the cerebral cortex and not only the spinal motor units. Some studies have reported improved force steadiness through non-invasive brain stimulation over the primary motor cortex (Massie et al. 2013; Montenegro et al. 2016). Furthermore, Watanabe and Kohn (2015) revealed that force steadiness can be influenced by cortical oscillations at frequencies at or above the beta band by using biologically inspired mathematical models of the neuromuscular system. This implied an effect of frequency band resulting from cortical activity on force control. These studies suggest that quantitative changes of motor command from the brain via the corticospinal pathway induced by plastic changes in the brain are important factors of force fluctuation. Farina et al. (2016) suggested that force steadiness has been used as a paradigm to compare motor control because the determinants of force steadiness have been of interest for decades. Therefore, quantifying this fluctuation helps reveal the underlying general and physiological condition of the individual, and is considered as one of the best evaluation indices for clarifying upper limb motor function in cSCI individuals.

We aimed to evaluate force steadiness in cSCI individuals in comparison to individuals with other lower limb disabilities and healthy controls. We hypothesized that cSCI individuals would produce steadier force than healthy controls and individuals with LLD.

Patients and methods

Participants

We conducted a hand grip force steadiness task for three groups: cSCI individuals (cSCI), individuals with lower limb disabilities (LLD), and healthy controls (Healthy). We used the LLD group to clarify the difference in the influence of brain reorganization and that of daily use of the upper limbs on upper limb performance. Since wheelchair users may use their upper limbs more frequently than healthy people, their performance in the force steadiness task may be higher than that of healthy people. All participants in the cSCI group used a wheelchair in their daily life; therefore, their task performance was thought to be influenced by both brain reorganization and wheelchair use. Therefore, we measured force steadiness in LLD individuals to determine the influence of wheelchair use alone. Fourteen cSCI individuals in the chronic phase (49.4 ± 5.8 years, 2 female), 15 LLD individuals (41.8 ± 14.1 years, 1 female), and 12 healthy controls (30.8 ± 7.7 years, 5 female) participated in this study. Table 1 shows demographics and relevant clinical information for each group. We recruited cSCI individuals and LLD individuals using the following inclusion criteria: (1) no paralysis in upper limb function and ability to apply force to a force transducer in the hand grip configuration and (2) use of a wheelchair in daily life and inability to move by standing or walking. Moreover, we recruited patients who were perfectly paralyzed (ASIA scale A, Table 1). Healthy controls did not have any neurological disorder and had normal hearing

Table 1 Population demographics and relevant clinical information for each group

Group cSCI								
Subject	Sex	Age (years)	Disease	Lesion level	ASIA	Injury years	Sports years	Grip force (kg)
1	M	58	SCI	Th 7	A	37	30	57.3
2	M	49	SCI	Th 5	A	32	17	58.9
3	M	58	SCI	Th 12	A	36	6	42.9
4	M	43	SCI	L 2	A	25	21	57.2
5	M	53	SCI	Th 11	A	16	13	45.1
6	M	41	SCI	Th 4	A	24	16	48.0
7	F	45	SCI	L 2	A	16	4	31.7
8	M	52	SCI	Th 12	A	35	12	35.2
9	M	42	SCI	Th 4	A	25	24	45.4
10	M	55	SCI	Th 12	A	36	4	41.3
11	M	55	SCI	Th 10	A	32	30	55.0
12	M	46	SCI	Th 9	A	17	0	33.3
13	M	49	SCI	Th 3	A	15	15	41.6
14	F	45	SCI	Th 10	A	5	2	45.7
Group LLD								
Subject	Sex	Age (years)	Disease	Lesion level	ASIA	Injury years	Sports years	Grip force (kg)
15	M	33	Spina bifida	—	—	33	20	41.9
16	M	40	Spina bifida	—	—	40	0	23.4
17	F	41	Spina bifida	—	—	41	0	31.0
18	M	30	Spina bifida	—	—	30	18	38.1
19	M	19	Spina bifida	—	—	19	3	42.6
20	M	28	Spina bifida	—	—	28	2	57.0
21	M	34	Femur head necrosis	—	—	4	0	37.4
22	M	34	Traumatic brain injury	—	—	17	10	42.9
23	M	39	Leukoencephalopathy	—	—	19	3	25.9
24	M	31	Cerebral palsy	—	—	31	0	33.0
25	M	64	Purulent spondylitis	—	—	3	3	43.3
26	M	60	Acute poliomyelitis	—	—	58	20	52.7
27	M	58	Stroke	—	—	8	3	35.9
28	M	63	Stroke	—	—	9	3	41.3
29	M	54	Stroke	—	—	6	4	39.7
Group healthy controls								
Subject		Sex		Age (years)		Sports years		Grip force (kg)
30		M		27		8		44.8
31		M		27		18		43.2
32		M		24		5		40.3
33		M		23		14		37.2
34		M		26		10		39.1
35		F		24		7		28.2
36		F		51		0		23.4
37		F		35		2		30.4
38		M		34		0		54.1
39		M		33		8		41.3
40		F		33		4		35.0
41		F		33		3		35.9

ASIA American Spinal Injury Association impairment scale, *cSCI* complete spinal cord injury, *LLD* individuals with lower limb disabilities

and vision. Prior to beginning the study, each subject read and signed informed consent that was approved by Graduate School of Arts and Sciences (2018, no. 581-2-2), The University of Tokyo, and was in accord with the Declaration of Helsinki.

