Invited review article

Effects of passive movement and mechanical tactile stimulation on corticospinal excitability

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Abstract

Passive limb movement and mechanical tactile stimulation of the skin can modulate corticospinal excitability. For example, repetitive passive finger movement at 5.0 Hz for 10 min reduces corticospinal excitability for 15 min after passive movement. However, corticospinal excitability increases when the subject pays attention to the passive movement of the finger. And mechanical tactile stimulation of the fingertip can increase or decrease corticospinal excitability, depending on the stimulation patterns used. For example, 20 min of repetitive simple tactile stimulation decreases corticospinal excitability, whereas repetitive complex tactile stimulation increases it. In addition, following repetitive complex tactile stimulation, motor function improves. In this review, we focus on cortical activity following passive movement and mechanical tactile stimulation and changes in corticospinal excitability after repetitive passive movement and mechanical tactile stimulation.

Introduction

Our research group is investigating cortical activities and corticospinal excitability following voluntary movement [1-11], passive movement [2, 3, 12-19], peripheral nerve stimulation [20-28], mechanical tactile stimulation [29-33], motor-point stimulation [4], water immersion [34-37], aerobic exercise [38-43], and noninvasive transcranial electrical brain stimulation [3, 21, 44-61] using electroencephalography (EEG), magnetoencephalography (MEG), transcranial magnetic stimulation (TMS), and near-infrared spectroscopy. In this review, we describe the effects of passive movement and mechanical tactile stimulation on corticospinal excitability.

Cortical Activation Following Passive Finger Movement

Numerous studies have measured brain activity following passive movement using functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) to reveal that passive movements without motor commands activate not only the primary somatosensory cortex (S1) but also the primary motor area (M1), supplementary motor area (SMA), posterior parietal cortex (PPC),

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and bilateral secondary somatosensory areas (S2) [62-67]. However, unlike MEG, PET and fMRI do not offer sufficient temporal resolution to elucidate the time course of activity in these cortical areas.

Some studies have used MEG systems to investigate the somatosensory evoked fields (SEFs) that accompany passive movement [68-72]. For example, Xiang et al. [72] identified four SEF components with peak latencies of 20, 46, 70, and 119 ms following the onset of passive finger movement. Several researchers have reported that the large SEF component observed following passive movement lasted for a long duration, with two peaks between 30 and 100 ms after the onset of movement [68-70]. The equivalent current dipoles (ECDs) of these two components were located in area 3b [68], area 4 [69], and areas 3b and 4 [70, 72]. However, many MEG studies have shown no evidence of activity in the SMA, PPC, or S2 following passive movements. In a previous study, we recorded SEFs following active and passive finger movements with a multiple dipole analysis system to examine the detailed time course for cortical activity and source localizations [2]. Consistent with earlier studies, two peaks of the MEG response associated with passive movement were recorded between 30 and 100 ms after the onset of movement. Figure 1 presents the resulting isocontour maps over the left hemisphere at 34, 89, and 121 ms and over the right hemisphere at 140 ms after the onset of active and passive movements. The earliest and second components showed peaks at approximately 36 and 86 ms after the onset of passive movement. The ECD of the earliest component was estimated to be in area 4, and the ECDs of the second component were estimated to be in area 4, the SMA, the PPC over the hemisphere contralateral to the movement and in S2 of both

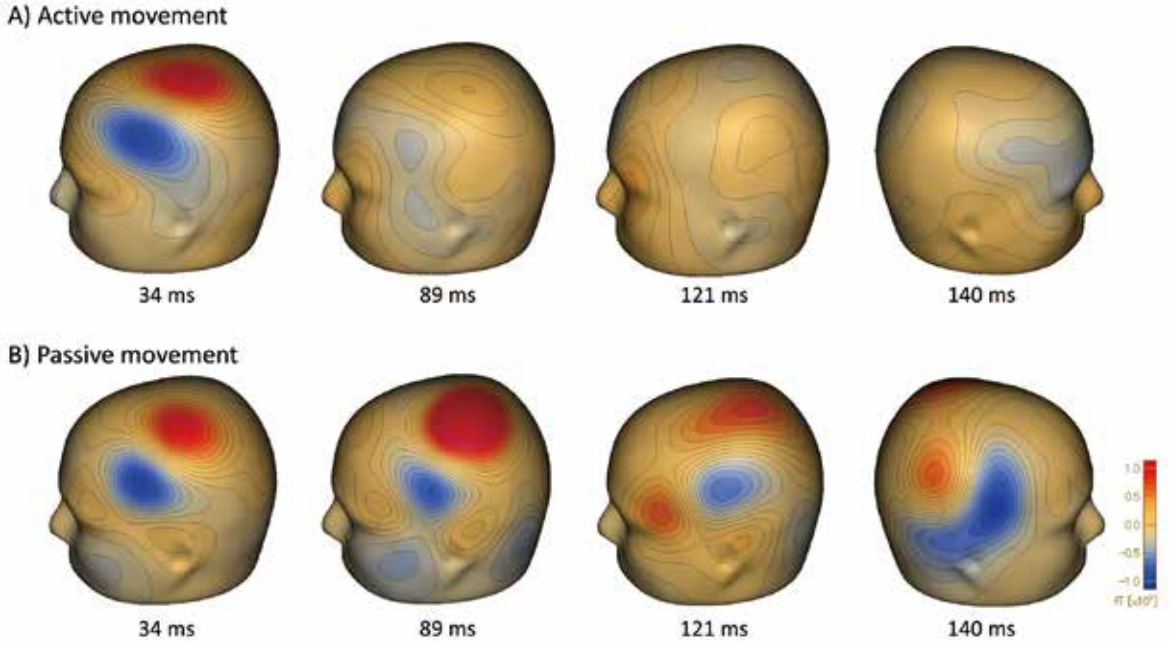

Figure 1. Isocontour maps following passive movement [2].
Isocontour maps over the left hemisphere at 34, 89, and 121 ms over the right hemisphere at 140 ms after the onset of active A) and passive B) movements in a representative subject. Red areas indicate magnetic flux exiting the head and blue areas indicate flux entering the head.

