Effects of Noise Electrical Stimulation on Proprioception, Force Control, and Corticomuscular Functional Connectivity

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***Abstract*— Sensory afferent inputs play an important role in neuromuscular functions. Subsensory level noise electrical stimulation enhances the sensitivity of peripheral sensory system and improves lower extremity motor function. The current study aimed to investigate the immediate effects of noise electrical stimulation on proprioceptive senses and grip force control, and whether there are associated neural activities in the central nervous system. Fourteen healthy adults participated in 2 experiments on 2 different days. In day 1, participants performed grip force and joint proprioceptive tasks with and without (sham) noise electrical stimulation. In day 2, participants performed grip force steady hold task before and after 30-min noise electrical stimulation. Noise stimulation was applied with surface electrodes secured along the course of the median nerve and proximal to the coronoid fossa EEG power spectrum density of bilateral sensorimotor cortex and coherence between EEG and finger flexor EMG were calculated and compared. Wilcoxon Signed-Rank Tests were used to compare the differences of proprioception, force control, EEG power spectrum density and EEG-EMG coherence between noise electrical stimulation and sham conditions. The significance level (alpha) was set at 0.05. Our study found that noise stimulation with optimal intensity could improve both force and joint proprioceptive senses. Furthermore, individuals with higher gamma coherence showed better force proprioceptive sense improvement with 30-min noise electrical stimulation. These observations indicate the potential clinical benefits of noise stimulation on individuals with impaired proprioceptive senses and the characteristics of individuals who might benefit from noise stimulation.**

***Index Terms*— Noise, stochastic resonance, neuromuscular control, EEG-EMG coherence.**

I. INTRODUCTION

SENSORY afferent inputs play an important role in neuromuscular functions. Within the sensory information, proprioceptive inputs, including joint and muscle force senses, heavily influence the modulation of sensorimotor control [1]. It has been reported that force control is impaired or reduced in temporary nerve block conditions [2], [3], [4], [5] and chronically deafferented patients [6], [7], [8]. The findings from these studies concluded that a lack of intact somatosensory information reduces maximal force production and precise force control. Proprioception dysfunction caused by aging or diseases can impair force control resulting in functional impairments [9]. Therefore, it is important to identify methods for modulating sensory afferent inputs to enhance or regain motor function.

Electrical stimulation applied to the periphery elicits sensory afferent input in the central nervous system. With direct and indirect neural connections between the sensory and motor cortices [10], sensory afferent inputs elicited by peripheral electrical stimulation can induce plastic changes in the healthy [11], [12] and injured brains [13], [14], [15]. It has been reported that repetitive peripheral electrical stimulation enhances the excitability, expands motor map of the motor cortex [16], [17], [18], [19], [20], [21], and increases neural activity in the sensorimotor cortex [22], [23], [24]. In addition, repetitive peripheral electrical stimulation has been found to improve motor learning [25] and motor function in healthy adults and patients with stroke [26], [27], [28].

Recently, a new type of electrical stimulation, noise stimulation, has been introduced. Noise inducing stochastic reso-

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nance phenomenon has been identified in the central nervous system [29] and has been observed in the human skin and muscle sensory organs [30], [31]. Noise in the nervous system induces trial-to-trial variability [32] and improves the detectability of weak neural signals [33]. Animal studies have found that noise stimulation can lower neural activation thresholds [34], [35] and enhance the sensitivity of subthreshold sensory stimuli detection [36], [37]. Human studies with noise stimulation applied to the lower extremity showed improvements in motor function, including balance or walking ability, in healthy adults [38], elderly [39], [40], and patients with neurologic or orthopedic disorders [41], [42].

Noise stimulation has been applied in the form of vibration and electrical stimulation. Previous studies have found that the intensity of noise electrical stimulation has a significant effect on the sensorimotor performance. Comparing noise stimulation with various intensities, a previous study reported that stimulation intensity below sensory thresholds improved balance performance, while stimulation intensity above sensory thresholds increased posture sway [43]. Furthermore, previous studies have used stochastic resonance stimulation with an intensity of 90% of the sensory threshold and showed that lower extremity muscle force control and balance were both improved [44], [45]. In addition, our previous work using noise stimulation over the mastoid process found that the treatment improved postural stability in patients with bilateral vestibular hypofunction [46].