Data collection

Prior to the experiment, we collected basic information using a questionnaire sheet for all subjects, including: (1) medical history—all the diseases they had ever had; (2) date of injury—when the main disease developed and the number of years that had passed and (3) sports history—type of sport played and the time spent playing after the main injury. In addition, a physiotherapist evaluated the patients using the ASIA impairment scale to assess injury level and severity (Table 1).

During the experiment, subjects were seated in front of an oscilloscope (National Instruments Japan Corporation, Tokyo, Japan) that was placed at a distance of 80 cm in front of the subjects with both arms flexed at the elbow by 70° while holding a gripping force transducer (FG-1002FA, Uchida Electronics, Osaka, Japan). The oscilloscope was set at 30° below the horizontal line to the eye of the subject. Additionally, the orientation of the monitor was corrected to face the front of the subject. When the hand and oscilloscope position were determined, the forearm was fixed with a belt to maintain its position (Fig. 1). At the beginning of the experiment, participants performed three brief handgrip maximum voluntary contractions (MVCs) (3–5 s) with the dominant hand. In the force steadiness task, we used four target levels (2%, 10%, 30%, and 65% MVC) with each task lasting 12 s from the point when the target was reached and repeated in 3 trials in random order (i.e., 3 trials/per force level, a total of 12 trials in about 15 min). After 3 trials for each level, each participant had a 1-min break. The tasks required the participants to move a cursor displayed on the monitor by performing isometric handgrip contractions. From a display, the subjects were able to see their actual hand grip force in real time as a horizontal yellow line and the required target force as a horizontal yellow dotted line. During the task, individuals were instructed to maintain the line of force to the target line as precisely as possible.

To precisely measure the force fluctuation so that the visual gain on the display is the same at each target level, a high sensitivity (0.051 V/N) mode was used for contractions that were less than 10% of the maximal voluntary contraction (MVC) force, and a low sensitivity (0.013 V/N) mode was used to measure contractions that were equal to or greater than 30% of the MVC force. Force signals were digitized at 1000 samples/s using an analog-to-digital (A/D) converter (Powerlab/16SP, AD Instruments, Castle Hill, Australia) and stored on a computer.

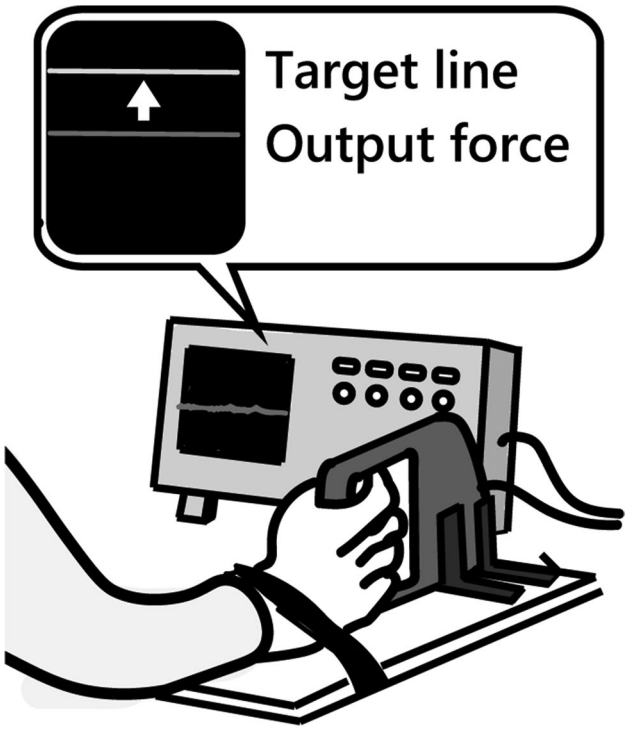

Fig. 1 Experimental setup. Brackets were attached to a 50-cm long, 20-cm wide, and 2-cm thick wooden base, and adjusted so that the force sensor could be fixed at any position. The force sensor was fixed before the experiment and placed on a desk. After the participant was seated, the elbow joint angle was fixed at 70° flexion, the forearm was placed in a neutral position, and the wrist was fixed with a detachable tape to restrict its movement. Subjects were instructed to gradually increase force exertion and to sustain the force line (bottom line on the oscilloscope monitor) around the target line (the line above) as steadily as possible for 12 s

Data analysis

For each task, the most stable 10-s data on the force, which were obtained by extracting the part where the force signal had the smallest standard deviation (SD), were used to calculate the SD and mean force and assess the magnitude of force fluctuation. Further, we normalized force fluctuation to the magnitude of force by computing the coefficient of variation [CV = (SD/mean) × 100].

