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Brain Mechanism for Enhanced Hand Function with Remote Sensory Stimulation

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BRAIN MECHANISM FOR ENHANCED HAND FUNCTION WITH REMOTE
SENSORY STIMULATION

by

Kishor Lakshmi Narayanan

A Dissertation Submitted in
Partial Fulfillment of the
Requirements for the Degree of

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in Engineering

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ABSTRACT

BRAIN MECHANISM FOR ENHANCED HAND FUNCTION WITH REMOTE SENSORY STIMULATION

by

Kishor Lakshmi Narayanan

The University of Wisconsin-Milwaukee, 2016
Under the Supervision of Professor Mohammad Habibur Rahman

The neurological bases for remote vibration enhanced sensory feedback and motor function are yet poorly understood. The purpose of this dissertation was to identify and examine the effect of vibration on finger tactile sensation in healthy adults and how imperceptible random vibration applied to the wrist changes cortical activity for fingertip sensation and precision grip. In a series of studies on healthy adults, white-noise vibration was applied to one of four locations (dorsum hand by the second knuckle, thenar and hypothenar areas, and volar wrist) at one of four intensities (zero, 60%, 80%, and 120% of the sensory threshold for each vibration location), while the fingertip sensation, the smallest vibratory signal that could be perceived on the thumb and index fingertip pads, was assessed. Vibration intensities significantly affected the fingertip sensation ($p < .01$) in a similar manner for all four vibration locations. Specifically, vibration at 60% of the sensory threshold improved the thumb and index fingertip tactile sensation ($p < .01$), while vibration at 120% of the sensory threshold degraded the thumb and index fingertip tactile sensation ($p < .01$) and the 80% vibration did not significantly change the fingertip sensation ($p > .01$), all compared with the zero vibration condition. The next step was to

examine the cortical activity for this vibration-enhanced fingertip sensation. We measured somatosensory evoked potentials to assess peak-to-peak response to light touch of the index fingertip with applied wrist vibration versus without. We observed increased peak-to-peak somatosensory evoked potentials with wrist vibration, especially with increased amplitude of the later component for the somatosensory, motor, and premotor cortex with wrist vibration. These findings corroborate an enhanced cortical-level sensory response motivated by vibration. It is possible that the cortical modulation observed here is the result of the establishment of transient networks for improved perception. Finally, we examined the effect of imperceptible vibration applied to the wrist on cortical control for precision grip. We measured β -band power to assess peak-to-peak response while subjects performed precision pinch with wrist vibration versus without. We observed increased peak-to-peak β -band power amplitude with wrist vibration, especially with event-related synchronization for the prefrontal, sensorimotor, motor, premotor, and supplementary motor areas with vibration. The enhanced motor function may possibly be a result of higher recalibration following movement and faster motor learning.

To
my parents,
my brother,
and God

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CHAPTER 1

INTRODUCTION

Finger tactile sensory feedback is a prerequisite for dexterous hand function including fine finger movements, gripping, and object manipulation [1]. Loss of finger tactile sensation via digital anesthesia immediately leads to declined grip force regulation, use of excessive grip force than needed for object lifting, and object slippage [2, 3, 4]. Deficits in tactile sensation following aging [5, 6, 7], stroke [8, 9], or diabetic neuropathy [10] can reduce sensory feedback from the fingers, resulting in inappropriate grip force control [11, 12], deteriorated manual dexterity [13] and fine object manipulation [14], unstable grip [15], and slippage of objects from the fingers [2, 16]. Therefore, methods to improve finger tactile sensation have the potential to facilitate hand dexterity and hand functions. Improving tactile sensation and dexterity represents a tremendous potential to enhance human performance in high precision manual dexterity tasks, such as cooking, gardening, assembling intricate parts, playing music, and performing surgical procedures.