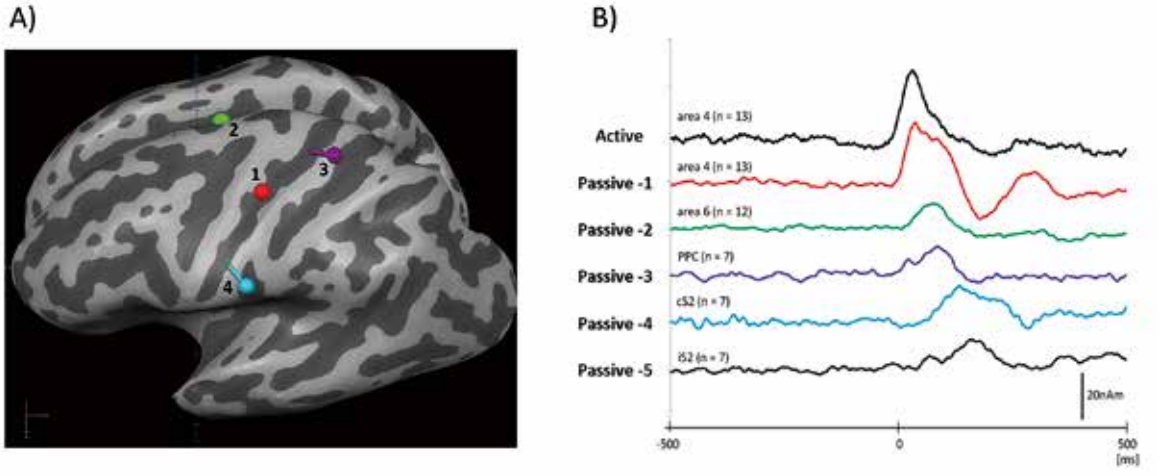

Figure 2. Cortical activities following passive movement [2].
A) Equivalent current dipoles (ECDs) following passive movement overlapped on the magnified brain of a representative subject. In this subject, the ECDs were estimated at the primary sensorimotor area (dipole 1), supplementary motor area (SMA, dipole 2), posterior parietal cortex (PPC, dipole 3), and contralateral secondary somatosensory cortex (cS2, dipole 4).
B) Time courses of averaged source activity following active and passive finger movements using brain electrical source analysis. "Active" shows the cortical activities at area 4 (n = 13) following active movement. "Passive -1, -2, -3, -4, and -5" shows the cortical activities in area 4 (n = 13), area 6 (n = 12), posterior parietal cortex (n = 7), contralateral secondary somatosensory cortex (S2, n = 7), and ipsilateral S2 following passive movement (n = 7), respectively.

hemispheres (Figure 2A). The peak latency of each source activity was obtained in the range of 54-109 ms in the SMA, 64-114 ms in the PPC, and 84-184 ms in the S2 (Figure 2B).

Cortical Excitability After Repetitive Passive Movements

In the field of rehabilitation, repetitive voluntary or passive movements are widely used to enhance muscle strength, improve range of motion, and promote motor learning or motor function in patients who have, for example, suffered from a stroke. Motor-evoked potentials (MEPs), which indicate corticospinal excitability, induced by single-intensity TMS temporarily decrease or increase after repetitive passive movements (RPMs). Miyaguchi et al.[3] reported that RPMs of the index finger for 10 min at 0.5 Hz reduced the MEP, whereas Mace et al. [73] reported that RPMs of the wrist for 60 min at an average frequency of 1.0 Hz increased the MEP; Lotze et al. and McDonnell et al. observed no changes in M1 excitability after 30 min of RPM [74, 75]. Table 1 summarizes six studies that investigated MEP changes associated with RPM. The differences in M1 excitability among the studies may have been influenced by differences in various stimuli such as the duration or speed of movement, presence or absence of a duty cycle of repeated movement and rest, and the degree of active attention given to the movement by the participant.

To determine the factors that influence M1 excitability, we first investigated the effect of passive movement speed on M1 excitability after 10 min of RPM [19]. We applied RPMs of different frequencies to examine whether movement frequen-

Table 1. Summary of studies investigating changes in motor-evoked potentials (MEP) after repetitive passive movements.

	Duration (min)	Number of movements	Velocity (degree/sec)	Joint of movement	Range of movement	Duty cycle	Attention	MEP
Mace [73]	60	1800	120	wrist	-45 ⇔ 45	+	+	increase
Lotze [75]	30	300	309	wrist	0 ⇔ 55	+	+	±
Miyaguchi [3]	10	300	20	index	0 ⇔ 20	−	−	decrease
Sasaki [19]	10	300	20	index	0 ⇔ 20	−	−	decrease
	10	600	40	index	0 ⇔ 20	−	−	decrease
	10	1800	120	index	0 ⇔ 20	−	−	decrease
	10	3000	200	index	0 ⇔ 20	−	−	decrease
Otsuka [15]	10	300	15	index	-15 ⇔ 0	−	−	decrease
	10	300	15	index	0 ⇔ 15	−	−	decrease
	10	150	15	index	-15 ⇔ 15	−	−	decrease
	10	300	15	index	15 ⇔ 30	−	−	decrease
Tsuiki [12]	10	600	40	index	0 ⇔ 20	−	−	decrease
	10	240	40	index	0 ⇔ 20	+	−	±
	10	600	100	index	0 ⇔ 20	+	−	decrease
	30	1800	40	index	0 ⇔ 20	−	−	decrease
	30	720	40	index	0 ⇔ 20	+	−	decrease
	10	240	40	index	0 ⇔ 20	+	+	increase
	10	240	40	index	0 ⇔ 20	+	−	±

