

## An Effect of Repetitive Ulnar Nerve Stimulation on Rapid Finger Movements in Cervical Spondylotic Myelopathy and Healthy Subjects : a Preliminary F-wave Study in Healthy Subjects

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### Abstract

**Objectives** : This study attempts to verify a beneficial effect of repetitive ulnar nerve stimulation (RUNS) at the wrist on rapidity of finger movements in cervical spondylotic myelopathy (CSM) patients and healthy subjects, followed by testing if RUNS alters the anterior horn cell excitability in healthy subjects.

**Methods** : The RUNS consisted of 0.1-ms width pulses with supramaximal intensity, delivered at 5/s for 5 minutes. We studied RUNS-induced changes in the repetitive finger movement rates in 9 CSM patients and 7 healthy subjects, followed by ulnar nerve F-wave studies on the first dorsal interosseous (FDI) and the first volar interosseous (FVI) muscles in 15 healthy subjects.

**Results** : The RUNS significantly increased the repetitive finger movement rates in both groups. Compared to the baseline, RUNS significantly decreased the F-wave persistence ( $41.1 \pm 23.1\%$  vs  $32.0 \pm 21.5\%$ ) and slightly but significantly shortened its mean latency ( $28.8 \pm 2.6\text{ms}$  vs  $28.0 \pm 1.6\text{ms}$ ) for the FVI, but not for the FDI.

**Conclusions** : A unilaterally applied RUNS increased the rate of rapid finger movements on both sides in CSM patients and healthy subjects. The RUNS preferentially suppressed the F-waves recorded from the FVI without equally affecting those from the FDI in healthy subjects, which may, at least partly, account for the RUNS-induced facilitative effects on rapid finger movements.

**Key words** : Cervical spondylotic myelopathy, finger spasticity, repetitive nerve stimulation, neuromodulation, motor neuron excitability, F-wave

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(Received July 20, 2016 and accepted August 18, 2016)

## Introduction

A velocity-dependent increase in tonic stretch reflex or muscle tone characterizes spasticity as one of the components of the upper motor neuron syndrome<sup>1</sup>, which causes functional impairment of fast movements and rapid repetitive movements of the limbs<sup>2</sup>. Upper limb involvement with this motor disorder affects fine finger movement in using tableware, doing up buttons and writing in the majority of patients with cervical spondylotic myelopathy (CSM)<sup>3-6</sup>. To quantitatively assess such disabilities, a simple test of how rapidly the patient can open and close the fists in 10 seconds (grip-and-release test) serves as a useful measure<sup>7</sup> (Fig. 1-A).

More recently, Yamada et al. (2004)<sup>8</sup> reported that repetitive ulnar nerve stimulation at the wrist (RUNS) transiently improved the grip-and-release rate in CSM patients. They also proposed a prognostic value of this technique by showing a significant correlation between the RUNS-induced improvement of grip-and-release rate and functional recovery after decompression surgeries. We further investigated this phenomenon on the assumption that RUNS might alter the anterior horn cell excitabilities of the finger extensors, flexors or both. First, the present study verified such a transient effect of RUNS on rapidity of repetitive finger movements in CSM patients and healthy subjects. We then used ulnar nerve F-waves to probe RUNS-induced excitability changes in the two groups of anterior horn cells innervating the first dorsal interosseous (FDI) and the first volar interosseous (FVI) muscles in healthy subjects. The FDI and the FVI function antagonistically to each other and synergistically to finger extensors and flexors, respectively.