Recently, it was shown that the application of sensory noise away from the hand (e.g., wrist, forearm) may also improve hand tactile sensation [17]. This effect is similar to ‘stochastic resonance’ [18, 19, 20, 21] in which minute, unperceivable noise improves signal detection by elevating the signal amplitude, while high intensity noise causes a suprathreshold sensation which masks the signal and disrupts signal detection [19]. Such minute sensory noise can be applied using a relatively low-cost, low-risk mechanical vibrator, with a rather instant effect [22]. However, a noise-generating device placed directly on the fingertip interferes with object manipulation and dexterous hand

movement by blocking physical contact between the finger and object. It was found that imperceptible vibrotactile noise, applied away from the fingertip, 'remotely' to the wrist improved fingertip tactile sensation in chronic stroke survivors [17]. Subthreshold vibrotactile noise applied to the forearm shortened muscle reaction time to hand tactile stimuli in healthy adults [23], thereby improving hand grip functions. Reduced sensation simulated by applying DuoDERM® bandages on the fingertips resulted in increased pinch grip force error, while subthreshold remote stimulation reduced pinch grip force error, when subjects attempted to maintain a set pinch force level at 5% of their pinch strength without visual feedback [24]. Such a remote effect has a practical implication of strategically placing a noise generator off the hand in order to expose the entire hand skin for tactile stimuli during dexterous manual tasks and also to not interfere with object manipulation.

However, the mechanism by which remote noise affects fingertip tactile sensation and motor control is unclear. A potential mechanism suggested is that the integration of signal and remote noise for stochastic resonance occurs at the spinal level and/or cortical level. However, such evidence for the signal and noise integration in the central nervous system based on electrical recordings of neural activities currently lacks in humans. Previous demonstration of the signal and noise integration in the central nervous system based on electrical recordings of neural activities was from cats [25]. Previous studies [17, 23] only demonstrated behavioral changes that suggest the signal and noise integration in the central nervous system. However, they did not demonstrate evidence in neural activity. The mechanism through which this remote sensory stimulation enhances hand function is

unknown, which is a hurdle for adoption of this new technology to enhance human performance in high precision manual dexterity tasks (cooking, gardening, assembling intricate parts, playing music, performing surgical procedures), helping aged people regain their hand functions, and serve as a rehabilitation tool for patients affected with neurological disorder (stroke, multiple sclerosis).

1.1 Research objectives

In order to achieve the objective of finding the neural mechanism for the effect of remote sensory stimulation on improved hand function, the following three specific aims were put forward. The central hypothesis is that the sensory and motor improvement with the stimulation at the wrist is mediated by increased primary sensorimotor cortical activity for finger touch sensing and precision grip.

- **Aim 1: To determine the effect of remote sensory noise on fingertip tactile sensation.**
 - ***Hypothesis 1:*** Remote sensory noise enhances fingertip tactile sensation when applied at a subthreshold level compared to without remote sensory noise application in healthy adults. The threshold is the sensory threshold of an individual at which they can barely distinguish the sensory noise being on or off. As a negative control, it is hypothesized that sensory noise applied at a suprathreshold level degrades fingertip tactile sensation.
- **Aim 2: To determine the effect of sensory manipulation on cortical control for fingertip touch sensing.**

- **Hypothesis 2:** Enhanced tactile sensation via remote sensory stimulation is mediated by an increase in the somatosensory evoked potential in the sensorimotor cortex EEG activity in response to fingertip touch events with the remote sensory stimulation compared to without it in healthy individuals.
- **Aim 3: To determine the effect of sensory manipulation on cortical control for precision pinch grip.**
 - **Hypothesis 3:** Enhanced tactile sensation via remote sensory stimulation increases the sensorimotor cortex EEG's β -band modulation during precision pinch grip compared to the control condition without the stimulation in healthy individuals.

1.2 Innovations

The first innovation in this dissertation was the approach of remote sensory stimulation. The preliminary work was the first to show improvement in finger tactile sensation and hand dexterity using remote sensory stimulation at the wrist. The approach allowed sensory noise to be applied away from the fingers, thereby enhancing tactile sensation and dexterity without interfering with the natural interaction between the fingers and the object. The second innovation was use of EEG to demonstrate brain mechanisms of enhanced or deteriorated hand function. Knowledge on the way the brain activity is modified by sensory manipulation which in turn affects hand function is scarce. This dissertation laid a foundation for EEG signals to be used for various cortical sensorimotor control and modulation with sensory manipulation.