All data are presented as mean ± standard error (SE). The R 2.8.1 (R Foundation for Statistical Computing, Vienna, Austria) was used to analyze all data. Prior to statistical analysis, Shapiro–Wilk normality tests were performed. The CV data sets of each group were confirmed to be normal. Furthermore, a mixed 3 (group) × 4 (target level) analysis of variance (ANOVA) with repeated measures was performed. All significant main effects or interaction were analyzed using Tukey–Kramer post hoc tests. Moreover, univariate relations between grip force control variables and injury years, sports years, grip force and age were examined using

Pearson's correlation coefficient. The correlation between the mean CV value of each target level and each factor was examined. The level of significance was set at $p < 0.05$. In addition to correlation analyses, multiple regression analyses (stepwise linear regression analyses) were conducted to determine how much of the variance in CV could be predicted by each factor. Injury years, sports years, grip force, and age were entered as independent variables.

Results

Force steadiness

There was no statistically significant difference in the MVC values obtained prior to the start of the experiment among the groups. Figure 2 shows the representative waveforms at 30% MVC in the cSCI, LLD, and Healthy groups. The waveform of the cSCI group exhibited fewer force fluctuations. Similarly, the cSCI group showed small fluctuations at other target levels, irrespective of the target force level. The mixed 3 (group) × 4 (target level) ANOVA revealed a significant main effect of group [F (2,40) = 9.86, $p = 0.0004$] and target level [F (3,40) = 26.2, $p = 0.0001$]. Moreover, there was a significant interaction between group and target level [F (6,40) = 2.67, $p = 0.034$]. We subsequently performed one-way ANOVA tests at each level for post hoc comparisons. Multiple comparisons (Tukey post hoc test) revealed that the CV was significantly lower in the cSCI group than in the Healthy group at all levels (2%: $p = 0.014$, 10%: $p = 0.032$, 30%: $p = 0.007$, 65%: $p = 0.008$) (Fig. 3). Furthermore, the CV was significantly lower in the cSCI group than in the LLD group at 10% and 65% level (10%: $p = 0.022$, 65%: $p = 0.005$), but not significantly different at the 30% level (Fig. 3). At 2% level, there was no significant difference in the CV between the cSCI and LLD group, but; the Healthy group had a higher CV compared to the cSCI and LLD group (Fig. 3).

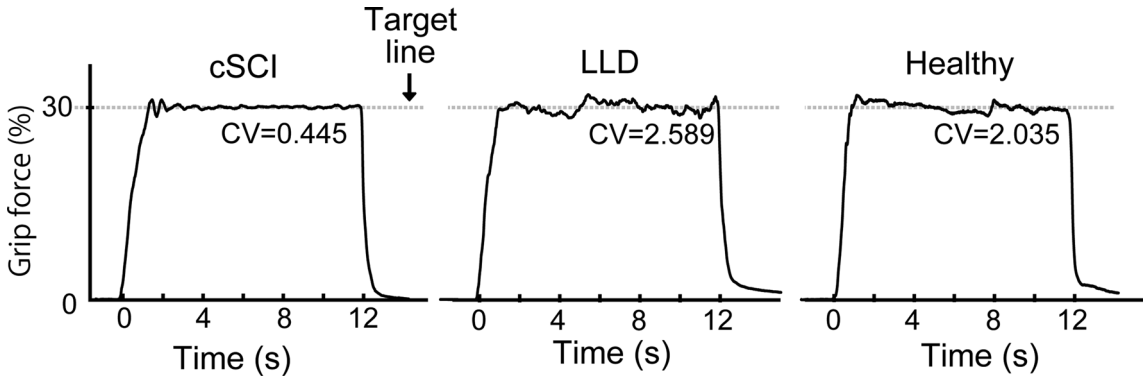

Fig. 2 Representative waveforms during the isometric contraction at 30% maximum voluntary contraction force. These traces represent handgrip force of cSCI (left), LLD (middle), and Healthy (right) subjects; the horizontal gray dotted line indicates the target line. The cSCI waveform showed less fluctuation and maintained higher stability. *cSCI* complete spinal cord injury, *LLD* lower limb disability, *CV* coefficient of variation