Notes: “Index” refers to index finger. Duty cycle + and – refer to the presence or absence, respectively, of a duty cycle, including rest periods. Attention + and – refer to attention being given or not given, respectively, to the joint being moved. “ ± ” indicate unchanged MEP.

cy contributed to the modulation of M1 excitability using a custom-made device comprising a controller (Figure 3A) to set the movement velocity and range and a motor device to deliver the set passive movement sequence (Figure 3B). The movement device comprised a plastic plate, rotating plate, and stepper motor. Subjects placed their right palms on the plastic plate, aligning the center of the metacarpophalangeal joint of the right index finger to the rotary shaft of the motor (Figure 3C). The right index finger was passively abducted and adducted for 10 min at 0.5, 1.0, 3.0, and 5.0 Hz. RPMs at 0.5 and 1.0 Hz both resulted in MEPs that were decreased relative to the baseline for 2 min, whereas 5.0-Hz RPMs reduced MEPs for 15 min; however, 3.0-Hz RPMs resulted in no change in MEPs (Figure 4). No F-wave changes were observed following any of the RPM interventions. Next, we used the paired-pulse TMS technique to investigate whether RPMs modulated the cortical

inhibitory circuit. We measured short interval intracortical inhibition (SICI) before and after 1.0, 3.0, and 5.0-Hz RPMs using paired-pulse TMS with an interstimulus interval of 3 ms. Both 1.0-Hz and 5.0-Hz RPMs resulted in an increase in SICI compared with that at baseline. These results suggest that M1 excitability decreases after RPM in a manner that depends on the movement frequency, possibly through frequency-dependent enhancement of the cortical inhibitory circuit in the M1. We next examined the influence of the range of passive movement (the extension amplitude of the muscle) on M1 excitability [15]. The index finger was passively moved from 15° abduction to 15° adduction, 15° abduction to 0°, 0° to 15° adduction, and 15° adduction to 30° adduction, with each movement at 15°/s for 10 min. MEPs and F-waves were measured before and after each RPM. The amplitudes of the MEPs significantly decreased after all the RPMs but the F-wave amplitude remained stable. These results suggest that the range of passive movement does not markedly influence the magnitude of the MEP decline after RPMs.

In another study involving peripheral electric stimulation, intermittent stimulation with a duty cycle of repeated stimulation and rest resulted in significantly increased corticospinal excitability [76]. Additionally, corticospinal excitability was shown to significantly decrease with continuous

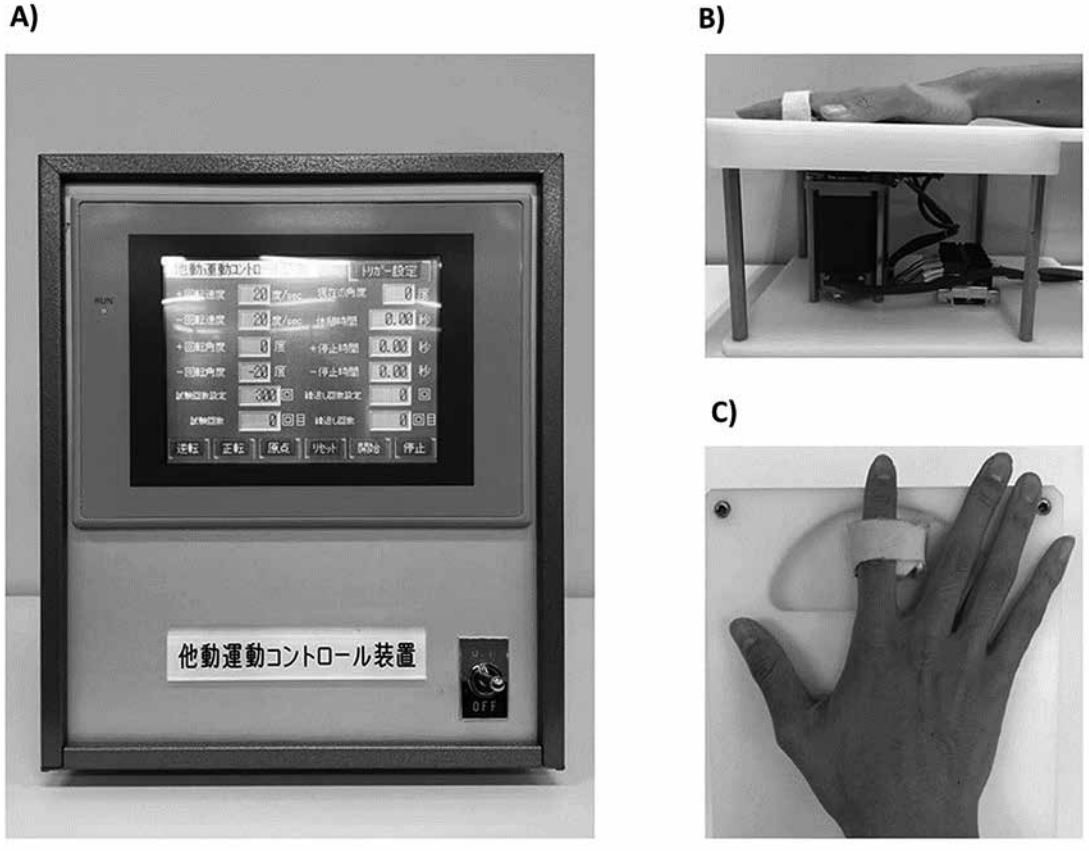

Figure 3. The passive movement control device [19].
A) The main device controls the velocity and range of movement. B), C) The secondary device produces repetitive passive movements of the right index finger.