Hand function is very important in daily living, and grip force control and hand/wrist proprioception are essential for hand function. From clinical perspective, both aging and central nervous system injuries affect upper extremity function, and distal part of the extremity (hand and wrist) are usually more severely affected. Although previous studies have shown the benefits of noise stimulation on lower extremity function, how sub-sensory level stochastic resonance stimulation improves upper extremity function and whether there are associated neural activities in the central nervous system remains unclear. Therefore, this study aimed to investigate the immediate effects of 30-min stochastic resonance electrical stimulation on hand force and joint proprioceptive sense, cortical activation, and functional connectivity between the cortex and muscles.

II. MATERIAL AND METHODS

A. Participants

Fourteen right-handed healthy adults (female: male = 6: 8; 23.6 ± 3.3 years old) without neurological and musculoskeletal disorders of their upper extremity voluntarily participated in this study. The study was conducted in accordance with the Declaration of Helsinki. Informed consent from all participants were obtained before the experiments. The experimental protocol was approved by Institute Review Board of Taipei Veteran General Hospital (2017-08 - 010C).

B. Experimental Procedures

This study consisted of 2 experiments and was conducted on 2 different days. Experiment 1 was conducted to investigate the immediate effects of noise stimulation on force and joint angle proprioceptive senses. Experiment 2 was conducted to investigate the effects of 30-minute continuous noise stimulation on grip force control and corticomuscular connectivity. During both experiments, participants sat comfortably in front of a computer screen with their dominant arm rested on a desk. Noise stimulation (neuroConn DC stimulator, neuroCare Group, Germany) was applied with surface electrodes secured along the course of the median nerve and proximal to the coronoid fossa (Figure 1). Hand grip force was measured using a dynamometer (Jamar, G200, Biometrics, UK). Wrist joint angle was measured using twin-axis electrogoniometer (SS20L/21L, Biopac, USA). EMG of finger flexors was recorded using surface electrodes (Foam Electrodes, Cardinal Health, USA) placed on the muscle belly. Grip force and EMG data were filtered, amplified (P511 AC Amplifier, Grass, USA) and digitized (Power 1401, CED, UK) for subsequent analysis. EEG of bilateral sensorimotor cortex was recorded simultaneously using 16-channel active electrodes (actiCAP and V-Amp, Brain Products, Germany).

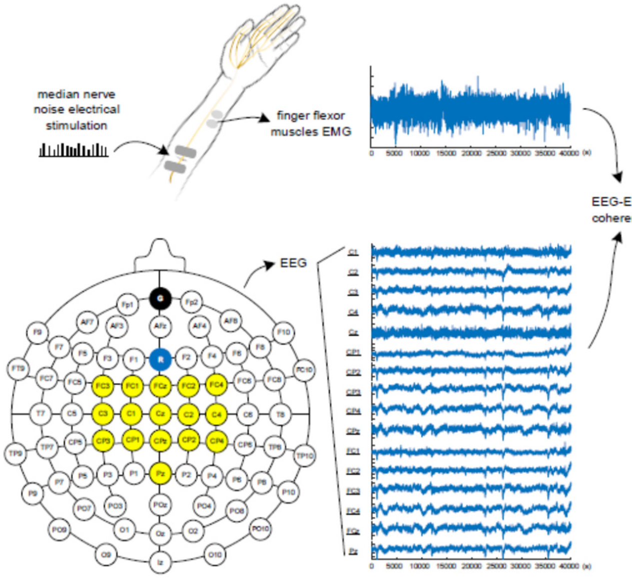

Fig. 1. Experimental setup. Bilateral sensorimotor cortex EEG signals and surface EMG of finger flexor muscles of the dominant hand were recorded and analyzed. Noise electrical stimulation was applied along the course of the median nerve above the coronoid fossa.