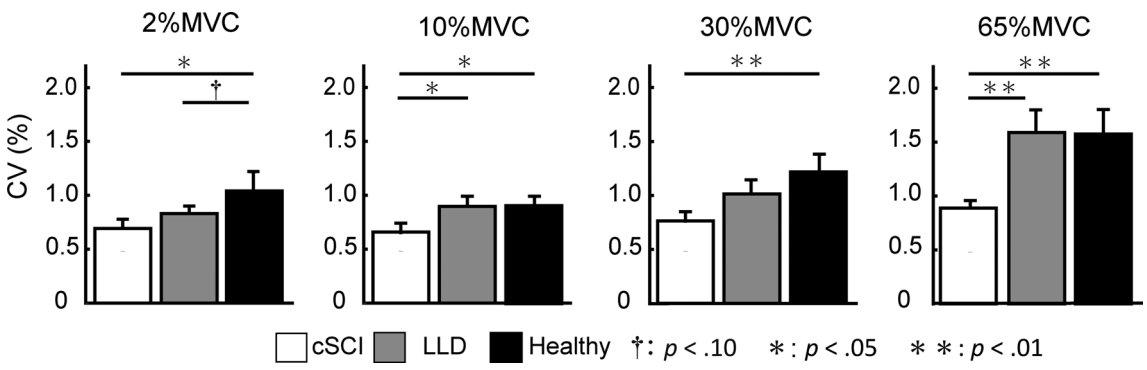

Fig. 3 Force steadiness of all groups. Mean ± SE of the CV during isometric contraction with four target forces (2%, 10%, 30%, and 65% MVC) compared between three groups (cSCI; white bar, LLD; gray bar, Healthy; black bar). †$P < 0.10$ compared between LLD and Healthy groups. *$p < 0.05$, **$p < 0.01$ compared between cSCI and LLD and Healthy groups. *cSCI* complete spinal cord injury, *LLD* lower limb disability, *CV* coefficient of variation, *MVC* maximum voluntary contraction

Correlations and linear regression

Pearson correlation analysis showed no significant relationship between the injury years and CV in the cSCI ($r=0.105$, $p=0.696$) and LLD group ($r=-0.351$, $p=0.198$) (Fig. 4). Similar results were obtained for grip force and CV in the cSCI ($r=-0.505$, $p=0.052$) and LLD group ($r=-0.247$, $p=0.374$) (Fig. 4). Furthermore, there was no significant relationship between age and CV in the cSCI ($r=-0.073$, $p=0.803$) and LLD group ($r=0.149$, $p=0.597$) (Fig. 4). However, we found significant negative correlations between the sports years and CV in the cSCI ($r=-0.626$, $p=0.009$) and LLD group ($r=-0.607$, $p=0.016$), but not in the Healthy group (Fig. 4). In addition to these analyses, the results of the stepwise regression revealed that only the sports years could predict the CV in the cSCI ($R=0.452$, $p=0.008$) and LLD group ($R=0.369$, $p=0.016$).

Discussion

The main findings of the present study were that the CV during the handgrip force steadiness task was significantly lower in the cSCI group than in the LLD (10%, 30%, and 65% MVC) and Healthy groups (2%, 10%, 30%, and 65% MVC), and that CV was significantly predicted by sports years. These results suggest that brain reorganization after spinal cord injury can functionally affect the remaining upper limb motor function. There was a significant age difference between the cSCI, LLD, and Healthy groups. At first glance, it seems that the group differences are not aligned, but this is more beneficial. It has been shown that aging affects force steadiness, and young adults exhibit the highest steady isometric hand muscle contraction among all the age groups (Enoka et al. 1999; Burnett et al. 2000; Laidlaw et al. 2000; Vaillancourt et al. 2003). In our study, however, the Healthy group of young adults (30.8 ± 7.7 years) had the highest CV. Therefore, if we had recruited healthy control individuals that were age-matched to the cSCI and LLD group, the difference in force steadiness between groups would probably be more prominent. This implies that the force steadiness of the cSCI group was especially good.

Previous studies have demonstrated that force steadiness is affected by aging, disuse, fatigue, and training intervention (Enoka et al. 2003; Saito et al. 2016). Furthermore, excitation of the motor neuron pool determines the force fluctuation (Taylor et al. 2003). Based on these findings, it is logical to speculate that the cSCI and LLD groups should exhibit a lower CV of force steadiness compared to the Healthy group, due to the frequent upper limb usage

