Application of Minute Electrical Noise to Muscle Proprioception Modulates Excitability of Alpha Motor Neuron Group

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Abstract It has been shown that injection of a minute electrical noise to an afferent input enhances the steadiness of force output, while reducing the variability of motor unit discharge intervals. To elucidate the involvement of alpha motor neurons in this noise effect, the effect of electrical noise injection into the soleus muscle (SOL) on the excitability of the alpha motor neuron group was examined. Nine young human subjects lying supine on a bed received a minute, subthreshold electrical white-noise-like stimulation to the SOL. In each subject, a 20-min trial with noise (Noise) and another 20-min trial without noise as control (Con) were performed in random order. The H-waves and M-waves were successively elicited at 1 Hz during each trial. The results showed that the static properties (mean, standard deviation, and coefficient of variation) of H-wave and M-wave amplitude fluctuations were not different between Noise and Con conditions ($p > 0.05$). On the other hand, the scaling exponent α , a dynamic property of the fluctuation of H- and M-wave amplitude, decreased significantly under Noise condition in H-wave amplitude ($p < 0.05$), but was unchanged in M-wave amplitude ($p > 0.05$). These results indicate that application of electrical noise to the afferent input affects the dynamic properties of motor neuron excitability, thus supporting the notion that the motor neurons are involved in the effect of noise injection on the motor control system.

Keywords: fractal, H-reflex, detrended fluctuation analysis.

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1. Introduction

A nonlinear system exhibits an enhanced response to a subthreshold input signal in the presence of minute noise [1]. There is an optimal intensity of noise below the activation threshold, a phenomenon known as stochastic resonance (SR). Based on the SR theory, artificial noise has been applied to human sensory receptors such as the somatosensory receptor to enhance their function [2–5].

Our recent study [6] showed that injection of a minute electrical noise into an afferent nerve (tibial nerve) reduced force fluctuation during an isometric force-matching task of plantar flexion at 5% of maximal voluntary contraction (MVC) intensity. This finding shows that noise intervention also affects motor control in human subjects. As the steadiness of low-intensity force output is an important parameter for daily activities such as postural control [7] and fine hand work [8], noise intervention to enhance motor control would be beneficial to frail individuals.

However, the detailed physiological mechanism underlying the noise intervention effect on motor control remains to be elucidated. One problem to be resolved is the site at which this noise effect actually takes place in the motor control system. A motor

unit is composed of an alpha motor neuron and muscle fibers innervated by this neuron. In our previous study using human subjects [6], we found that fluctuation of the motor unit discharge interval, a determinant of force steadiness, was attenuated by injection of electrical noise into the afferent nerve during a force-matching task at 5% MVC. A previous study demonstrated that the motor neurons in the spinal cord intrinsically showed considerable fluctuation in inter-spike intervals, and this fluctuation was attributed mainly to the synaptic noise that reflects random variations of the membrane potential [9]. The synaptic noise in that study was enhanced by stretching a muscle, and was suggested to be presynaptic in origin; i.e., a summation of small and rapid postsynaptic potentials asynchronously induced by impulses at the presynaptic terminals [9]. Based on these previous results, we hypothesized that the excitability of alpha motor neurons is stabilized by injection of electrical noise into Ia nerve fibers, which transmit the afferent signals from the muscle spindles to the alpha motor neurons. It is possible that the artificial noise transmitted above Ia neurons affect the motor neurons via the monosynaptic input, thus cancelling smaller intrinsic synaptic noise in the resting membrane potential of each neuron. In cat muscle, it has already been reported that the optimal level of mechanical (stretching) noise applied to the synergistic muscles (lateral gastrocnemius and soleus muscles) effectively enhances the H-wave amplitude in the medial gastrocnemius muscle, indicating the presence of the SR phenomenon in the motor system [10]. From the intracellular recordings of action potentials in the motor neurons, the authors attributed the SR effect to the postsynaptic interaction between the noise and the input signal in the motor neurons [10]. Therefore, the effect of applying electrical noise to the afferent nerve on the motor control system may be due to the interaction between noise and motor command in motor neurons.

The purpose of this study was therefore to determine wheth-

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er noise application to the afferent input affects the excitability of motor neuron groups in human subjects. We assessed the static and dynamic properties of excitability of the alpha motor neurons, with or without injection of artificial electrical noise.