In Experiment 1, the participants' force and joint proprioceptive sense were evaluated under noise electrical stimulation and sham. For the force sense experiment, each participant held the dynamometer with their grip force displayed in real time on a computer screen in front of them. Three maximal voluntary contractions (MVC) with a 3-minute rest in between were performed first. The target of each participant's 30% MVC was displayed along with the real time grip force on the screen before they practiced generating grip force to match the target line for 1 minute. The screen was then turned off and each participant was asked to generate a grip force of 30% MVC for 5 times. They were asked to press a switch button each time when they "felt" their grip force was at 30% MVC. Pressing the switch button generated a TTL (Transistor-transistor logic) signal, which was recorded simultaneously with the force signal for subsequent analysis. This procedure was repeated 4 times at 4 different noise stimulation intensities (0, 70, 90 and 100% of sensory threshold) with random order. A similar procedure was executed for joint proprioceptive sense testing. The target wrist flexion angle for the participant to reach was 30°. Each participant practiced flexing the wrist to 30° for 1 minute with visual feedback from a computer screen. The screen was then turned off and each participant was asked to generate 30° wrist flexion for 5 times. They were asked to press a switch button each time they "felt" that they had reached 30° wrist flexion. This procedure was repeated 4 times at 4 different noise stimulation intensities (0, 70, 90 and 100% of sensory threshold) applied with random order.

In Experiment 2, the effects of noise stimulation on force control and corticomuscular connectivity were investigated. Participants were positioned in the same experimental setup as described in Experiment 1. Participants performed a 30-second steady hold contraction at 30% of MVC before, during and after a 30-minute session of noise stimulation, with visual feedback of real-time grip force and 30% of MVC target line displayed on a screen in front of the participant. It has been demonstrated that this experimental protocol could successfully detect beta and gamma corticomuscular coherence in healthy adults [47]. The intensity of noise stimulation was determined based on the best force proprioception results among the 4 noise stimulation intensities from Experiment 1 for each participant. EEG of bilateral sensorimotor cortex and EMG of finger flexors were collected during the 30-second steady hold contraction.

C. Data Analysis

For Experiment 1, the time points when the participants pressed the switch button were first identified. Next, force and joint proprioceptive senses were evaluated by calculating the difference between the targeted line (30 degrees and 30% of MVC) and the actual joint angle and force output at each of the time points. The results from 5 trials were averaged for each of the noise stimulation intensities for each participant.

For Experiment 2, the accuracy and stability of the steady hold grip force, as well as EEG and EMG activities were analyzed for both the pre- and post-noise stimulation conditions. The accuracy of the steady hold force was calculated by the averaged differences between the actual and target forces over the 30-second period. The stability of the steady hold force was determined by calculating the variance (squared deviation from the mean) of the actual force output over the entire 30-second session. EEG signals from bilateral sensorimotor cortex were filtered and eye-blinking artifact were removed using Independent Component Analysis (EEGLAB) [48]. To focus on the sensorimotor cortex area corresponding to the right hand, we selected EEG channel C3 for subsequent analysis. The mean power in alpha (8-12 Hz), beta (15-30 Hz) and low gamma (30-60 Hz) frequency bands were calculated and compared.

The connectivity between the motor cortex and muscles was determined by corticomuscular coherence (CMC, EEG-EMG coherence). EEG of C3 electrode and EMG signals were processed offline with MATLAB (The MathWorks, USA) to calculate the CMC based on the following equation [49]:

$$|Cxy(f)| = \frac{|\overline{\mathrm{P}xy(f)}|^2}{\mathrm{P}xx(f)\cdot\mathrm{P}yy(f)} \tag{1}$$

C_{xy}(f) is the coherence between x and y in frequency domain and can be calculated via Equation (1). In this study, P_{xx}(f) and P_{yy}(f) represent the power spectral density (PSD) of EEG or EMG in frequency domain; P_{xy}(f) represents the cross PSD between EEG and EMG in frequency domain. The signals were analyzed within a 2048-sample epoch with 50% overlap. The length of the signal is 30 seconds and the resolution of frequency is 0.98 Hz.