## Methods

### 1. Subjects

We studied 9 CSM patients selected on the basis of having moderate to severe spastic limb paresis with

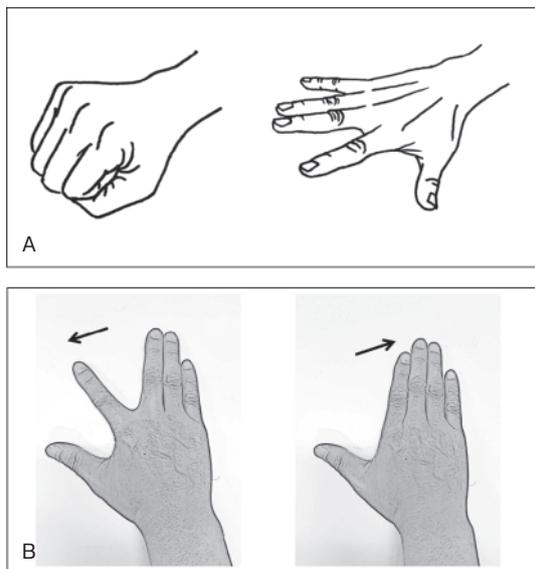
MRI evidence of maximal cord involvement at C3-4 or C4-5, and a total of 22 healthy subjects without a history of peripheral or central nervous system disease or abnormalities on neurological examination. All agreed in writing to participate in the study after reading an informed consent form approved by the hospital ethics committee.

### 2. Repetitive ulnar nerve stimulation (RUNS)

We applied a conditioning RUNS to the ulnar nerve on the side affected by myelopathic symptoms more than the other in CSM patients, and on a side chosen arbitrarily in healthy subjects. A bipolar surface stimulator (NM-420S, Nihonkohden, Tokyo, Japan), with the cathode placed proximal to the anode, served for RUNS. Electrical stimulation consisted of 0.1-ms width pulses with intensity 20% greater than that for just eliciting maximal compound muscle action potentials (CMAPs) from the FDI and the FVI, delivered to the ulnar nerve at the wrist at 5Hz for 5 minutes.

### 3. Experiment 1 (Effects of RUNS on the grip-and-release rate in CSM patients and healthy subjects)

We tested 9 CSM patients (5 women) aged 51 to 83 years (mean, 66.9 years) and 7 healthy subjects (4 men) aged 30 to 75 years (mean, 52.9 years). The subjects sat on an adjustable chair with the shoulder slightly abducted, the elbow flexed at 90 degrees and the forearm pronated. We requested them to open and close their fists as rapidly as possible in 10 seconds (grip-and-release test) (Fig. 1-A). Following a few practice trials, the subjects carried out the subsequent test trial. They performed the test for both sides separately twice each : once before and once after RUNS.

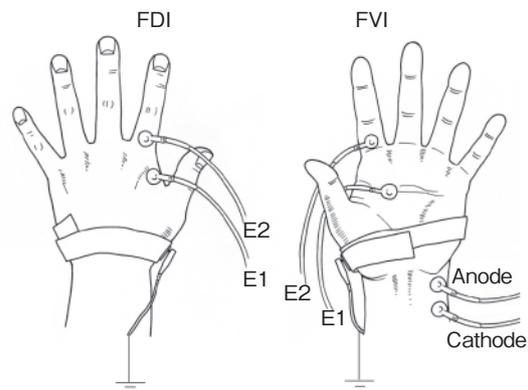


**Figure 1**

(A) A grip-and-release test [Ono et al., 1987]. The subject opens and closes the fists repeatedly as rapidly as possible in 10 seconds. (B) An abduction-and-adduction test of the index finger. With the palm spread on the desk, the subject abducts his/her index finger towards the bisector of the angle between the thumb and the middle finger and then adducts it back to the side of the middle finger repeatedly as rapidly as possible in 10 seconds.

#### 4 . Experiment 2 (Effects of RUNS on the abduction-and-adduction test of the 2nd digit in healthy subjects)

To make the target muscles for testing the rapidity of repetitive finger movements consistent with the F-wave study, we devised the abduction-and-adduction test of the index finger, as a substitute for the grip-and-release test. We studied the same 7 healthy subjects as tested in Experiment 1. The subjects sat on an adjustable chair in front of a desk with their palm spread on the desk. We requested them to perform a repetitive motion of the index finger, abducting it towards the bisector of the angle between the thumb and the middle finger with FDI contraction and then adducting it back to the side of the middle finger with FVI activation as rapidly as possible in 10 seconds (Fig. 1-B). Following a few practice trials, the subjects carried out the subsequent test trial. They



**Figure 2**

Technique for recording the F-waves simultaneously from the first dorsal interosseous (FDI) muscles (left) and the first volar interosseous (FVI) muscles (right) after ulnar nerve stimulation at the wrist with the cathode proximal to the anode.

performed the test for both sides separately twice each ; once before and once after the RUNS.