1.3 Outline

We saw a brief introduction in this chapter and in the next chapter, the effect of both imperceptible and perceptible white-noise vibration applied to different locations within the distal upper extremity on the fingertip pads' tactile sensation in healthy adults were examined. In Chapters 3 and 4, we shall see how imperceptible random vibration applied to the wrist changed cortical activity for fingertip sensation and motor function respectively. Finally, Chapter 5 is the summarized findings from all the studies in this dissertation.

CHAPTER 2

EFFECT OF VIBRATORY NOISE APPLIED TO WRIST AND HAND SKIN ON FINGERTIP TACTILE SENSATION

The objective of this study in the dissertation was to investigate the way the fingertip pads' tactile sensation is affected by white-noise vibration applied to the distal upper extremity in healthy adults. Specifically, the effects of both imperceptible and perceptible white-noise vibration intensities applied at one of four locations (dorsum hand by the second knuckle, thenar and hypothenar areas, and volar wrist) were examined to improve understanding of its influence on fingertip pad tactile sensation.

2.1 Introduction

Finger tactile sensation is a prerequisite for dexterous hand function including fine finger movements, gripping, and object manipulation [1]. Anesthesia of the fingers results in immediate decline in grip strength, increase in safety margin, and slippage of an object from the hand in healthy adults [3, 2, 4]. Likewise, deficits in tactile sensation, such as following peripheral nerve injuries, aging [7, 6, 5], or stroke [8, 9, 26], can reduce sensory feedback from the fingers, resulting in inappropriate grip force control [11, 12], deteriorated manual dexterity and fine object manipulation [13, 14], unstable grip [15] and dropping of objects [16].

Given the direct connection between finger tactile sensation and hand function, it is important to know potential sources that affect tactile sensation. Sensory manipulation exploiting these sources could be used to facilitate or degrade hand dexterity and hand functions depending on the application. One of the sensory manipulation techniques involves imperceptible vibration. Application of imperceptible vibration to the fingertips

has been shown to improve the fingertip pad's tactile sensation and reduce excessive grip force during object lifting [22]. Such a wearable vibrating device can be realized using a low-cost, low-risk mechanical vibrator, with an instant effect [22] to enhance human performance in high precision manual dexterity tasks, such as assembling intricate parts, playing music or sports, and performing surgical procedures.

This vibration is thought to work based on a concept from traditional control theory in which presence of low-level random noise increases the signal to noise ratio and the system's ability to respond to signals. Such a phenomenon is also referred to as 'stochastic resonance' [20]. In the human tactile sensory system, application of imperceptible white-noise vibration to the tactile signal resulted in improved detection of the tactile signal for the fingertip [19, 27] as well as foot sole [21]. This effect on sensation was supported by electrophysiological data showing that white-noise vibration resulted in increased signal to noise ratios in EEG somatosensory evoked responses [25]. Furthermore, there appears to be an optimal level of white-noise vibration for improving human tactile sensation: Wells et al. [21] showed an inverted U shaped relationship between noise intensity and sensation in which white-noise vibration at the intensities of 33%, 50% and 67% of the sensory threshold improved tactile sensation to a greater extent than did vibration at intensities of 83% and 100% of the sensory threshold compared with baseline sensation with no vibration in healthy adults. White-noise vibration above sensory threshold was shown to degrade sensation, likely by masking the tactile signal and interfering with signal detection [19]. Based on these results, Wells et al. [21]

concluded that white-noise vibration should be high enough to facilitate a weak tactile signal to cross a sensory threshold but not too high to mask the tactile signal.

Recent studies show that application of imperceptible white-noise vibration away from the fingertips such as the wrist or the dorsum of the hand may also improve fingertip tactile sensation: Imperceptible white-noise vibration applied to the dorsal and volar wrist as well as the dorsum of the hand by the first and second knuckles was found to improve the index and thumb fingertip pads' light touch sensation in chronic stroke survivors [17]. Imperceptible white-noise vibration applied to the thenar eminence and the volar and dorsal forearm skin shortened muscle reaction time to hand tactile stimuli in healthy adults, as did white-noise vibration applied to the middle fingertip [23].