2. Method

2.1 Subjects

Four males and five females (22–33 yrs) volunteered for this study. No subjects had experienced any neurological disease. This study was performed in accordance with the Declaration of Helsinki. The study protocol was approved by the Ethics Review Board, Ritsumeikan University Biwako-Kusatsu Campus. Each subject received an explanation of the nature and purpose of the study, and gave written informed consent to participate in it. The subjects were asked to avoid intense exercise, coffee, tea, and alcohol for 24 h before testing.

2.2 Experimental procedures

All measurements were completed in one visit to the laboratory. Each subject lay supine on a bed during the measurement. When each subject arrived at the laboratory, the location of the stimulation electrode (14 mm diameter, P-00-S, Ambu, Denmark) and the stimulation intensity of the electrical noise were determined. A pair of stimulation electrodes was placed at the lateral and medial portions of the soleus muscle (SOL), with the interelectrode distance made as long as possible for injecting the noise into the whole muscle belly (**Fig. 1(a)**). The test leg (right or left) was randomly assigned. The stimulation electrode was connected to a stimulator (SEN-7203, Nihon-Kohden, Japan) that outputs a white-noise-like electrical stimulation (unipolar rectangular pulse, frequency range 5–1000 Hz, pulse duration 0.5 ms) through an isolator device (SS-104J, Nihon-Kohden) [4]. The noise intensity was fixed at well below the individual M-wave-generating threshold in SOL, and was also below the sensory threshold. The subjects all responded that they could not distinguish

which was the trial with noise stimulation when they were asked after completing all measurements (two trials, one with and the other without noise stimulation, as explained below). On the other hand, in order to record H-reflex during noise stimulation, the tibial nerve of the test leg was electrically stimulated by a pair of surface electrodes. H-reflex is a common method to measure the excitability of alpha motor neurons. When the tibial nerve is stimulated by a given intensity of electrical current, the motor axons are activated and the action potentials (M-wave) are recorded by surface electromyography (sEMG) of the SOL (**Fig. 1(b)**). The electrical current also activates Ia fibers and thus causes monosynaptic reflex response (H-wave) in the SOL, following the M-wave (**Fig. 1(b)**). As shown in **Fig. 1(a)**, the cathode (11 mm diameter, N-00-S, Ambu) was placed on the tibial nerve at the popliteal fossa, and the anode (75 mm × 47 mm, HV-BIGPAD, OMRON, Japan) on the anterior thigh, both connected to a stimulator (SEN-7203, Nihon-Kohden) through an isolator device (SS-104J, Nihon-Kohden). The stimulus was a unipolar rectangular pulse at 110% intensity of the M-wave generation threshold with a pulse duration of 0.5 ms. EMG bipolar electrodes (Ag/AgCl, 4 mm diameter, 2 cm interelectrode distance) were fixed to the posterior portion of the SOL, between the electrodes for noise injection (**Fig. 1(a)**). The reference electrode was placed on the lateral malleolus. The EMG signal was differentially amplified and high-pass filtered at 5 Hz (AB-610J, Nihon-Kohden). The EMG data were sampled at 10 kHz (PowerLab 16/30, AD Instruments, Sydney, Australia).

For each subject, two 20-min trials were performed; one with noise-like electrical stimulation (Noise) and the other without as control (Con). The two trials were performed in random order, with a 20-min rest interval. During each trial, we elicited H-reflexes consecutively at a frequency of 1 Hz (**Fig. 1(b)**) [11, 12]. The peak-to-peak amplitude was determined for each of the M- and H-wave. Consequently, time series of peak-to-peak amplitude data (1200 points long) was obtained separately for M- and H-waves.

In our previous study [6], the electrical noise was injected into the tibial nerve at the popliteal fossa. On the other hand, our pilot study revealed that simultaneous stimulation of the tibial nerve for both injecting electrical noise and eliciting the H-reflex failed to ensure a constant stimulation intensity for the H-reflex, as indicated by nonconstant M-wave amplitude. We therefore decided to apply noise stimulation to the muscle belly of the SOL, because other reports suggest that percutaneous electrical noise stimulation also affects the underlying proprioceptive receptors [4, 13, 14]. Another previous study [9] showed that the synaptic noise in the alpha motor neuron was enhanced by stretching a muscle via synaptic input, by activating the underlying muscle proprioception.