#### 5 . Experiment 3 (Effects of RUNS on the ulnar nerve F-waves in healthy subjects)

Fifteen healthy subjects (13 men) aged 23 to 57 years (mean, 32.0 years) underwent the ulnar nerve F-wave studies on the side of RUNS. The subject lay supine on a table in a quiet room. Electrophysiological study consisted of supramaximally stimulating the ulnar nerve at the wrist and recording the F-wave from the FDI and the FVI simultaneously. We utilized the same bipolar surface stimulator as used for RUNS with the cathode proximal to the anode<sup>9-10</sup>, delivering 0.1-ms width pulses at 120% of the intensity required to elicit the largest CMAPs at 0.2Hz. Two pairs of disk electrodes of 12mm in diameter (NE-142B, Nihonkoh-den, Tokyo, Japan) placed after lowering skin impedance with an abrasive solution served for F-wave acquisition. The recording arrangement comprised the active electrodes (E1) placed over the belly for the FDI and slightly lateral to the midpoint of the volar aspect of the 3rd metacarpal for the FVI<sup>11</sup>, referenced to the electrodes (E2) over the dorsal and the volar aspects of the proximal phalanx of the 2nd digit for the FDI and the FVI, respectively (Fig. 2). A 2-cm wide strap,

**Table 1 Effect of RUNS on grip-and-release rate in CSM patients(Experiment 1).**

Case No	Age(y)/Sex	Level of max cord involvement	Grip-and-release rate(times/10sec)					
			Ipsilateral side to RUNS			Contralateral side to RUNS		
			Baseline	Post-RUNS	<i>P value</i> *	Baseline	Post-RUNS	<i>P value</i> *
1	51/M	C3/4	14	20	NA	35	38	NA
2	53/M	C3/4	12	16	NA	11	14	NA
3	58/F	C4/5	16	19	NA	15	16	NA
4	63/M	C3/4	18	18	NA	19	19	NA
5	67/M	C3/4	13	14	NA	12	12	NA
6	75/M	C3/4	16	17	NA	14	16	NA
7	75/F	C3/4	18	20	NA	20	19	NA
8	77/F	C3/4	11	9	NA	11	11	NA
9	83/F	C4/5	11	15	NA	10	12	NA
Mean ± SD	NA	NA	14.3 ± 2.8	16.4 ± 3.5	<0.02	16.3 ± 7.8	17.4 ± 8.2	<0.03

RUNS, repetitive ulnar nerve stimulation

NA, not applicable

\*Calculated according to the Wilcoxon's signed rank test

wrapped around the hand between the stimulating and recording electrodes, served as the ground electrode. An evoked potential analyzer (Neuropack MEB-9102, Nihonkohden, Tokyo, Japan) registered the evoked potentials with a sampling rate of 10kHz and a filter setting of 20Hz-3KHz.

We measured F-wave defined as a late response with a peak-to-peak amplitude of at least 70 μV<sup>12)</sup>, excluding the late responses with a constant latency and waveform, known as the A-wave, from the evaluation<sup>13-14)</sup>. The subjects underwent the F-wave study twice with 100 stimuli each : once before and once after RUNS.

F-wave measurements included (1) persistence (i. e., the number of definable F responses per 100 stimuli), (2) the minimal onset latency, (3) the mean onset latency and (4) the mean F/M amplitude ratio<sup>15)</sup> (i. e., peak-to-peak F-wave amplitude averaged for only those trials with detectable F responses, termed 'response average'<sup>16-17)</sup>, divided by baseline-to-peak M-wave amplitude).