Such a remote effect offers a practical benefit by strategically placing a vibrator off the hand in order to expose the entire hand skin for tactile stimuli during dexterous manual tasks and also to not interfere with object manipulation. In addition, this remote effect has the potential to expand our current understanding of sensory manipulation in the following way. We often assume that small vibratory noise on the base of the palm or wrist from laying the hand on a table or a wristband-type device would not affect finger sensation and dexterity. This assumption will be greatly challenged if we find that small vibratory noise around the palm or wrist effectively changes fingertip tactile sensation. Currently, it is unknown if imperceptible white-noise vibration applied to the upper extremity other than the fingertips can affect fingertip tactile sensation in healthy adults. In addition, it is currently unclear how this practical benefit of the remote effect is accrued.

This study aimed to investigate further the effect of white-noise vibration applied to the upper extremity other than the fingertips on fingertip tactile sensation in healthy adults by varying the noise locations and intensities. Specifically, to examine if connections between specific nerves are mediating the remote effect, we tested four vibration locations of the thenar eminence, hypothenar region, volar wrist, and dorsum of the hand just proximal to the second knuckle that are innervated by the median nerve, ulnar nerve, lateral musculocutaneous nerve, and radial nerve, respectively. The greatest effect of the vibration when applied to the thenar eminence compared to other locations may indicate involvement of median nerve sharing, whereas equal extents of sensory effects for all vibration locations may indicate involvement of higher level neural connections. In addition, three different noise intensities of 60%, 80%, and 120% of the sensory threshold were tested to examine if the remote vibration affects the fingertip tactile sensation in a manner similar to stochastic resonance.

2.2 Methods

2.2.1 Subjects

Twelve healthy right-handed adults (four females and eight males) with a mean age of 29 ± 5 ranging from 20 to 40 years participated in the study. All subjects verbally disclosed that they had no history of upper limb injury or musculoskeletal or neurologic disorders. The protocol was approved by the Institutional Review Board (Study: 15.079-UWM). Subjects read and signed a written informed consent form before participating in the experiment.

2.2.2 Procedure

Subjects' tactile sensation for the thumb and index fingertips was compared with vs. without remote white-noise vibration at three vibration intensities (60%, 80%, and 120% of the sensory threshold) and four remote vibration locations (dorsal hand just proximal to the second knuckle, thenar eminence, hypothenar region, and volar wrist as shown in Figure 1). The non-dominant hand was used because the non-dominant hand is thought to be more sensitive to somatosensory feedback than the dominant hand [28, 29, 30].

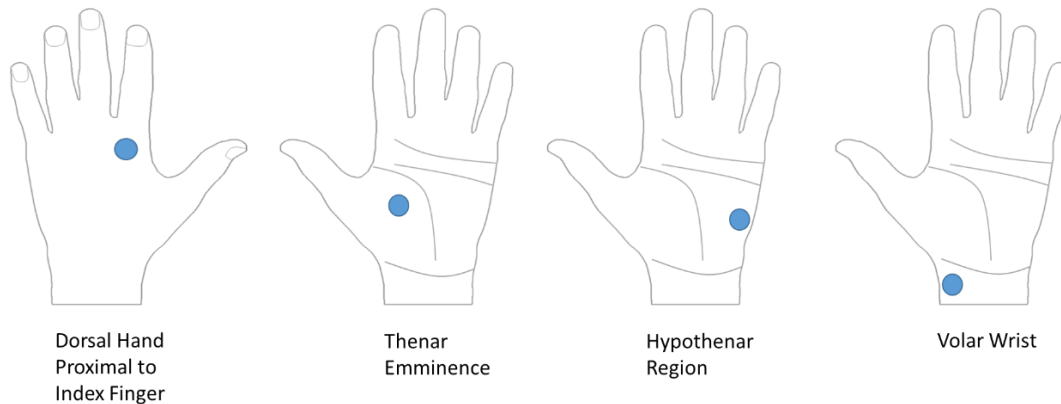


Figure 1: Four remote location for vibration application during thumb and index finger tactile sensation score recording