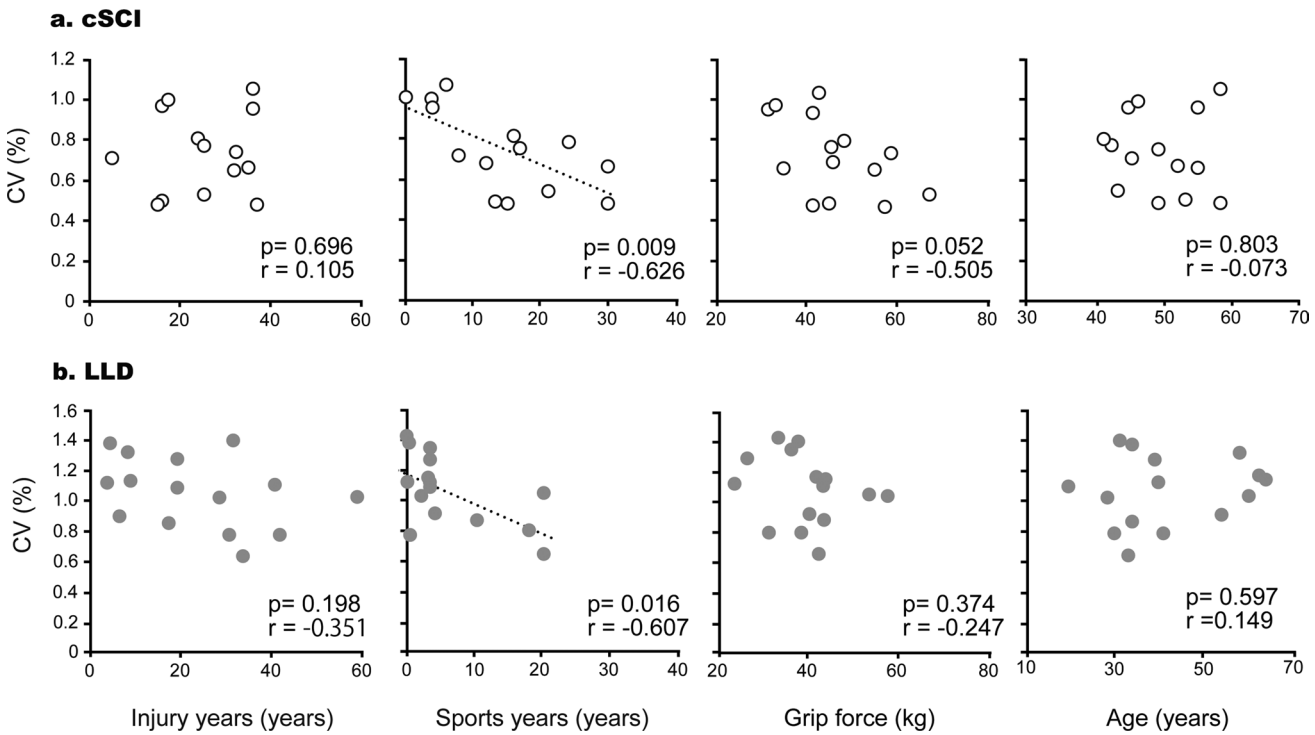

Fig. 4 Correlation among all groups. The correlation between the mean CV value of each target level and injury years, sports years, grip force, and age. The straight dotted line is shown only for significant correlations. **a**, **b** The relationship between CV and injury years, sports years, grip force, and age in the cSCI (**a**) and LLD group (**b**). *cSCI* complete spinal cord injury, *LLD* lower limb disability, *CV* coefficient of variation

in daily living and the subsequent adaptation of the motor unit. However, the results for both wheelchair groups were clearly different, which indicates that the frequency of upper limb usage cannot explain the results. Therefore, it is possible that the higher central nervous system affected the lower CV in the cSCI group. In cSCI individuals, the afferent sensory signal input from below the injury level is completely blocked (Freund et al. 2011) and the cortical reorganization in the dominant area of the remaining body parts has also been found to be larger in cSCI patients than in patients with incomplete injuries (Lotze et al. 2006). Further, the previous studies using animal models have reported that drastic changes in the somatotopy in 3b area could be induced in cSCI subjects compared with those with incomplete injury (Jain et al. 1998; Aguilar et al. 2010). It is likely that complete blocking of the afferent sensory signal increases the cortical response of the brain. Herbert et al. (2007) used EEG to confirm that brain reorganization is likely to occur for complete SCI individuals. Significant and consistent decreased alpha wave (8–13 Hz) and increased beta wave activity (13–30 Hz) were found in the cortex of cSCI patients. Beta wave activity has been shown to lead to an increase in the steady-state force generated by muscles (Watanabe and Kohn 2015). Therefore, these findings suggest that the specific reorganization process in cSCI patients contributes to the improved motor function in the remaining upper limbs.

