Bio-Medical Materials and Engineering 26 (2015) S803–S809
DOI 10.3233/BME-151372
IOS Press

Sensory electrical stimulation for suppression of postural tremor in patients with essential tremor

Jae-Hoon Heo[a, 1], Ji-Won Kim[a, 1], Yuri Kwon[a], Sang-Ki Lee[a], Gwang-Moon Eom[a,b,*], Do-Young Kwon[c,*], Chan-Nyeong Lee[d], Kun-Woo Park[d] and Mario Manto[e]
[a]*School of Biomedical Engineering, Konkuk University, Choongju, 380-701, Korea*
[b]*Research Institute of Biomedical Engineering, Konkuk University, Choongju, 380-701, Korea*
[c]*Department of Neurology, College of Medicine, Korea University, Ansan, Korea*
[d]*Department of Neurology, College of Medicine, Korea University, Anam, Korea*
[e]*Université libre de Bruxelles, Belgium*

Abstract. Essential tremor is an involuntary trembling of body limbs in people without tremor-related disease. In previous study, suppression of tremor by sensory electrical stimulation was confirmed on the index finger. This study investigates the effect of sensory stimulation on multiple segments and joints of the upper limb. It denotes the observation regarding the effect's continuity after halting the stimulation. 18 patients with essential tremor (8 men and 10 women) participated in this study. The task, "arms stretched forward", was performed and sensory electrical stimulation was applied on four muscles of the upper limb (Flexor Carpi Radialis, Extensor Carpi Radialis, Biceps Brachii, and Triceps Brachii) for 15 seconds. Three 3-D gyro sensors were used to measure the angular velocities of segments (finger, hand, and forearm) and joints (metacarpophalangeal and wrist joints) for three phases of pre-stimulation (Pre), during-stimulation (On), and 5 minute post-stimulation (P5). Three characteristic variables of root-mean-squared angular velocity, peak power, and peak power frequency were derived from the vector sum of the sensor signals. At On phase, RMS velocity was reduced from Pre in all segments and joints while peak power was reduced from Pre in all segments and joints except for forearm segment. Sensory stimulation showed no effect on peak power frequency. All variables at P5 were similar to those at On at all segments and joints. The decrease of peak power of the index finger was noted by 90% during stimulation from that of On phase, which was maintained even after 5 min. The results indicate that sensory stimulation may be an effective clinical method to treat the essential tremor.

Keywords: Essential tremor, postural tremor, sensory stimulation, arms stretched forward, gyro sensor

1. Introduction

Essential tremor is an involuntary trembling of body limbs people without specific diseases known

[1] Jae-Hoon Heo and Ji-Won Kim contributed equally to this work as co-first authors.

[*] Address for correspondence: Gwang-Moon Eom, School of Biomedical Engineering, Konkuk University, Choongju, 380-701, Korea. Tel.: +82-43-840-3764; Fax: +82-43-851-0620; E-mail: gmeom@kku.ac.kr.
Do-Young Kwon, Department of Neurology, College of Medicine, Korea University, Ansan, Korea. Tel.: +82-10-3389-0954; Fax: +82-31-412-5659; E-mail: kwondoya@hanmail.net.

to cause tremor [1]. Essential tremor occurs in 0.3-1.7% of the world's population, 5.5% of 40 to 64 year old, and 10.2% of 65 year olds or over [2]. Important symptoms of essential tremor include postural tremor and action tremor [1, 3-4]. Traditional treatment of essential tremor includes medication and surgery. Medication is ineffective in many cases and has a risk of side-effects, while surgery poses a risk of cerebral hemorrhage, seizure, and schizophrenia [5]. Recently, rTMS was proposed to suppress tremor [6], but it would be impractical for daily use because it is need to long time and big space for observation of suppression of tremor.

Many engineering attempts were made to overcome the limitations in medical approaches. First, mechanical systems were tested on body limbs to add mechanical resistance, such as inertial load [7-8], viscous load [9], and both inertial and viscous load [10], which reduced tremor by 40-80% [7-10]. However, mechanical systems are not entirely prepared to be used in daily life, because they are bulky, with burdensome weight, and not aesthetic.