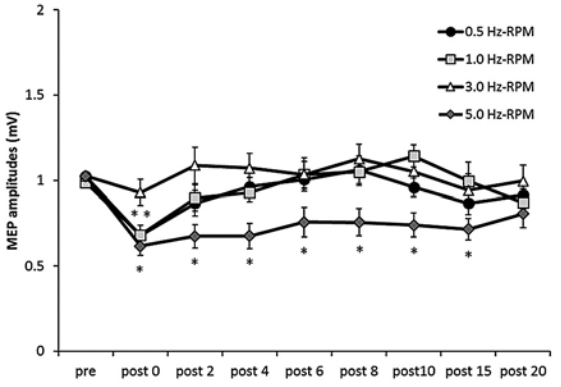

Figure 4. Effects of RPM frequency on MEP amplitudes [19].
The effect of the frequency of repetitive passive movement (RPM) on MEP amplitudes. Time course of change in mean ± standard error MEP amplitudes for all subjects (n = 15) following 0.5, 1.0, 3.0, and 5.0-Hz RPM.
*p < 0.05 compared with the pre-value.

theta burst stimulation but increase when the theta burst stimulation was intermittent [77]. These findings suggest that continuous and intermittent interventions with duty cycles of repeated stimuli and rest have different effects on corticospinal excitability. Therefore, we examined the effect of the presence or absence of a duty cycle for the RPM on corticospinal excitability. The results confirmed that a decline in corticospinal excitability does not depend on the presence or absence of the duty cycle [12].

Attention is closely related to cortical excitability. For example, during paired associative stimulation interventions, corticospinal excitability significantly increased when attention was directed to the stimulated side but there was no change when focusing on the other hand. It was also reported that SICI decreased and corticospinal excitability increased when attention was paid to the target hand during a movement task [78], repetitive TMS [79], or vibration stimulation [80]; however, there was no change in corticospinal excitability when there was no attention paid to the stimulated hand. These findings suggest that attention to the stimulated side during an intervention increases corticospinal excitability. Therefore, we assessed the influence of paying attention to passive movement on corticospinal excitability and found that when attention was paid to the moving finger during RPM, corticospinal excitability increased, whereas corticospinal excitability did not change under conditions where no attention was directed to the passive finger movements (Figure 5) [12].

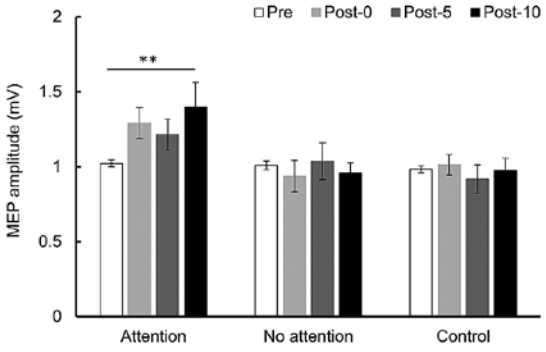

Figure 5. MEP amplitude before and after the repetitive passive movement [12].
Motor-evoked potential (MEP) amplitudes before and after repetitive passive movements (RPMs) under three conditions. The MEP amplitude significantly decreased at Post-0 and Post-5 compared with Pre. Mean MEP amplitude (mean ± SE) at Pre, Post-0, Post-5, and Post-10. When paying attention, the MEP amplitude significantly increased at Post-10 compared with Pre ($p < 0.01$). In contrast, when not paying attention and in the control condition, there was no significant change in MEP amplitude before and after the intervention.

Cortical Activation Following Mechanical Tactile Stimulation

Tactile input from the periphery activates several cortical areas. The primary somatosensory cortex (S1) in the postcentral gyrus performed the initial cortical processing of the somatosensory

stimuli. The secondary somatosensory cortex (S2) is in the upper wall of the sylvian fissure. Several cortical imaging tools such as fMRI, PET, and MEG have provided unequivocal evidence of the activity in sensory processing areas such as S1 and S2. Compared with fMRI and PET, MEG has excellent temporal resolution and has been successfully used to analyze the temporal aspects of cortical sensory information processing [81, 82]. In some MEG studies, intra-epidermal and transcutaneous electrical stimulation [83], YAG- or CO2-laser stimulation [84], mechanical stimulation using air puffs (pneumatic stimulation) [85, 86], brushes [87, 88], plastic pieces driven by airflow [89], and mechanical pins driven by piezoelectric actuators [32, 33] have been used to analyze the cortical activity following nociceptive or non-nociceptive stimulation. Because laser and intra-epidermal stimulation can activate nociceptors of thin myelinated A-delta fibers without stimulating tactile afferent fibers, these stimulators are ideal for investigations of the nociceptive system.

Pneumatic stimulation is a useful tool for recording the SEF in response to face or lip stimula-