We had initially hypothesized that force steadiness would spontaneously increase over time with brain and body adaptation after injury in the cSCI group. However, there was no correlation between the injury years and CV in both the cSCI and LLD groups. On the other hand, there was a significant correlation between the sports years and CV, especially in the cSCI group (Figs. 3, 4). Although correlation does not imply causality, it is evident that there was a decrease in CV with increase in sports years. This suggests that sports exercise can promote motor function improvement via brain reorganization. Many studies have revealed that motor learning exercise can favorably affect structural and functional plasticity in the motor cortex (Karni et al. 1995; Pascual-Leone et al. 1995; Pearce et al. 2000; Sampaio-Baptista et al. 2013; Taubert et al. 2015). A study on spinal cord injury patients demonstrated that subjects with exercise habits had a higher sense of self-ownership to recognize their upper limbs than those without exercise habits (Pernigo et al. 2012). We considered that brain somatotopic reorganization was caused by exercise repetition, efferent signal output along with motor execution, and afferent signal input by sensory feedback. In summary, (1) blocking afferent sensory signal input can trigger brain reorganization, and (2) repetition of body movements by exercise promotes plastic changes in the central nervous system. We speculate that the combination of these two significant features of plastic changes contributed to the lower CV observed in the cSCI group during the force steadiness task.

At 2% MVC intensity, there was no significant difference in the CV between the cSCI and LLD groups, but it was lower than that in the Healthy group, which was different from the findings in other target levels. The force steadiness task used in this study has been reported to monitor information on the adjustment of the gripping force based on the skin sensation signal of the fingertip (Macefield et al. 1996). Although 2% and 65% intensity are the levels used experimentally, 2% intensity requires little force output and more sensitive sensory input feedback; therefore, the proprioceptive acuity is needed to hold the fingers in the same position. If the finger's position does not move, no fluctuation of the force waveforms occurs. Elderly individuals were reported to have a high CV of force in index finger abduction, elbow flexion, and knee extension when performing a force steadiness task at 2.5% MVC level, which was attributed to weakening of their sensory acuity (Graves et al. 2000; Burnett et al. 2000; Tracy and Enoka 2002). This is similar to the results at the 2% level obtained in the present study. We speculate that this tendency is due to increased sensitivity in the hands of individuals in both the cSCI and LLD groups given their daily use of wheelchairs.

Limitation of this study

We only measured the force output signal without obtaining the neurophysiological index, and the study does not provide any direct evidence on the correlation between high force steadiness and brain reorganization.

In our next study, we plan to measure actual brain activity during a similar force steadiness task and compare the results of cSCI individuals, LLD individuals, and healthy subjects.

Conclusion

In conclusion, we were able to determine motor function characteristics in cSCI individuals using the force steadiness task. This study revealed that (1) cSCI individuals show a lower CV during the force steadiness task than LLD individuals and healthy subjects, and (2) this improvement in ability for force adjustment depends on long-term exercise, but not the number of years since injury. These results suggest that brain reorganization triggered by blocking afferent sensory signal input can trigger brain reorganization and that repetition of body movements by exercise contributed to the greater force steadiness in the cSCI group. We speculate that these features promote plastic changes in the central nervous system of cSCI individuals. These findings may have great implications in the clinical rehabilitation field, such

as occupational rehabilitation of the upper limbs. They also indicate that individuals with complete spinal cord injury, based on their enhanced force adjustment skills, would excel at fine motor tasks such as manufacturing and handicrafts.

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Author contributions TN, HK, and KeN designed the study. TN, HK, and HO collected the data. TN analyzed and interpreted the data and wrote the article. All authors have revised the article for intellectual content and approved the final manuscript.

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Compliance with ethical standards

Conflicts of interest We declare that we have no conflicts of interest.

References

Aguilar J, Humanes-Valera D, Alonso-Calvino E, Yague JG, Moxon KA, Oliviero A, Foffani G (2010) Spinal Cord Injury Immediately Changes the State of the Brain. J Neurosci 30(22):7528–7537. https://doi.org/10.1523/JNEUROSCI.0379-10.2010

Burnett RA, Laidlaw DH, Enoka RM (2000) Coactivation of the antagonist muscle does not covary with steadiness in old adults. J Appl Physiol 89:61–71. https://doi.org/10.1152/jappl.2000.89.1.61

Callan DE, Naito E (2014) Neural processes distinguishing elite from expert and novice Athletes. Cogn Behav Neurol 27(4):183–188. https://insights.ovid.com/pubmed?pmid=25539037

Capogrosso M, Milekovic T, Borton D, Wagner F, Moraud EM, Mignardot JB et al (2016) A brain–spine interface alleviating gait deficits after spinal cord injury in primates. Nature 539:284-288. https://www.nature.com/articles/nature20118

Enoka RM, Duchateau J (2017) Rate coding and the control of muscle force. Cold Spring Harb Perspect Med 7(10):a029702. https://doi.org/10.1101/cshperspect.a029702