## 6 . Statistical analysis

We analyzed the data, given as mean ± SD, using Wilcoxon's signed rank test with p<0.05 considered

significant. The software program, GraphPad InStat Version 3.00 (GraphPad software Inc.), was used to conduct all statistical analyses.

## Results

### 1 . Experiment 1

In the spastic CSM patients, RUNS significantly increased the grip-and-release rate on both sides : from the baseline value of 14.3 ± 2.8 times/10sec to 16.4 ± 3.5 times/10sec (p<0.02) on the side of RUNS and from 16.3 ± 7.8 times/10sec to 17.4 ± 8.2 times/10sec (p<0.03) on the contralateral side (Table 1). RUNS similarly affected the grip-and-release rate in the healthy subjects, increasing from the baseline value of 25.0 ± 5.2 times/10sec to 29.0 ± 5.7 times/10sec (p<0.02) on the side of RUNS and from 25.6 ± 4.1 times/10sec to 29.7 ± 5.6 times/10sec (p<0.02) on the contralateral side (Table 2).

### 2 . Experiment 2

In the healthy subjects, RUNS significantly increased abduction-and-adduction rate of the index finger on both sides ; from the baseline value of 21.4 ± 6.1 times/10sec to 24.6 ± 4.8 times/10sec (p<0.03)

**Table 2** Effect of RUNS on grip-and-release rate and abduction-and-adduction rate in healthy patients (Experiments 1 and 2).

Case No	Age (y)/Sex	Grip-and-release rate (times/10sec)					
		Ipsilateral side to RUNS			Contralateral side to RUNS		
		Baseline	Post-RUNS	p value*	Baseline	Post-RUNS	p value*
1	31/M	29	33	NA	29	33	NA
2	48/M	25	27	NA	26	29	NA
3	70/M	25	30	NA	22	28	NA
4	30/M	33	39	NA	32	40	NA
5	74/F	21	23	NA	24	25	NA
6	42/F	25	28	NA	26	30	NA
7	71/F	17	23	NA	20	23	NA
Mean ± SD	NA	25.0 ± 5.2	29.0 ± 5.7	0.0156	25.6 ± 4.1	29.7 ± 5.6	0.0156

Case No	Age (y)/Sex	Abduction-and-adduction rate (times/10sec)					
		Ipsilateral side to RUNS			Contralateral side to RUNS		
		Baseline	Post-RUNS	p value*	Baseline	Post-RUNS	p value*
1	31/M	20	25	NA	24	25	NA
2	48/M	17	20	NA	20	23	NA
3	70/M	24	24	NA	24	25	NA
4	30/M	30	33	NA	37	40	NA
5	74/F	14	23	NA	18	24	NA
6	42/F	28	28	NA	29	31	NA
7	71/F	17	19	NA	17	20	NA
Mean ± SD	NA	21.4 ± 6.1	24.6 ± 4.8	<0.03	24.1 ± 7.0	26.9 ± 6.7	<0.01

RUNS, repetitive ulnar nerve stimulation

NA, not applicable

\*Calculated according to the Wilcoxon's signed rank test

on the side of RUNS and from  $24.1 \pm 7.0$  times/10sec to  $26.9 \pm 6.7$  times/10sec ( $p < 0.01$ ) on the contralateral side (Table 2).

### 3 . Experiment 3

F-wave persistence for the FVI significantly ( $p < 0.01$ ) decreased from the baseline value of  $41.1 \pm 23.1\%$  to  $32.0 \pm 21.5\%$  after RUNS in contrast to the corresponding values for the FDI, which showed no difference ( $44.5 \pm 28.4\%$  vs  $43.0 \pm 24.2\%$ ;  $p > 0.76$ ) (Table 3 and Figs. 3A and B). F-wave mean latency for the FVI significantly ( $p < 0.03$ ) shortened from the baseline value of  $28.8 \pm 2.6$ ms to  $28.0 \pm 1.6$ ms after RUNS, whereas the corresponding measure for the FDI remained unchanged ( $29.0 \pm 2.4$ ms vs  $28.8 \pm 2.3$ ms;  $p > 0.12$ ). RUNS significantly altered neither

F-wave minimal latency nor the response average of F-wave amplitude (F/M ratio) for both the FVI ( $p > 0.63$  and  $p > 0.42$ , respectively) and the FDI ( $p > 0.40$  and  $p > 0.12$ , respectively) (Table 3).