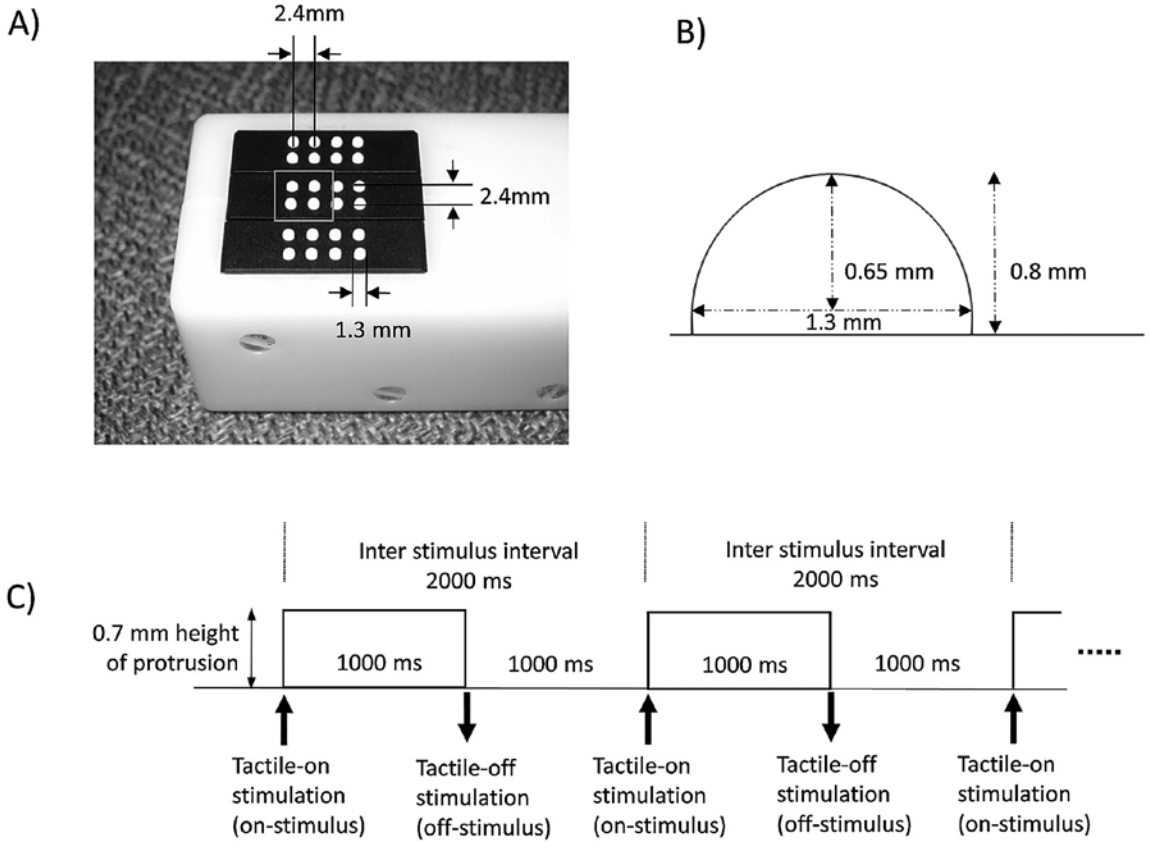

Figure 6. Tactile stimulator and stimulation parameter [33].
A) An array of four tiny plastic pins (2.4 × 2.4 mm) on the tactile stimulator was driven by piezoelectric actuators. The pins were each 1.3 mm in diameter and protruded to 0.8 mm. The distance between pins was set to 2.4 mm. B) Schema of a mechanical pin. C) The interstimulus interval was set to 2000 ms, including 1000 ms of constant stimulus.

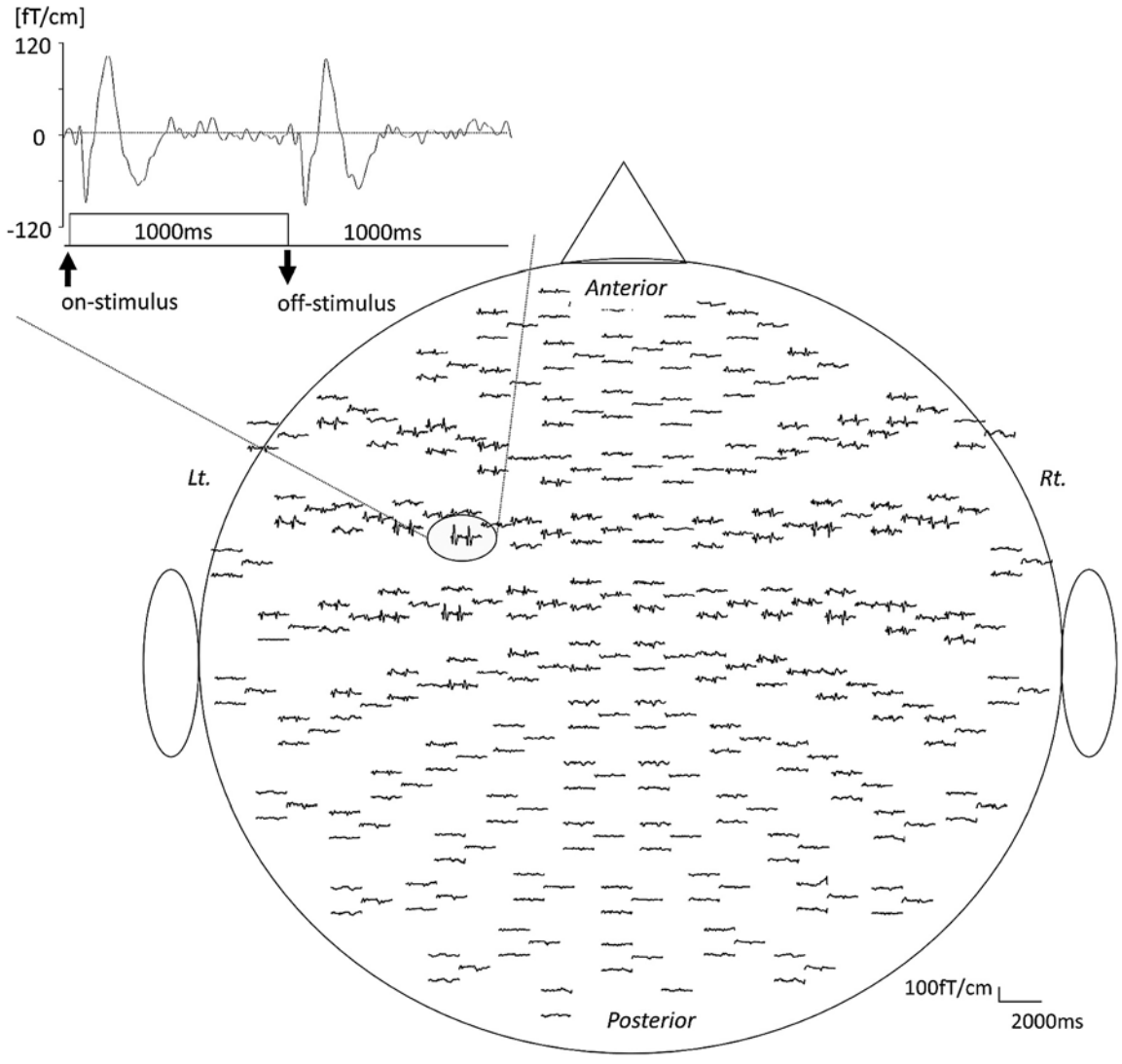

Figure 7. Representative whole-scalp SEF waveforms after the onset of tactile-on stimulation [33]. Representative whole-scalp SEF waveforms from a period of between 20 ms before and 2000 ms after the onset of tactile-on stimulation obtained from Subject 2. The recording period comprised 1000 ms of constant stimulus and 1000 ms following the removal of the constant stimulus.