2.3 Data analysis

The static and dynamic properties of H-wave amplitude fluctuation were evaluated under Noise and Con conditions. As measures of the static properties, the mean, standard deviation (SD), and coefficient of variation (CV) of the 1200-point data were calculated. On the other hand, as the time series of the H-wave amplitude has been shown to be fractal [11], we employed detrended fluctuation analysis (DFA), a fractal analysis [15, 16], to assess the dynamic properties of the fluctuation. The DFA was a modified root

Fig. 1 (a) Diagram showing locations of the sEMG bipolar electrodes and reference electrode, and a pair of electrodes for noise injection in SOL. H-reflex is evoked by electrical stimulation of tibial nerve at the popliteal fossa. (b) Typical example of the M- and H-waves evoked at a frequency of 1 Hz (upper panel) and an enlarged portion of a single pair of M- and H-waves (lower panel). Stimulation artifact is also recorded.

mean square analysis of a random walk, specifically developed for biological data that quantifies the scaling exponent α for the integrated time series [15, 16].

The same measures (mean, SD, CV, and scaling exponent α) were calculated for the time series of M-wave amplitude to assess whether the changes in the static and dynamic properties of the H-wave amplitude fluctuation were accounted for by those of M-wave amplitude. In addition, surrogate H-wave data created by randomly shuffling the order of the original sequences were also analyzed by DFA to confirm whether the result of DFA actually reflects its dynamic property.

In the statistical analysis, the normality of data distribution was checked by a Kolmogorov-Smirnov test. As a result, a Wilcoxon signed-ranks test was performed to compare each measure between Noise and Con conditions. Statistical significance was set at $p < 0.05$. Descriptive statistics included the group mean and SD.

3. Results

As summarized in Table 1, the mean, SD, and CV of the H-wave amplitude were not different between Noise and Con conditions ($p > 0.05$). There were also no differences in mean, SD, and CV of the M-wave amplitude. Thus, noise injection did not change the static properties of the H-wave or M-wave amplitude.

The DFA for the H-wave amplitude showed that the scaling exponent α decreased significantly under Noise condition [0.96 (0.09) and 0.91 (0.05) for Con and Noise, respectively, $T = 5$, effect size $d = 0.69$, $p < 0.05$] (Fig. 2). On the other hand, α was not different between Con and Noise conditions for the M-wave amplitude ($p > 0.05$). The α value for the shuffled H-wave time series was close to 0.5 under each condition, with no significant difference ($p > 0.05$). These findings indicated that the shuffled time series were random white noise under each condition, with no relationship between consecutive data points. Thus, the result for shuffled data confirmed that the difference in α for the H-wave amplitude actually reflects the difference in the dynamic properties of the fluctuation between the two conditions.

4. Discussion

In the present study, the effect of noise injection into the SOL on the excitability of the alpha motor neuron group was studied in young human subjects. The results showed, for the first time, that

noise injection changed the dynamic properties of H-wave amplitude fluctuation but did not change its static properties (mean, SD, and CV). It may be argued that the small number of subjects may have affected the statistical results of the present study. A previous study on seven subjects whose age distribution was similar to the subjects of the present study revealed a significant effect of noise application on the static measures of the motor control system, such as CVs of force fluctuation and motor unit inter-spike interval during force-matching task [6]. It is therefore unlikely that the non-significant changes in static properties of the M- or H-wave amplitude time series by noise injection (Table 1) was due to an insufficient number of subjects.

Another concern is that the change in H-wave dynamic property observed in the present study was due to the changes in electrical properties of the muscle membrane or neuromuscular junction. Regarding this point, we demonstrated that the static and dynamic properties of M-wave amplitude, which reflect the electrical properties of the muscle membrane and neuromuscular junction, were not different between Noise and Con conditions. These results therefore indicate that the change in the dynamic property of H-wave amplitude fluctuation was not due to the muscle membrane or neuromuscular junction, but actually reflects changes in the excitability of motor neurons (Table 1).