Enoka RM, Burnett RA, Graves AE, Kornatz KW, Laidlaw DH (1999) Task- and age-dependent variations in steadiness. Prog Brain Res 123:389–395

Enoka RM, Christou EA, Hunter SK, Kornatz KW, Semmler JG, Taylor AM, Tracy BL (2003) Mechanisms that contribute to differences in motor performance between young and old adults. J Electromyogr Kinesiol 13(1):1–12. https://doi.org/10.1016/S1050-6411(02)00084-6

Farina D, Negro F, Muceli S, Enoka RM (2016) Principles of motor unit physiology evolve with advances in technology. Physiology 31(2):83–94. https://doi.org/10.1152/physiol.00040.2015

Feeney DF, Meyer FG, Noone N, Enoka RM (2017) A latent low-dimensional common input drives a pool of motor neurons: a probabilistic latent state-space model. J Neurophysiol 118(4):2238–2250. https://doi.org/10.1152/jn.00274.2017

Floyer-Lea A, Wylezinska M, Kincses T, Matthews PM (2006) Rapid modulation of GABA concentration in human sensorimotor cortex during motor learning. J Neurophysiol 95(3):1639–1644. https://doi.org/10.1152/jn.00346.2005

Freund P, Weiskopf N, Ward NS, Hutton C, Gall A, Ciccarelli O, Thompson AJ (2011) Disability, atrophy and cortical reorganization following spinal cord injury. Brain 134(6):1610–1622. https://doi.org/10.1093/brain/awr093

Graves AE, Kornatz KW, Enoka RM (2000) Older adults use a unique strategy to lift inertial loads with the elbow flexor muscles. J Neurophysiol 83:2030–2039. https://doi.org/10.1152/jn.2000.83.4.2030

Henderson LA, Gustin SM, Macey PM, Wrigley PJ, Siddall PJ (2011) Functional reorganization of the brain in humans following spinal cord injury: evidence for underlying changes in cortical anatomy. J Neurosci 31(7):2630–2637. https://doi.org/10.1523/JNEUROSCI.2717-10.2011

Herbert D, Tran Y, Craig A, Boord P, Middleton J, Siddall P (2007) Alterd brain eave activity in persons with chronic spinal cord injury. Int J Neurosci 117(12):1731–1746. https://doi.org/10.1080/00207450701242826

Hou J, Xiang Z, Yan R, Zhao M, Wu Y, Zhong J, Wu J (2016) Motor recovery at 6 months after admission is related to structural and functional reorganization of the spine and brain in patients with spinal cord injury. 2209(March): 2195–2209. https://doi.org/10.1002/hbm.23163

Ionta S, Villiger M, Jutzeler CR, Freund P, Curt A, Gassert R (2016) Spinal cord injury affects the interplay between visual and sensorimotor representations of the body. Sci Rep 6:20144. https://doi.org/10.1038/srep20144

Jain N, Florence SL, Kaas JH (1998) Reorganization of somatosensory cortex after nerve and spinal cord injury. Physiology 13(3):143–149. https://doi.org/10.1152/physiologyonline.1998.13.3.143

Jurkiewicz MT, Mikulis DJ, Fehlings MG (2009) Sensorimotor cortical activation in patients with cervical spinal cord injury with persisting paralysis. Neurorehabil Neural Repair 24(2):136–140. https://doi.org/10.1177/1545968309347680

Karni A, Meyer G, Jezzard P, Adams MM, Turner R, Ungerleider LG (1995) Functional MRI evidence for adult motor cortex plasticity during motor skill learning. Nature 377:155-158. https://www.nature.com/articles/377155a0

Laidlaw DH, Bilodeau M, Enoka RM (2000) Steadiness is reduced and motor unit discharge is more variable in old adults. Muscle Nerve 23(4):600–612

Lotze M, Laubis-Herrmannb U, Topkac H (2006) Combination of TMS and fMRI reveals a specific pattern of reorganization in M1 in patients after complete SCI. Restor Neurol Neurosci 24(2):97–107

Macefield VG, Fuglevand AJ, Bigland-Ritchie B (1996) Contractile properties of single motor units in human toe extensors assessed by intraneural motor axon stimulation. J Neurophysiol 75(6):2509–2519. https://doi.org/10.1152/jn.1996.75.6.2509

Massie CL1, Tracy BL, Paxton RJ, Malcolm MP (2013) Functional repetitive transcranial magnetic stimulation increases motor cortex excitability in survivors of stroke. Clin Neurophysiol 124(2):371–378. https://content.iospress.com/articles/neurorehabilitation/nre944

Montenegro RA, Midgley MR, Bernardes W, Okano AH, Farinatti P (2016) Bihemispheric motor cortex transcranial direct current stimulation improves force steadiness in post-stroke hemiparetic patients: a randomized crossover controlled trial. Front Hum Neurosci 10:1–9. https://doi.org/10.3389/fnhum.2016.00426