Since only CMC values that exceed a theoretical threshold represent physiologically meaningful functional connections [49], theoretical threshold of coherence $\gamma_{th}^2(\alpha)$ was calculated at the significance level of 0.05 (α) with equation 2 and the value was corrected with equation 3-5 [50].

$$\gamma_{\mathrm{th}}^2(\alpha) = 1-\alpha^{\frac{1}{\tilde{k}-1}} \tag{2}$$

$$\tilde{k} = \frac{k}{Cw(D)} \tag{3}$$

$$\mathrm{Cw}(\mathrm{D}) = 1 + 2\left(\frac{\mathrm{k}-1}{\mathrm{k}}\right)\rho_{\mathrm{w}}^2(\mathrm{D}) \tag{4}$$

$$\rho_w(D) = \frac{\sum_{t=0}^{L-D-1} w_L(t)\, w_L(t+D)}{\sum_{t=0}^{L-1} w_L^2(t)} \tag{5}$$

In the equations, k is the number of non-overlapping segments, and $\tilde{k}$ indicates the number of segments with 50% overlapping. D is the non-overlapping length (delay time) of each two segments, and L is the length of each segment. $W_L(t)$ is a window function with t = 0, …, L-1. The CMC was evaluated between 0-60 Hz. Because the motor task performed in this study was steady hold contractions at 30% MVC, we focused on beta (15-30 Hz) and lower gamma (30-60 Hz) band CMC, as these frequency bands are found to be more dominant during moderate, [51] static, [52] and isometric [53] muscle contractions. The summation of the area that is above the critical threshold within each frequency band was calculated and referred to as the CMC value.

D. Statistical Analysis

Because our data showed non-parametric distributions, Wilcoxon Signed-Rank Tests were used to compare the differences of proprioception, force control, EEG PSD and corticomuscular coherence between noise electrical stimulation and sham. The significance level (alpha) was set at 0.05.

III. RESULTS

The current study investigated the effects of noise electrical stimulation on force and joint proprioceptive sense of the hand. Across the 4 different noise stimulation intensities, we observed a tendency that better force and joint proprioceptive performances were respectively achieved with 70% and 100% of the sensory threshold stimulation. However, the optimal noise stimulation intensity was different among the participants. For our 14 participants, the number of participants had their optimal stimulation intensity at 70%, 90% and

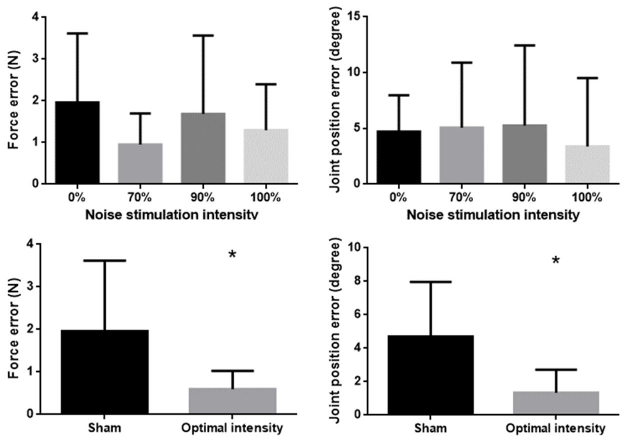

Fig. 2. Force (left) and joint (right) proprioceptive senses performance across different noise electrical stimulation intensities. The upper panels show force and joint proprioceptive sense performance during intensities at 0, 70, 90 and 100% of sensory thresholds. The lower panels show the comparison of proprioceptive sense performance between sham (0% intensity) versus the noise electrical stimulation at optimal intensity (optimal intensity was different for different participants). * indicates statistical significance.

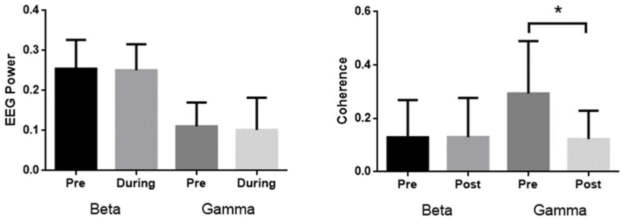

Fig. 3. EEG power spectrum density (PSD, left) and corticomuscular coherence (CMC) (right) in beta and gamma bands during noise electrical stimulation. * indicates statistical significance.

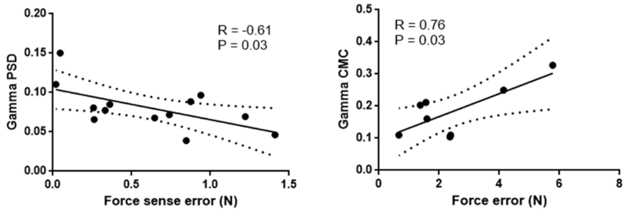

Fig. 4. Left panel: Relationship between EEG gamma band power and force proprioceptive sense errors during noise electrical stimulation. Right panel: relationship between Gamma CMC and force control error after noise stimulation.