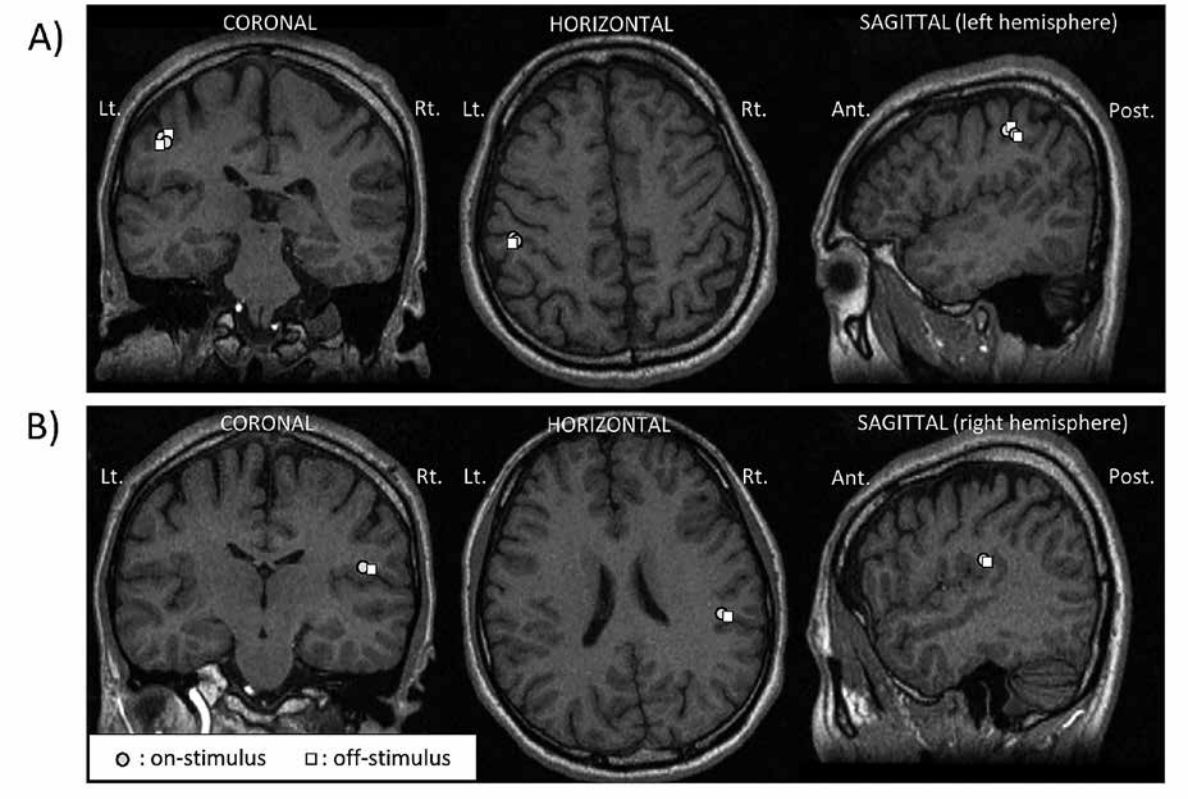

Figure 8. ECD locations following tactile on-stimulation and off-stimulation [33].
The locations of the ECDs are superimposed on the same subject's MR images. A) The contralateral hemisphere to the right finger stimulation. ECDs corresponding to the on-stimulation as well as off-stimulation were all located in SI. B) The ipsilateral hemisphere to the stimulation. ECDs corresponding to the on-stimulation and off-stimulation were observed in SII. The yellow circle and white box correspond to the on-stimulus and off-stimulus, respectively.

tion. However, the rise time for pneumatic stimulation is relatively long (>10 ms); hence, the early phase of cortical activity cannot be measured as clearly as the responses generated by electrical stimulation. In contrast, the rise time for mechanical pins driven by piezoelectric actuators is <1 ms and the stimulus is precise and consistent. Therefore, this device is useful for investigating the early time course of cortical activity following life-like tactile sensation, tactile-off responses, and responses to multiple stimuli distributed over a region in sensory paradigms such as two-point discrimination. We investigated the effects of tactile-off stimulation generated by the removal of a constant mechanical pressure (Figure 6) to activate SI and SII cortices using a 306-ch whole-head MEG system and a tactile stimulator driven by a piezoelectric actuator [33]. Consequently, prominent SEFs from the contralateral hemisphere were recorded at 57.5 ms and 133.0 ms after the onset of tactile-on stimulation and at 58.2 ms and 138.5 ms after the onset of tactile-off stimulation (Figure 7). All ECDs were located in S1 (Figure 8A). Moreover, long-latency responses (168.7 ms after tactile-on stimulation and 169.8 ms after tactile-off stimulation) were detected from the ipsilateral