In the DFA, when the scaling exponent α equals 0.5, the original time series is considered a white noise. The $1/f$ fluctuation (pink noise) and brown noise have $\alpha = 1$ and $\alpha = 1.5$, respectively [15, 16]. Therefore, the present result showing that the electrical noise reduced the averaged α value from nearly 1.0 indicated that the H-wave amplitude fluctuation shifted from pink to white noise. As the physiological mechanism and meaning of pink noise in the physiological parameters remain to be elucidated, how much the change in the α value in the present study influences the physiological parameters of the motor control system cannot be determined. However, it should be noted that the dynamic property of the fluctuation of H-wave amplitude; i.e., the excitability of the alpha motor neuron group, differed between the Noise and Con trials, providing evidence that the noise injection procedure actually affects the excitability of the alpha motor neuron group. Previous study has shown that the H-wave amplitude in the cat medial gastrocnemius muscle was enhanced by the optimal intensity of mechanical noise applied to the peripheral synergistic muscles, due to the postsynaptic interaction between in-

Table 1 Group means of static property measures in H-wave and M-wave amplitude under Con and Noise conditions and results of statistical analyses. Values are expressed as group means (SD). p values obtained by Wilcoxon signed-ranks tests are indicated.

		Mean (SD)		p
		Con	Noise	
Mean	H-wave	2.30(1.15)	2.13(0.92)	0.678
	(mV)			
	M-wave	0.584(0.428)	0.581(0.494)	0.374
	(mV)			
SD	H-wave	0.478(0.313)	0.400(0.190)	0.213
	(mV)			
	M-wave	0.0972(0.0980)	0.0814(0.0846)	0.441
	(%)			
CV	H-wave	22.7(10.0)	20.5(8.8)	0.260
	(%)			
	M-wave	14.7(6.5)	13.0(8.0)	0.314
	(%)

Fig. 2 Group data for scaling exponent α obtained from DFA for time series of H-wave, M-wave, and shuffled H-wave under Con (open bar) and Noise (closed bar) conditions. * $p < 0.05$. The data are expressed as means and SD.

put noise and monosynaptic reflex input in the alpha motor neurons [10]. Generally, the receptor potential of sensory neurons is converted to action potential at the trigger zones of the axon [17]. Therefore, it can be speculated that, in the present study, the impulses of artificial electrical stimulation are transmitted from the large-diameter peripheral afferent nerves located under the stimulating electrodes, converted to afferent action potentials at the trigger zones of axons with random discharge intervals, and finally transmitted to the motor neurons via monosynaptic input. Thus, the dynamic property of noise stimulation (white-noise-like stimulation between 5–1000 Hz) would be reflected by changes in the dynamic property of H-wave amplitude fluctuation, quantified by the scaling exponent α . On the other hand, our previous study found that the electrical noise injection attenuated both the fluctuation of the motor unit discharge interval and that of the force output during the force matching task at 5% MVC [6]. Regarding this point, further experimental or simulation studies are required to assess the mechanism by which the shift of dynamic properties to white noise in alpha motor neurons accounts for the stability of motor unit discharges during low muscle force output.

Application of the noise effect to sensorimotor control systems such as postural control system has been extensively reported. Specifically, enhancement of somatosensation in the control system has been studied. For example, postural sway was attenuated by noise-like vibration applied to the soles of the feet [18, 19] or to the fingertip [5], and by electrical noise injected into the knee joint [4, 20]. Also, the effect of noise intervention on the dynamic property of postural fluctuation was reported [19]. Thus, while previous studies have revealed the noise effect on postural sway measures, our recent study [6] showed that injection of a minute electrical noise into an afferent nerve attenuated the fluctuation of the motor unit discharge interval during a force-matching task at 5% MVC. Furthermore, the present result showed that the injected noise significantly changed the dynamic property of the H-wave amplitude. Therefore, the present result, suggesting a possible change in excitability of alpha motor neurons in the presence of noise stimulation, would be helpful for further understanding of the neural mechanism of the noise effect, especially the dynamic property of the sensorimotor control system. From the viewpoint of biomedical engineering, the present findings would help further develop noise intervention as a flexible method. In other words, understanding of the neural mechanism underlying the noise intervention effects would be helpful for practically optimizing its modality, intensity, frequency range, and dynamic property in order to achieve maximal effects of noise, which may vary from subject to subject.

5. Conclusion

Electrical noise injected into the skin over the muscle affects the dynamic property of the H-wave amplitude fluctuation, with the possibility that the noise is transmitted to the alpha motor neurons by monosynaptic input. Further studies are needed to explore how the change in the dynamic property influences the motor control system.

Conflict of Interest

The authors declare that they have no conflict of interest.