## DISCUSSION

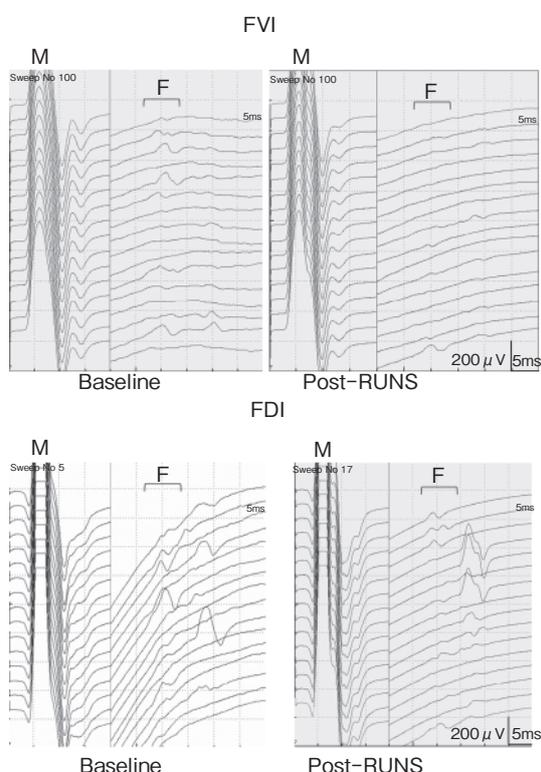
The phenomenon, in which RUNS causes a transient recovery of rapid repetitive finger movements impaired in CSM patients, has received little attention since originally reported by Yamada et al. (2004)<sup>8</sup>. The present study verified and further investigated the effects of RUNS. Our Experiment 1 not only confirmed their findings, but also revealed its similar effect on the contralateral side in CSM patients. The experiment also demonstrated in healthy subjects that a

**Table 3** Effects of RUNS on F-waves in healthy subjects (Experiment 3).

	FVI muscle			FDI muscle		
	Baseline (Mean ± SD)	Post-RUNS (Mean ± SD)	p value *	Baseline (Mean ± SD)	Post-RUNS (Mean ± SD)	p value *
Persistence (%)	41.1 ± 23.1	32.0 ± 21.5	<0.01	44.5 ± 28.4	43.0 ± 24.2	>0.76
Mean F/M amplitude ratio (Response average of amplitude)	1.14 ± 0.3	1.1 ± 0.3	>0.42	0.98 ± 0.4	1.0 ± 0.4	>0.12
Minimal onset latency (msec)	25.5 ± 1.7	25.3 ± 1.6	>0.63	26.0 ± 1.9	26.2 ± 1.4	>0.40
Mean onset latency (msec)	28.8 ± 2.6	28.0 ± 1.6	<0.03	29.0 ± 2.4	28.8 ± 2.3	>0.12

RUNS, repetitive ulnar nerve stimulation

\*Calculated according to the Wilcoxon's signed rank test



**Figure 3**

Raster mode display of 16 consecutive traces showing M responses and F-waves recorded from the first volar interosseus muscle (A) and the first dorsal interosseus muscle (B) before (left) and after (right) conditioning repetitive ulnar nerve stimulation (RUNS) at the wrist in a 29-year-old healthy subject.

unilaterally applied RUNS increased the grip-and-release rate on both sides.