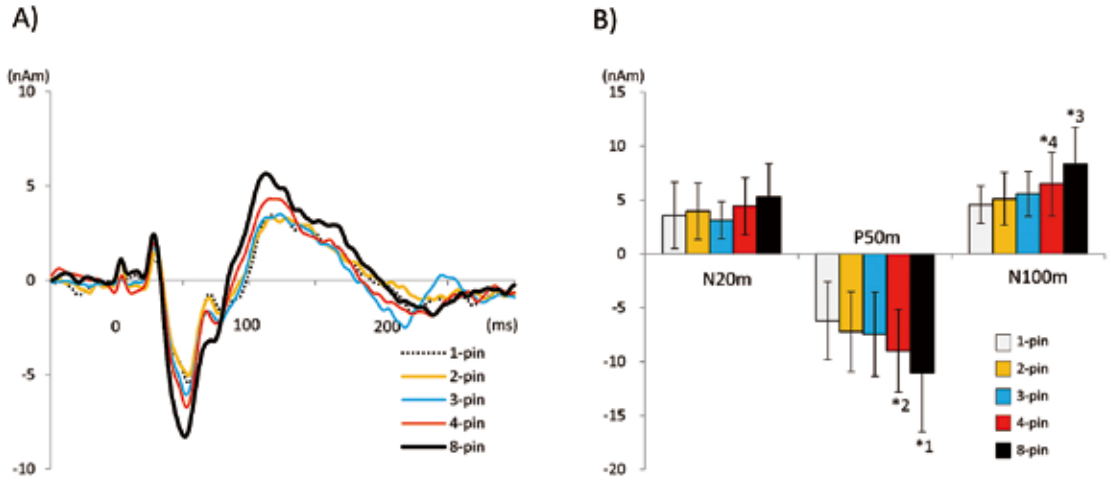

Figure 9. Effect of the number of stimulation pins on cortical activities [32].
A) Grand averaged source waveforms across subjects elicited by each number of pins of mechanical stimulation. B) The mean source activities of each component were summarized to compare the source activities among the pin numbers for mechanical stimulation.
*1: P50 m: 8-pins > 4-pins ($p < 0.01$), 3-pins ($p < 0.01$), 2-pins ($p < 0.01$), 1-pin ($p < 0.01$)
*2: P50 m: 4-pins > 2-pins ($p < 0.05$), 1-pin ($p < 0.01$)
*3: N100 m: 8-pins > 4-pins ($p < 0.05$), 3-pins ($p < 0.01$), 2-pins ($p < 0.01$), 1-pin ($p < 0.01$)
*4: N100 m: 4-pins > 1-pin ($p < 0.05$)

hemisphere. The ECDs of these signals were identified in the S2 (Figure 8B). The SEF waveforms elicited by the two tactile stimuli (tactile-on and tactile-off) with a mechanical stimulator were strikingly similar. These mechanical stimuli elicited both contralateral SI and ipsilateral SII activities.

In addition, we investigated the effect of the number of mechanical pins and inter-pin distance on SEFs following mechanical stimulation [32]. SEFs were elicited through tactile stimuli with 1-, 2-, 3-, 4-, and 8-pins using healthy participants. Tactile stimuli were applied to the tip of the right index finger. Prominent SEFs were recorded from the contralateral hemisphere approximately 54 ms (P50 m) and 125 ms (P100 m) after mechanical stimulation, regardless of the number of pins. ECDs were located in the S1. The source activities for P50 m and P100 m significantly increased in tandem with the number of pins for mechanical stimulation (Figure 9). Additionally, source activities significantly increased when the inter-pin distance increased from 2.4 to 7.2 mm. The number of stimulated receptors was considered to have increased with an increase in the inter-pin distance as well as an increase in the number of pins. These findings clarified the effect of the number of pins and inter-pin distance for mechanical stimulation on SEFs.

Cortical Excitability After Repetitive Tactile Stimulation

Prolonged and/or repetitive somatosensory stimulation, including electrical stimulation and tactile stimulation, may be useful rehabilitation tools because they reportedly modulate cortical and corticospinal excitability [90-92], motor function [93, 94], and sensory skills [95-97] in both healthy subjects and stroke patients [98-101]. For example, the MEP increased for 15 min following

electrical stimulation of the ulnar nerve for 2h [102]. Thirty minutes of vibration on the palm increased corticospinal excitability for 2h [103]. In addition, mechanical stimulation for 3h was shown to decrease the two-point discrimination threshold, while increasing S1 activity, with a corresponding correlation observed between these effects [96, 97].

A previous study using tactile stimulation showed that cortical activity differed depending on the pattern of tactile stimulation. An fMRI analysis demonstrated that cortical activity depends on the pattern of mechanical stimulation, and simple and complex mechanical stimulations activated S1, whereas complex mechanical stimulations activated not only S1 but also the M1 [67]. Therefore, we investigated whether the effects of repetitive mechanical tactile stimulation on corticospinal excitability [30, 31] and motor function [30] depend on different pin protrusion patterns. Two types of mechanical tactile stimulation were used: a repetitive global stimulus (RGS) was used to stimulate the finger using 24 pins installed on a finger pad and a sequential stepwise displacement stimulus (SSDS) was used to stimulate the finger by moving a row of six pins between the left and right sides on a finger pad (Figure 10). Mechanical tactile stimuli were applied to the right index finger for 20 min (stim on/stim off, 1s/5s) at a frequency of 20 Hz. MEPs were observed to be significantly smaller after RGS intervention than pre intervention MEPs (Figure 11A); however, motor