On the other hand, electrical systems were also used for tremor suppression as Javidan, Prochazkal, and Maneski suggested functional electrical stimulation (FES) as a method for tremor suppression [12-14]. In these studies, electrical motor stimulation (with the intensity greater than motor threshold) was applied to the muscles acting in the direction opposite to the joint movement. The electrical stimulation was controlled in real-time, with the feedback of the movement. It was found that the electrical stimulation was effective in suppressing tremor and would have aesthetical advantage over the mechanical system. However, continuous muscle contraction due to electrical stimulation above motor threshold induces muscle fatigue significantly faster than the voluntary muscle contraction Moreover, real-time control is critical for a reliable performance due to the possible time-delay in the control loop. Another potential difficulty would be the risk of control divergence if the property of the plant (musculoskeletal system) changes.

To overcome the problem in FES methods, sensory stimulation (with the intensity between sensory threshold and motor threshold) to antagonistic muscle pairs with constant intensity was suggested for the tremor suppression, where the suppression was confirmed on the index finger [15]. Sensory stimulation has an advantage over FES it does not induce muscle contraction, leading to muscle fatigue being minimal. Moreover, it does not have a risk of controller divergence because it utilizes constant stimulation. However, the efficacy of sensory stimulation was confirmed only regarding the index finger. Furthermore, the effect was investigated only during stimulation, and the carry-over effect remains unknown.

The aims of this study were to investigate the effect of sensory stimulation on multiple segments and joints of the upper limb and to observe if the effect continues after the simulation was discontinued. The study was performed for the postural tremor, with the task of "arms stretched forward" commonly utilized in the clinical tests [16].

2. Methods

2.1. Subjects

18 outpatients with essential tremor (8 men and 10 women) participated in this study (Table 1). Patients withhold medication for 12 hours before stimulation. Patients were recruited only if they do not have disease related to tremor. This study was approved by the institutional review board of Korea University Hospital and written informed consent was provided by all patients.

Table 1

Subject information

Subject	Gender	Age	Disease Duration	Family history
18	8 Male / 10 Female	68.8 ± 7.7 yrs	17.8 ± 17.6 yrs	11 Yes / 7 No

2.2. Experimental system and procedure

As shown in Figure 1, 3-D gyrosensor (L3G4200D, STMicroelectronics, Germany) was attached dorsally on three segments of the upper limb (index finger, hand, and forearm). Angular velocity measured by sensor was sampled by 100 Hz and wirelessly transmitted to a personal computer via Bluetooth.

Two commercially available electrical stimulators (Walking man 2, Cybermedic, Korea) were used for the stimulation of four muscles (Flexor Carpi Radialis, Extensor Carpi Radialis, Biceps Brachii, and Triceps Brachii), associated with the movements of finger, wrist, and elbow [14-15]. Electrodes of 50 mm×50 mm size were attached on the motor points of target muscles. Constant-current, monopolar, and rectangular stimulation were applied with the frequency of 100 Hz and the pulse-width of 300 μs. The current intensity was increased from 0 mA in 0.2 mA step, until the subjects felt discomfort or the muscle contraction occurred. Then the optimal intensity was defined as the maximum current in this range for each muscle in each subject.

"Arms stretched forward" task was performed for three sessions: pre-stimulation (Pre), during-stimulation (On), and 5 min post-stimulation (P5). One session consisted of three 15s trials, resulting in a total of 9 trials (3 sessions * 3 trials). Five minutes of rest was given to patients between sessions. Both the stimulation and the measurement were performed on the most affected limb.

2.3. Analysis

Digital bandpass filter with passband of 3-12 Hz was used to eliminate low frequency drift and high frequency noise in the sensor signal [17]. Angular velocity of a joint ω_j was derived from those of

Fig.1 Experiment setup

segments as in Eq. (1). In case of metacarpophalangeal (MP) joint, the lower segment was finger and the upper segment was hand. Likewise, for the wrist joint, the lower segment was hand and the upper segment was forearm.

$$\omega_j = \omega_{ls} - \omega_{us} \quad (1)$$

ω_{ls}, ω_{us} : angular velocities of the lower and upper segment of the joint, respectively.

Vector sum of 3-D angular velocities were derived for each segment and joint, and was used for further analyses. Three characteristic variables of root-mean-squared (RMS) angular velocity for 15 s of vector sum, peak power, and peak power frequency were derived from the vector sum. Peak power was defined as a maximum in power spectrum of the vector sum and the peak power frequency as a frequency manifesting the peak power.

Two-way ANOVA was performed for the characteristic variables with two factors of the phase (Pre, On, P5) and segments (finger, hand, and forearm), and also with two factors of phase and joints (MP and wrist). Post-hoc pairwise comparisons (Tukey HSD) were performed for each segment or joint, if any phase effect or interaction was significant. Reduction ratio was also calculated for characteristic variables, if phase effect was significant.