The remote vibration was applied by attaching a C-3 Tactor (Engineering Acoustics, Inc. Casselberry, FL) on one of the four locations using tape. The C-3 Tactor generated white-noise vibration low pass filtered at 500Hz. The remote vibration intensity was adjusted to zero (no vibration), 60%, 80%, or 120% of the sensory thresholds of each remote location. The sensory threshold was the minimal vibration intensity that could be felt by the subject. The sensory threshold was determined by incrementally increasing or decreasing the voltage input to the vibrator (vibration intensity) repeatedly until the

subject was barely able to distinguish vibration on versus off as in the method of ascending and descending limits [19, 31]. Subjects were verbally asked if they can distinguish vibration on versus off. The average root mean square vibration intensity for the sensory threshold was 0.41V, 0.35V, 0.37V, and 0.55V for the dorsal hand just proximal to the second knuckle, thenar eminence, hypothenar region, and volar wrist, respectively. Voltage input linearly changes the peak-to-peak vibration displacement, and the average remote vibration at 0.42V corresponds to peak-to-peak vibration displacement of 0.08mm according to the manufacturer datasheet.

Simultaneously with the remote vibration, another C-3 Tactor was attached to either the thumb or index fingertip to measure fingertip tactile sensation (Figure 2). The thumb and index fingertip tactile sensation score was quantified as the minimum root mean square voltage (V) driving the C-3 Tactor whose stimuli could be barely felt by the subject. The same sensory threshold determination method as described above for the remote vibration was used to determine the fingertip tactile sensation score. During measurement of the fingertip tactile sensation score, the remote vibration was continuously on, whereas the vibration to the fingertip was turned on and off frequently to ask subjects whether they could feel the fingertip vibration or not. A smaller fingertip tactile sensation score indicates better sensation.



Figure 2: Placement of C-3 Tactors

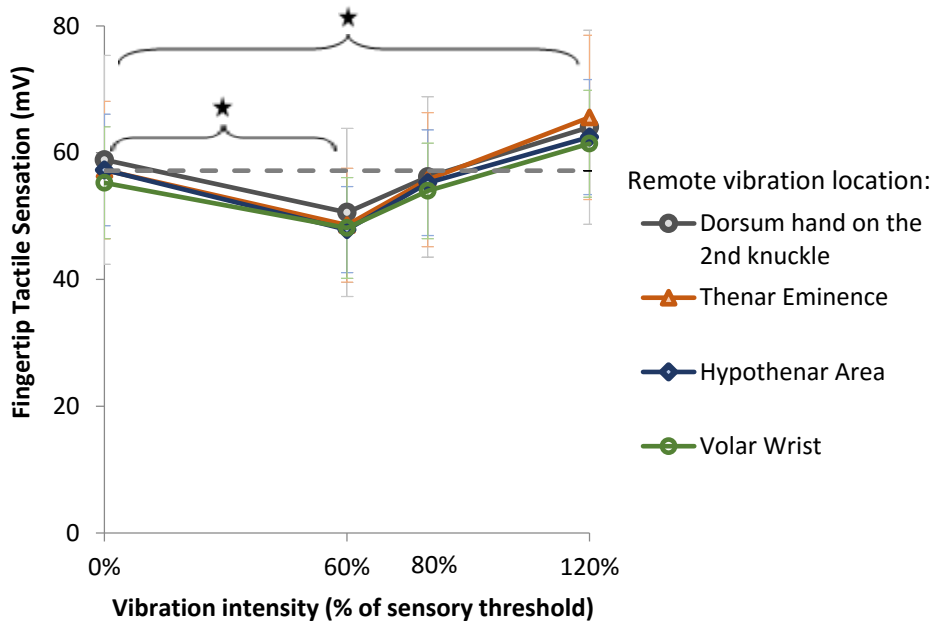
The testing order of the four remote vibration locations was randomized. Within each location, the testing order of the vibration intensities (zero, 60%, 80%, and 120%) and fingers (thumb and index) was randomized. The testing session for each subject lasted for approximately two hours.