100% of the sensory threshold were 5, 3, and 6 participants, respectively.

Comparing the effects of optimal stimulation intensity vs sham (0% intensity) on proprioceptive senses, we observed significantly better performance in both force and joint proprioceptive senses (both p values < 0.05) (Fig 2). On average, force and joint proprioceptive sense improved 69% and 71%, respectively

We investigated how the participants' force control performance (maintaining grip force at 30% MVC) was affected by noise electrical stimulation. Compared to sham, we observed a trend of 6% decrease and a 15% increase in force control error respectively during and after noise electrical stimulation; however, these comparisons were not statistically significant, suggesting that the participants did not perform better either during or after the 30-min noise stimulation.

This study also investigated how noise stimulation at the optimal intensity level affects the central nervous system. Our results demonstrated that noise stimulation did not induce immediate change in EEG beta or gamma band power. Nevertheless, after 30-minute noise stimulation, our data indicated that the functional connectivity between the motor cortex and active muscles was modulated. We found that the CMC of the C3 electrode and finger flexor EMG in the gamma band decreased significantly when compared to the value before the stimulation ($P < 0.05$) (Fig 3).

We also investigated whether motor performance and neural activities in the motor cortex are correlated when noise stimulation is applied. We observed that the participants' force proprioception error during noise stimulation was negatively and moderately correlated with EEG gamma band power ($r = -0.61$; $P = 0.03$), which suggested that participants demonstrating better force proprioceptive performance during noise electrical stimulation exhibited greater EEG gamma band power. It was also observed that after the 30-minute noise electrical stimulation, force control error was positively correlated with CMC gamma band ($R = 0.76$; $P = 0.03$), suggesting a connection between better force control performance with lower gamma band coherence (Fig 4).

IV. DISCUSSIONS

Noise stimulation has been used to improve motor performance in humans [38]. In the form of vibration, noise stimulation from the insole has been found to reduce postural sway, improve balance [39], and reduce gait variability [40] in the elderly and individuals with diabetes and stroke [41]. Noise stimulation can also be applied in the form of an electrical stimulation. A previous study indicated that patients with ankle instability had improved postural stability when noise electrical stimulation was applied over the triceps surae muscle belly [42]. Noise stimulation can also improve the hand motor performance. A visuomotor task that involved using a finger to control the position of a manipulandum had higher accuracy when stochastic noise was applied on the manipulandum [54]. Moreover, this study also reported that noise stimulation in the periphery induced neural responses in the cortex. The investigators found that the EEG power in the beta-gamma band and functional connectivity between the motor cortex and finger muscles (EEG-EMG coherence) increased during noise stimulation. The benefits of noise stimulation were also observed in post-stroke individuals. Vibrotactile stimulation with noise improved light touch sensation of the fingertips, and improvements were observed in all stimulation intensities (from 40 to 80% of the sensory threshold) tested [55]. Furthermore, vibrotactile stimulation with noise applied to the wrist during motor tasks improved hand motor function in post-stroke individuals [56].

Noise stimulation is a key parameter that influences stimulation-induced neural responses. Compared to other techniques of neuromodulation such as transcranial direct current stimulation (tDCS) or transcranial alternating current stimulation (tACS), it does seem that random noise stimulation provides an advantage [57]. One possibility is that this technique has a larger effect on attentional networks [58] and another possibility is that these random noise stimulations generate a wider spread of power in the frequency domain [59]. Although noise stimulation can be delivered in the form of tactile vibration and electrical stimulation, the current study used electrical stimulation to broaden the types of peripheral nerves being stimulated. When applied on the skin surface, both tactile vibration and electrical stimulation activated cutaneous neurons. However, if electrical stimulation is applied to a nerve trunk at a more proximal site, various types of sensory nerves, including the cutaneous and proprioceptive nerves, are likely to be activated. Sensory afferent inputs are important in motor control and play an important role in promoting proprioceptive integration and effective motor learning [60]. Expanding the effects of noise stimulation to diverse types of sensory neurons could be an advantage of electrical stimulation over tactile vibration.