3. Results

Interaction of phase and segment or phase and joint was significant ($p<0.05$) for all characteristic variables except for the peak power frequency. Even for the peak power frequency, phase effect was significant for the segments. Therefore, post-hoc comparisons of phase pairs were performed for all variables. Figure 2 shows the change in characteristic variables with phases and the post-hoc test results. Table 2 shows the reduction ratio for RMS velocity and peak power.

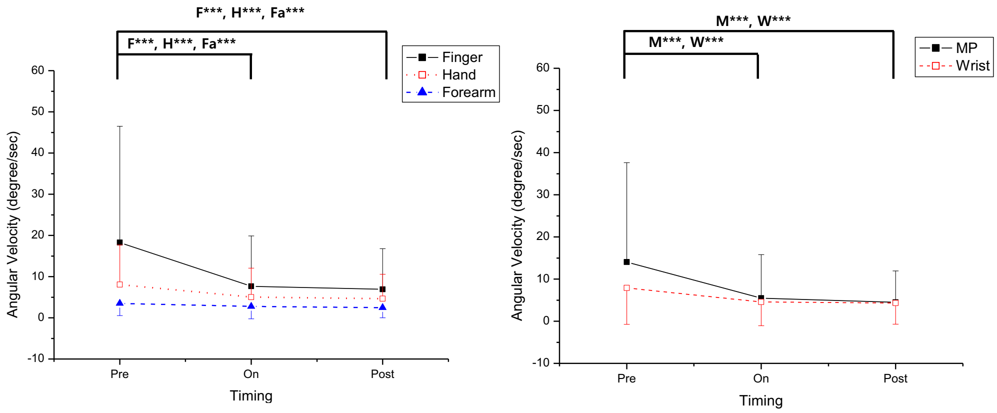
At On phase, both RMS velocity and peak power were reduced from those of Pre in all segments and joints, except for forearm segment ($p<0.05$). Specifically, the reduction ratio of peak power at finger, MP, and wrist was 90%, 77%, and 77%, respectively (Table 2). Peak frequency was not different from Pre phase ($p>0.05$).

P5 phase showed identical results for both RMS velocity and peak power. Specifically, the reduction ratio of peak power at finger and MP were 88% and 89%, which is even better than on phase (Table 2). Peak frequency was reduced at finger segment ($p<0.05$). All characteristic variables at P5 were not different from those at On at all segments and joints ($p>0.05$).