2.2.3 Data Analysis

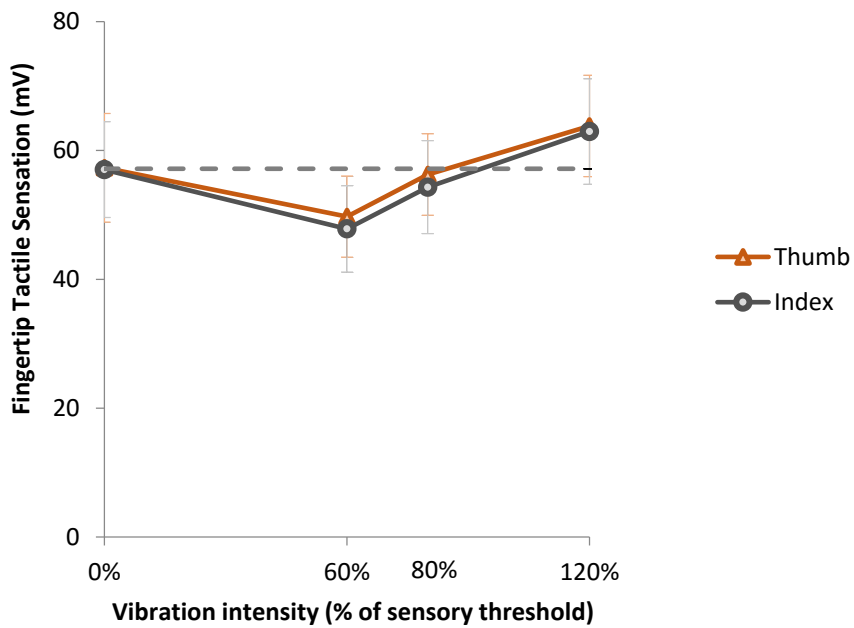
Repeated measures analysis of variance (ANOVA) was performed to determine if the fingertip tactile sensation score varied significantly with remote white-noise vibration. An inverse transformation was applied to the fingertip tactile sensation score data to ensure normality [32]. ANOVA was performed on the transformed data with the factors of vibration intensity (zero, 60%, 80%, and 120% of sensory threshold), vibration location (dorsal hand just proximal to the second knuckle, thenar eminence, hypothenar region, and volar wrist), finger (thumb and index), and their interactions. A conservative significance level of .01 was used. Tukey post-hoc analysis was performed for pairwise comparisons for significant factors.

2.3 Results

The fingertip tactile sensation score significantly varied with vibration intensity (Figure 3, $F_{3,341}=79.11$, $p<.0005$ in ANOVA). All other effects of vibration location ($F_{3,341}=1.30$, $p=.273$), finger ($F_{1,341}=1.07$, $p=.301$), and interactions were not found to be significant. Specifically for the effect of vibration intensity, the mean fingertip sensation improved by 15% with vibration at 60% of the sensory threshold compared to no vibration (Figure 3A, $T_{341}=-4.335$, $p=.0001$ in posthoc). The vibration intensity of 80% did not result in a significant change in fingertip tactile sensation compared to no vibration ($T_{341}=-0.970$, $p=.7667$ in posthoc). Fingertip tactile sensation degraded by 11% with 120% vibration intensity compared to no vibration ($T_{341}=3.213$, $p=.0072$ in posthoc). Such an effect of the vibration intensity was observed for all vibration locations (Figure 3A, C, $F_{9,341}=0.16$, $p=.997$ for the interaction between vibration intensity and vibration location in ANOVA). Also, the effect of the vibration intensity was observed for both fingertips (Figure 3B, $F_{3,341}=0.16$, $p=.925$ for the interaction between vibration intensity and finger in ANOVA). Individual subjects' data are also shown in Figure 4. All subjects showed improved fingertip sensation with vibration at 60% of the sensory threshold compared to no vibration (0%) for all vibration locations. All subjects showed worsened fingertip sensation with vibration at 120% of the sensory threshold compared to no vibration for all vibration locations, except for one subject for dorsum hand proximal to the second knuckle.