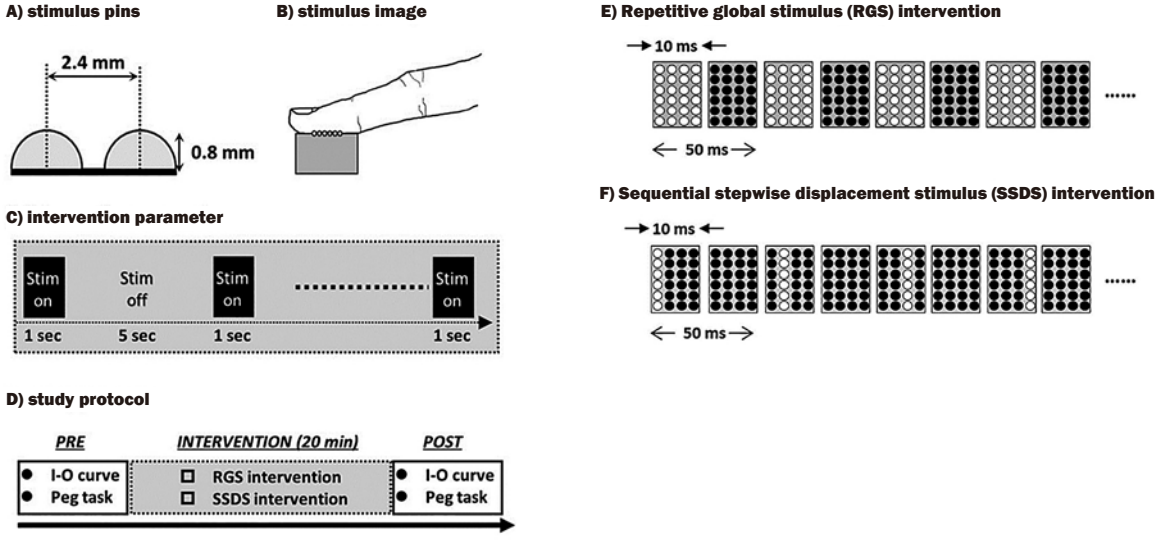

Figure 10. Mechanical tactile stimulation and stimulus protocol [30].
A) The mechanical tactile stimulator. Each pin was 1.3 mm in diameter and protruded to 0.8 mm. B) The mechanical tactile stimulator comprised 24 tiny plastic pins applied to the tip of the right index finger. C) Mechanical stimulation was applied for 20 min (stim on/stim off, 1 s /5 s) at a frequency of 20 Hz. D) I-O curve and motor function were measured prior to intervention (PRE). Each mechanical stimulation (either RGS or SSDS) was applied for 20 min. After mechanical stimulation (POST), the I-O curve and motor function were measured again. E) RGS intervention stimulated the index finger with 24 pins installed in the finger pad. F) SSDS intervention stimulated the finger by moving the row of six pins between the left and right sides on the finger pad. I-O curve (Input-Output curve), RGS (repetitive global stimulus), SSDS (sequential stepwise displacement stimulus)

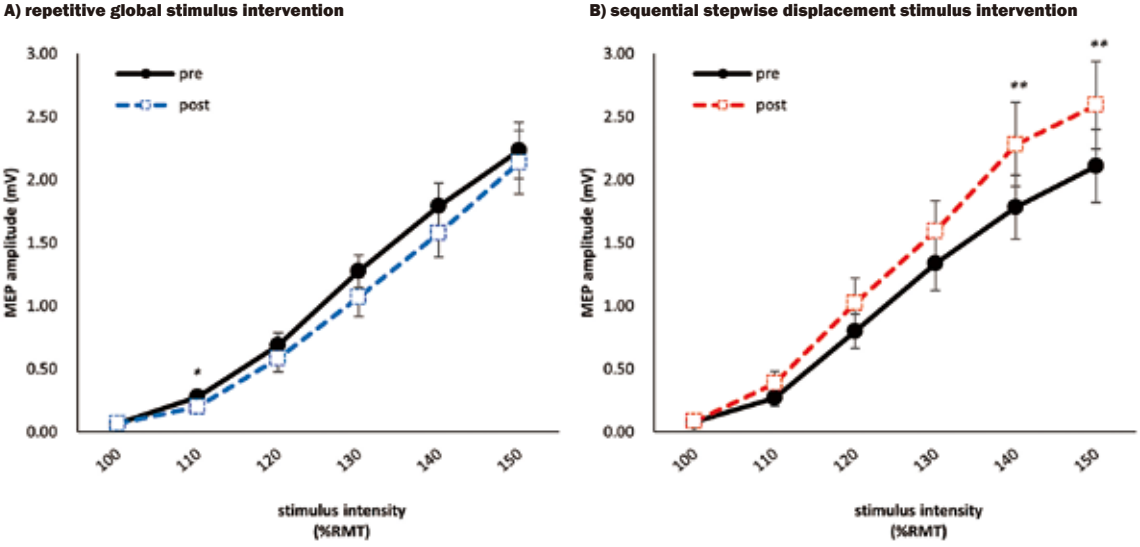

Figure 11. Pre-to post-intervention changes in the Input-Output curve plotting the MEP amplitude (mean ± standard error of mean) [30].
A) In the RGS intervention, post hoc analysis showed a significant decrease in the MEP amplitude evoked by 110% RMT PRE compared with POST ($p = 0.005$). B) In the SSDS intervention, post hoc analysis showed a significant increase in the MEP amplitude evoked by 140% and150% RMT PRE compared with POST (140% RMT; $p = 0.00057$, 150% RMT; $p = 0.00078$).
RMT (resting motor threshold), PRE(prior to intervention), POST(after mechanical stimulation), I-O curve(Input-Output curve), RGS(repetitive global stimulus), SSDS(sequential stepwise displacement stimulus)

function using the grooved pegboard task remained unchanged. After SSDS intervention, MEPs were significantly larger (Figure 11B) and motor function significantly improved compared with pre intervention values. Our results demonstrate that mechanical tactile stimulation can modulate corticospinal excitability and motor function and that the effects of mechanical stimulation depend on stimulation patterns.

Conclusion

In this review, we summarized the cortical activity and corticospinal excitability associated with passive movement and mechanical tactile stimulation. Corticospinal excitability following RPM is believed to be influenced by various factors, including the duration and velocity of the movement and the presence or absence of a duty cycle of repeated movement/stimulation and rest. Therefore, we performed several experiments involving RPMs which showed that whether or not there was a duty cycle of repeated movement and rest, RPM resulted in a temporary decrease in cortical excitability when no attention was paid to the passive movement but an increase in cortical excitability when attention was directed at the movement. Furthermore, we investigated the effects of mechanical tactile stimulation on corticospinal excitability and motor function. We found that repetitive simple mechanical stimulation decreased corticospinal excitability but did not change motor function, whereas complex mechanical stimulation increased both corticospinal excitability and motor function. Collectively, repetitive mechani-

cal stimulation can modulate corticospinal excitability and motor function and the effects of the intervention depend on the pattern of stimulation.

Acknowledgments

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