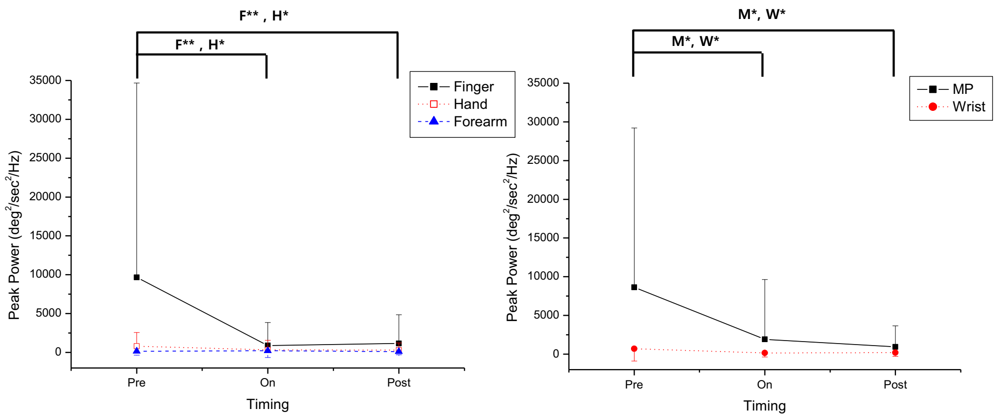
Table 2

Reduction ratio of RMS Angular velocity & peak power compared to Pre phase

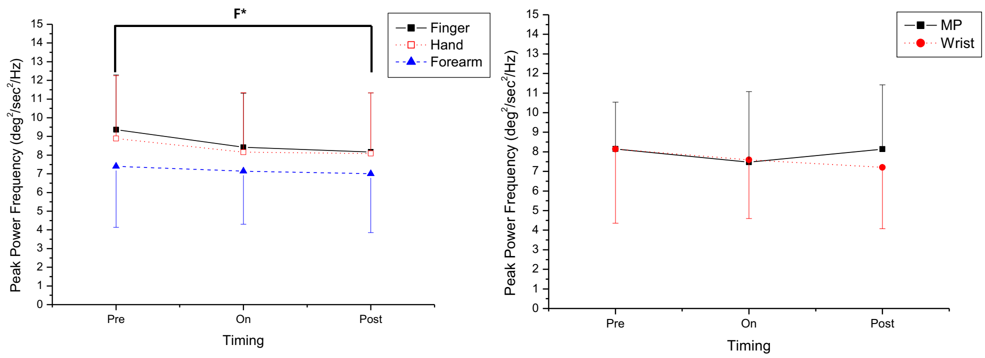
		RMS Average		Peak Power	
		On	P5	On	P5
Segments	Finger	57%	62%	90%	88%
	Hand	37%	41%	58%	61%
	Forearm	21%	29%	-50%	27%
Joint	MP	60%	67%	77%	89%
	Wrist	40%	45%	77%	73%



(a) RMS



(b) Peak power



(c) Peak power frequency

Fig. 2 The effect of sensory stimulation at each segment and joint

Note: *p<0.05, **p<0.01, ***p<0.001. Letter F, H, FA, M, and W preceding the asterisk indicate significant difference existed for each finger, hand, forearm, metacarpophalangeal joint, and wrist joint.

4. Discussion

The main findings of this study are, 1) RMS velocity and peak power are reduced by sensory stimulation in all segments and joints of upper limb (except for the peak power at forearm), and 2) the suppression effect of tremor lasts for at least 5 min.

The reduction in mean (RMS) velocity and peak power is regarded to be closely related. Peak power is the power of the main component of oscillation which has the greatest influence on tremor. Therefore, the reduction of peak power would result in mean velocity, again this indicates the involuntary tremor movement became slower and smaller (tremor amplitude is the integration of the velocity so lower mean velocity leads to smaller mean amplitude).

By the sensory stimulation of four muscles, RMS mean of the tremor velocity was reduced in all segments. The reduction was the greatest in finger segment. This could be due to the reduction of joint movement. The tremor at the upper segment would propagate to the lower segment through interlinking joint. If the joint angular motion is zero, both segments would have the same angular movement. Any nonzero joint motion would worsen or amplify the tremor at the lower segment. Therefore, it is highly probable that the reduction of the joint motion led to reduction of the worse trembling of the lower segment, up to similar tremoring amplitude with the upper segment. This tendency can be clearly observed in Figure 2. The effect of essential tremor on concurrent joint motion and segment motion could be investigated for the first time in this study, owing to simultaneous measurement of multi-segment motion, which is argued to have significance. Information of muscle activities concurrently measured with the motion data would be very helpful to get insight into how the tremor is reduced by sensory stimulation. However, measuring muscle activities during electrical stimulation leads to a complicated experimental setup for elimination of stimulation artifact emerging on the muscle activities. Further study using this setup is encouraged for better understanding of tremor and its reduction.

Another significance of this study is that the suppression effect lasted at least 5 min after the stimulation. This is an impressive result, because it implies the possibility of sensory stimulation as a therapeutic method. However, further investigation is required including the investigation of the long term effect for the therapeutic usage of the sensory stimulation.

It is noted that the main frequency of the movement (peak power frequency) did not change much in this study (Figure 2). On the contrary, the movement frequency decreased by attachment of mechanical resistance such as inertial load [7, 18]. Change in inertial load would alter the resonant frequency of the mechanical system, however sensory stimulation is considered to work on a different mechanism because the main frequency did not change much.

The mechanism of the tremor reduction by sensory stimulation is unknown. The feedback signal through the afferent pathway might have affected the cerebrum, which was suggested to be the source of tremor [4, 11]. Reflex on the spinal level evoked by the electrical stimulation [19] might have reduced the efferent motor commands to the muscles related to the tremor. Further study is required to reveal the detailed mechanism, i.e., if one of or both pathways are responsible for the tremor reduction.

The sensory stimulation system could be easily applied in daily life, by making the system small, light weighted, and aesthetic. Moreover, a demand-type system would also be possible, which applies stimulation only when significant tremor is detected.

The limitations of this study include that the effect was investigated only for the postural tremor, that the elbow joint motion was not measured, and that the long term effect was not investigated.

Acknowledgment

This research was supported by Basic Science Research Program through the National Research Foundation (NRF) of Korea funded by the Ministry of Education (2014R1A1A2057508).