In addition, stimulation intensity is also an important factor in determining the effectiveness of noise electrical stimulation on motor function. Previous studies have used stimulation intensities ranging from 40% up to 100% of the sensory thresholds. Therefore, at the beginning of our experiment, we first determined the optimal noise stimulation intensity level for each participant. Our results showed that the optimal level of noise stimulation intensity varied among the participants, with 36%, 21%, and 43% having optimal intensities at 70%, 90%, and 100% of the sensory threshold, respectively. This observation suggested that optimal noise stimulation intensity is required to achieve better sensorimotor function improvement with noise stimulation.

Although no significant changes in EEG power spectrum density with noise stimulation were observed, we found that during noise stimulation, better force proprioceptive sense was associated with higher gamma band EEG. A limited number of reports have discussed the effects of peripheral ES on EEG in the contralateral motor cortex. EEG power spectrum density in the gamma frequency band has been linked to motor performance. Using a visuomotor reaction time task, prior studies found that people with faster reactions exhibited stronger gamma oscillation in the sensorimotor region of the cortex [61], [62]. Notably, this gamma oscillation is likely related to attention control, which mediates reaction speed [63]. Another recent study suggested that gamma oscillation is associated with motor performance following action observation [64]. Our findings were consistent with those of the above-mentioned studies. Although our experimental paradigm reproduced grip force without visual feedback (force proprioceptive sense), this type of motor task requires a high level of attention control to achieve accuracy and consistency during grip force reproduction. Furthermore, individuals with greater EEG gamma power during the force proprioception task showed better force sense. Our observations indicated that EEG gamma power is associated with noise stimulation-induced improvement in force sense, which suggests that noise stimulation might help enhance movement-related attention control. Furthermore, EEG gamma power can potentially serve as a biomarker to reflect force sense performance responsiveness to noise stimulation.

The motor cortex and muscles exhibit synchronized neural oscillations, which can be observed through corticomuscular (EEG-EMG) coherence. CMC represents the functional connectivity between the motor cortex and active muscles and has been used to reflect the functional status of the neuromuscular system [65], [66]. CMC is dynamic and can be modulated by interventions or physiological changes in the neuromuscular system. For example, it has been found that motor training increases CMC [67]. In contrast, lesions in the central nervous system [68], [69], [70] and muscle fatigue [71], [72], [73] modulate CMC levels. The current study observed a reduction in gamma band CMC during noise stimulation, and two potential reasons contribute to this. First, sensory afferent inputs play an essential role in CMC. A previous study that investigated the factors that influence CMC found that during peripheral electrical stimulation, an alternative rhythm generator in the neuromuscular system may activate and subsequently interfere with and reduce CMC [74]. In the current study, although we used subsensory level stimulation intensity, sensory neurons in the vicinity of the noise stimulation electric field could become more sensitive [36], [37] and discharge higher levels of sensory afferent inputs back to the CNS. This results in altered neural oscillation frequency during noise stimulation and CMC interference. Second, gamma band CMC is influenced by motor learning and enhanced motor performance. It has been reported that gamma band CMC is associated with feedback gain with motor learning [75], which is presumably due to reduced feedback gain after the motor task has been acquired. In addition, our previous work investigated the effects of eight-week peripheral electrical stimulation intervention on CMC and motor recovery in patients with stroke. We found that after the intervention, patients with stroke showed improvement in upper limb motor function and decreased gamma band CMC [76]. Nevertheless, the current study found that, after 30-min noise stimulation, better force control performance was associated with lower gamma CMC. This finding further supports the association between motor learning, motor performance, and gamma band CMC.

V. CONCLUSION

Our study found that noise stimulation with optimal intensity could improve both force and joint proprioceptive senses. Furthermore, individuals with higher gamma coherence showed better force proprioceptive sense improvement with 30-min noise electrical stimulation. These observations indicate the potential clinical benefits of noise stimulation, and future development could focus on a portable/wearable device that can deliver sub-sensory level noise electrical stimulation to help individuals with impaired proprioceptive senses, as well as utilizing EEG-EMG signals as biomarker to identify optimal intervention protocol and individuals who might benefit from noise stimulation.

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