We postulated that RUNS might alter the anterior horn cell excitabilities of the finger extensors, the

flexors or both. In fact, earlier studies demonstrated that supramaximal electrical stimulation of a mixed peripheral nerve or cutaneous nerves suppressed the anterior horn cell excitability<sup>12),18-22)</sup>. Measurement of the F-wave, which results from the backfiring of antidromically-activated anterior horn cells<sup>14)</sup>, provides a useful means to assess excitability changes of the anterior horn cells as previously reported<sup>14),16-17),23-27)</sup>. This technique, however, has a practical limitation when applied to the forearm muscles such as the finger flexors and extensors, because the F-waves from those muscles partially overlap with the M wave, thereby precluding accurate evaluation of the F-waves. Testing the forearm muscles has the additional disadvantage of requiring a comparison of separately conducted F-wave studies on the finger extensors with radial nerve stimulation and on the finger flexors with median or ulnar nerve stimulation. To circumvent these problems, we tested the FDI and FVI muscles simultaneously activated by ulnar nerve stimulation, allowing a direct comparison of excitability changes between the two groups of anterior horn cells, functionally antagonistic to each other.

To evaluate rapid repetitive finger movements for the same muscles as used for the F-wave study, we devised the abduction-and-adduction test of the index finger, as a substitute for the grip-and-release test. Applying this new test on healthy subjects, unilateral RUNS significantly increased abduction-and-adduction rate on both sides (Experiment 2). Associated with this RUNS-induced facilitative effect on the

index finger movements, RUNS reduced the F-wave persistence and shortened its mean latency for the FVI, whereas the corresponding measures for the FDI remained unchanged.

A reduction of F-wave persistence only for the FVI indicates that RUNS preferentially suppressed the anterior horn cells innervating the FVI without equally affecting those supplying the FDI. The response average of F-wave amplitude, however, failed to show the same tendency of suppression possibly because of the large variability in amplitude as suggested previously<sup>12/28)</sup>. A shortening of the mean latency of the F-waves for the FVI coupled with no significant changes in the minimal latency may imply that RUNS-induced suppression affects smaller anterior horn cells having slower-conducting axons. This finding supports the notion that the preferential generation of F-waves by large, fast-conducting motor units prevails even when the motor neuron pool become hypoexcitable<sup>17/29)</sup>.

Considering all these findings revealed in healthy subjects, we postulate that RUNS induces hypoexcitability of anterior horn cells innervating the FVI, which, in turn, may cause facilitative effects on rapid index-finger movements. Because the FVI likely functions as a synergist to the finger flexors, RUNS may also induce suppressive effects on the finger flexors leading to an RUNS-induced increase in the grip-and-release rate in healthy subjects as shown in Experiment 1. A similar mechanism may also underlie the phenomenon of the RUNS-induced recovery of the grip-and-release rate impaired in spastic CSM patients, although the mechanisms of motor control would be different between healthy subjects and CSM patients. If so, the RUNS-induced suppressive influences on the finger flexors may partially rectify 'finger spasticity' where muscle tone of the finger flexors increases more than extensors.

The facilitative effects of the RUNS on the contralateral side demonstrated in Experiments 1 and 2 deserve brief mention. In an earlier study, voluntary muscle activation of the ipsilateral abductor pollicis

brevis significantly facilitated F-waves recorded from the contralateral muscle<sup>30)</sup>. Peripheral afferent input produced by RUNS may alter the excitability in not only ipsilateral but also contralateral anterior horn cells<sup>19)</sup>. This cross effect of RUNS requires further F-wave study on the contralateral side.

## Study Limitation

There is a limitation to our Experiments 1 and 2 that subjects performed a series of test trials only once, after a few practice trials. Analyzing test-retest reproducibility would have excluded the possibility that the improvement in number of repetitions after RUNS might be a learning effect.

## Conclusions

A unilaterally applied RUNS at the wrist with a square wave, 0.1ms in duration and of supramaximal intensity, delivered at a rate of 5/s for 5 minutes, increased the rate of rapid finger movements on both sides in CSM patients and healthy subjects. The RUNS preferentially suppressed the F-waves from the FVI muscle without equally affecting those from the FDI in healthy subjects. This finding may, at least partly, account for the RUNS-induced facilitative effects on rapid repetitive finger movements in CSM patients as well as healthy subjects.

Conflicts of interest and Funding Source (s) : None were declared for all authors.

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