Reference

[1] G. Deuschl, P. Bain and M. Brin, Consensus statement of the movement disorder society on tremor, Ad Hoc Scientific Committee, Movement Disorders: Official Journal of the Movement Disorder Society **13** (1998), 2-23.
[2] E.D. Louis and J.J. Ferreira, How common is the most common adult movement disorder? Update on the worldwide prevalence of essential tremor, Movement Disorders: Official Journal of the Movement Disorder Society **25** (2010), 534-541.
[3] E.D. Louis, Essential tremor, Lancet Neurology **4** (2005), 100-110.
[4] G. Deuschl, R. Wenzelburger, K. Löffler, J. Raethjen and H. Stolze, Essential tremor and cerebellar dysfunction clinical and kinematic analysis of intention tremor, Brain **123** (2000), 1568-1580.
[5] K. Busenbark, P. Barnes, K. Lyons, D. Ince, F. Villagra and W.C. Koller, Accuracy of reported family histories of essential tremor, Neurology **47** (1996), 264-265.
[6] T.A. Zesiewicz, R. Elble, E.D. Louis, R.A. Hauser, K.L. Sullivan, R.B. Dewey, Jr., W.G. Ondo, G.S. Gronseth and W.J. Weiner, Practice Parameter: Therapies for Essential Tremor: Report of the Quality Standards Subcommittee of the American Academy of Neurology, Neurology **64** (2005), 2008-2020.
[7] R.L. Hewer, R. Cooper and M.H. Morgan, An investigation into the value of treating intention tremor by weighting the affected limb, Brain: A Journal of Neurology **95** (1972), 579-590.
[8] M.E. Heroux, G. Pari and K.E. Norman, The effect of inertial loading on wrist kinetic tremor and rhythmic muscle activity in individuals with essential tremor, Clinical Neurophysiology. **122** (2011), 1794-1801.
[9] J. Kotovsky and M.J. Rosen, A wearable tremor-suppression orthosis, Journal of Rehabilitation Research and Development **35** (1998), 373-387.
[10] E. Rocon, J.M. Belda-Lois, A.F. Ruiz, M. Manto, J.C. Moreno and J.L. Pons, Design and validation of a rehabilitation robotic exoskeleton for tremor assessment and suppression, IEEE Transactions on Neural Systems and Rehabilitation Engineering : A Publication of the IEEE Engineering in Medicine and Biology Society **15** (2007), 367-378.
[11] A. Gironell, J. Kulisevsky, J. Lorenzo, M. Barbanoj, B. Pascual-Sedano and P. Otermin, Transcranial magnetic stimulation of the cerebellum in essential tremor: A controlled study, Archives of Neurology **59** (2002), 413-417.
[12] A. Prochazka, J. Elek and M. Javidan, Attenuation of pathological tremors by functional electrical stimulation, I: Method, Annals of Biomedical Engineering **20** (1992), 205-224.
[13] M. Javidan, J. Elek and A. Prochazka, Attenuation of pathological tremors by functional electrical stimulation, II: Clinical evaluation, Annals of Biomedical Engineering **20** (1992), 225-236.
[14] L.P. Maneski, N. Jorgovanovic, V. Ilic, S. Dosen, T. Keller, M.B. Popovic and D.B. Popovic, Electrical stimulation for the suppression of pathological tremor, Medical & Biological Engineering & Computing **49** (2011), 1187-1193.
[15] S.K. LEE, J.W. Kim, Y.R. Kwon, Y.J. Lee, J.H. Lee, G.M. Eom, D.Y. Kwon, C.N. Lee, Y.M. Seo, M.K. Kim, K.W. Park, H.C. Jeong and M. Manto, The effect of sensory stimulation on postural tremor at index finger of patients with essential tremor (ET), Journal of Biomedical Engineering Research **34** (2013), 129-134.
[16] S.E. Fahn, E. Tolosa and C. Marin, Clinical rating scale for tremor, Parkinson's Disease and Movement Disorders **2** (1993), 271-280.
[17] P.H. Mansur, L.K. Cury, A.O. Andrade, A.A. Pereira, G.A. Miotto, A.B. Soares and E.L. Naves, A review on techniques for tremor recording and quantification, Critical Reviews in Biomedical Engineering **35** (2007), 343-362.
[18] Martin Bilodeau, Douglas A. keen, Patrick J. Sweeney, Robert W. Shwelds and Rogers M. Enoka, Strength training can improve steadiness in persons with essential tremor, Muscle & Nerve, 2000, pp.771-778.
[19] B.L. Day, H. Riescher, A. Struppler, J.C. Rothwell and C.D. Marsden, Changes in the response to magnetic and electrical stimulation of the motor cortex following muscle stretch in man, Journal of Physiology **433** (1991), 41-57.