Negro F, Holobar A, Farina D (2009) Fluctuations in isometric muscle force can be described by one linear projection of low-frequency components of motor unit discharge rates. J Physiol 587(24):5925–5938. https://doi.org/10.1113/jphysiol.2009.178509

Pascual-Leone A, Nguyet D, Cohen LG, Brasil-Neto JP, Cammarota A, Hallett M (1995) Modulation of muscle responses evoked by transcranial magnetic stimulation during the acquisition of new

fine motor skills. J Neurophysiol 74(3):1037–1045. https://doi.org/10.1152/jn.1995.74.3.1037

Pearce AJ, Thickbroom GW, Byrnes ML, Mastaglia FL (2000) Functional reorganisation of the corticomotor projection to the hand in skilled racquet players. Exp Brain Res 130:238–243. https://doi.org/10.1007/s002219900236

Pernigo S, Moro V, Avesani R, Miatello C, Urgesi C, Aglioti SM (2012) Massive somatic deafferentation and motor deafferentation of the lower part of the body impair its visual recognition: a psychophysical study of patients with spinal cord injury. Eur J Neurosci 36(11):3509–3518. https://doi.org/10.1111/j.1460-9568.2012.08266.x

Perrey S (2013) Promoting motor function by exercising the brain. Brain Sci 3(1):101–122. https://doi.org/10.3390/brainsci3010101

Sabre L, Tomberg T, Kõrv J, Kepler J, Keple K, Linnamägi Ü, Asser T (2016) Brain activation in the chronic phase of traumatic spinal cord injury. Spinal Cord 54(1):65–68. https://doi.org/10.1038/sc.2015.158

Saito A, Ando R, Akima H (2016) Effects of prolonged patellar tendon vibration on force steadiness in quadriceps femoris during force-matching task. Exp Brain Res 234(1):209–217. https://doi.org/10.1007/s00221-015-4447-x

Sampaio-Baptista C, Khrapitchev AA, Foxley S, Schlagheck T, Scholz J, Jbabdi S, Johansen-Berg H (2013) Motor skill learning induces changes in white matter microstructure and myelination. J Neurosci 33(50):19499–19503. https://doi.org/10.1523/JNEUROSCI.3048-13.2013

Solstrand Dahlberg L, Becerra L, Borsook D, Linnman C (2018) Brain changes after spinal cord injury, a quantitative meta-analysis and review. Neurosci Biobehav Rev 90:272–293. https://doi.org/10.1016/j.neubiorev.2018.04.018

Taubert M, Villringer A, Lehmann N (2015) Endurance exercise as an "endogenous" neuro-enhancement strategy to facilitate motor learning. Front Hum Neurosci 9:1–16. https://doi.org/10.5700/rege373

Taylor AM, Christou EA, Enoka RM (2003) Multiple features of motor-unit activity influence force fluctuations during isometric contractions. J Neurophysiol 90:1350–1361. https://doi.org/10.1152/jn.00056.2003

Thompson CK, Negro F, Johnson MD, Holmes MR, McPherson LM, Powers RK, Farina D, Heckman CJ (2018) Robust and accurate decoding of motoneuron behaviour and prediction of the resulting force output. J Physiol 596(14):2643–2659. https://doi.org/10.1113/JP276153

Tracy BL, Enoka RM (2002) Older adults are less steady during submaximal isometric contractions with the knee extensor muscles. J Appl Physiol 92(3):1004–1012. https://doi.org/10.1152/japplphysiol.00954.2001

Vaillancourt DE, Larsson L, Newell KM (2003) Effects of aging on force variability, single motor unit discharge patterns, and the structure of 10, 20, and 40 Hz EMG activity. Neurobiol Aging 24:25–35. https://doi.org/10.1016/S0197-4580(02)00014-3

Wagner FB, Mignardot JB, Le Goff-Mignardot CG, Demesmaeker R, Komi S, Capogrosso M et al (2018) Targeted neurotechnology restores walking in humans with spinal cord injury. Nature 563(7729):65–71. https://doi.org/10.1038/s41586-018-0649-2

Watanabe RN, Kohn AF (2015) Fast oscillatory commands from the motor cortex can be decoded by the spinal cord for force control. J Neurosci 35(40):13687–13697. https://doi.org/10.1523/JNEUROSCI.1950-15.2015

Wrigley PJ, Press SR, Gustin SM, Macefield VG, Gandevia SC, Cousins MJ, Siddall PJ (2009) Neuropathic pain and primary somatosensory cortex reorganization following spinal cord injury. Pain 141(1–2):52–59. https://doi.org/10.1016/j.pain.2008.10.007