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References

1. Douglass JK, Wilkens L, Pantazidou E, Moss F: Noise enhancement of information transfer in crayfish mechanoreceptors by stochastic resonance. *Nature*. **365**(6444), pp. 337–340, 1993.
2. Collins JJ, Imhoff TT, Grigg P: Noise-enhanced tactile sensation. *Nature*. **383**(6603), pp. 770, 1996.
3. Collins JJ, Imhoff TT, Grigg P: Noise-mediated enhancements and decrements in human tactile sensation. *Phys Rev E*. **56**(1), pp. 923–926, 1997.
4. Kimura T, Kouzaki M: Electrical noise to a knee joint stabilizes quiet bipedal stance. *Gait Posture*. **37**(4), pp. 634–636, 2013.
5. Kimura T, Kouzaki M, Masani K, Moritani T: Unperceivable noise to active light touch effects on fast postural sway. *Neurosci Lett*. **506**(1), pp. 100–103, 2012.
6. Kouzaki M, Kimura T, Yoshitake Y, Hayashi T, Moritani T: Sub-threshold electrical stimulation reduces motor unit discharge variability and decreases the force fluctuations of plantar flexion. *Neurosci Lett*. **513**(2), pp. 146–150, 2012.
7. Kouzaki M, Shinohara M: Steadiness in plantar flexor muscles and its relation to postural sway in young and elderly adults. *Muscle Nerve*. **42**(1), pp. 78–87, 2010.
8. Marmon AR, Pascoe MA, Schwartz RS, Enoka RM: Associations among strength, steadiness, and hand function across the adult life span. *Med Sci Sports Exerc*. **43**(4), pp. 560–567, 2011.
9. Calvin WH, Stevens CF: Synaptic noise and other sources of randomness in motoneuron interspike intervals. *J Neurophysiol*. **31**(4), pp. 574–587, 1968.
10. Martinez L, Perez T, Mirasso CR, Manjarrez E: Stochastic resonance in the motor system: effects of noise on the monosynaptic reflex pathway of the cat spinal cord. *J Neurophysiol*. **97**(6), pp. 4007–4016, 2007.
11. Nozaki D, Nakazawa K, Yamamoto Y: Fractal correlation in human H-reflex. *Exp Brain Res*. **105**(3), pp. 402–410, 1995.
12. Nozaki D, Nakazawa K, Yamamoto Y: Supraspinal effects on the fractal correlation in human H-reflex. *Exp Brain Res*. **112**(1), pp. 112–118, 1996.
13. Magalhaes FH, Kohn AF: Imperceptible electrical noise attenuates isometric plantar flexion force fluctuations with correlated reductions in postural sway. *Exp Brain Res*. **217**(2), pp. 175–186, 2012.
14. Magalhaes FH, Kohn AF: Effectiveness of electrical noise in reducing postural sway: a comparison between imperceptible stimulation applied to the anterior and to the posterior leg muscles. *Eur J Appl Physiol*. **114**(6), pp. 1129–1141, 2014.
15. Peng CK, Hausdorff JM, Goldberger AL: Fractal mechanism in neuronal control: human heartbeat and gait dynamics in health and disease. In: Walleczek J ed. *Self-Organized Biological Dynamics and Nonlinear Control*, Cambridge University Press, UK, pp. 66–96, 2000.
16. Peng CK, Havlin S, Stanley HE, Goldberger AL: Quantification of scaling exponents and crossover phenomena in nonstationary heartbeat time series. *Chaos*. **5**(1), pp. 82–87, 1995.
17. Kandel ER: Nerve cells and behavior. In: Kandel ER, Schwartz JH, Jessell TM ed. *Principles of Neural Science*, McGraw-Hill, New York, pp. 19–35, 2000.
18. Priplata A, Niemi J, Salen M, Harry J, Lipsitz LA, Collins JJ: Noise-enhanced human balance control. *Phys Rev Lett*. **89**(23),

pp. 238101, 2002.

19. Priplata AA, Niemi JB, Harry JD, Lipsitz LA, Collins JJ: Vibrating insoles and balance control in elderly people. *Lancet*. **362**(9390), pp. 1123–1124, 2003.
20. Gravelle DC, Laughton CA, Dhruv NT, Katdare KD, Niemi JB, Lipsitz LA, Collins JJ: Noise-enhanced balance control in older adults. *Neuroreport*. **13**(15), pp. 1853–1856, 2002.

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