(A)



(B)

Figure 3: (A): Fingertip tactile sensation scores without and with white-noise vibration at different intensities. (B):

Fingertip tactile sensation scores without and with white-noise vibration at both fingertips

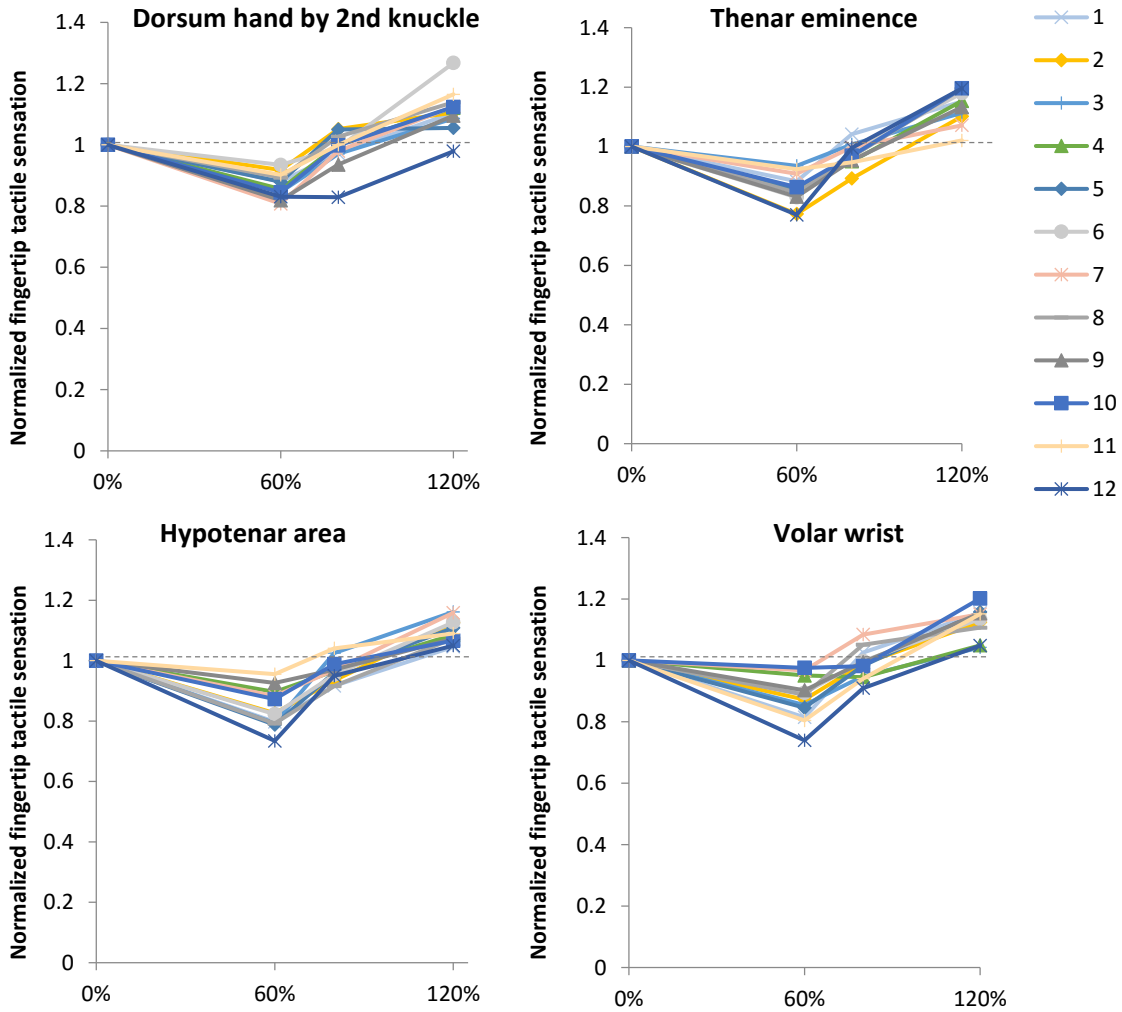


Figure 4: Fingertip tactile sensation scores without and with white-noise vibration at different locations

2.4 Discussions

2.4.1 Effect of remote white-noise vibration on fingertip tactile sensation

The main finding of this study is that tactile sensation of the thumb and index fingertip pads was affected by application of white-noise vibration to upper extremity skin sites other than fingertips at both imperceptible and perceptible intensities in healthy adults. Specifically, fingertip tactile sensation improved with remote imperceptible vibrations at the intensity of 60% of the sensory threshold. Imperceptible vibrations with

the intensity at 80% of sensory threshold did not significantly change fingertip tactile sensation. Perceptible white-noise vibration at 120% of sensory threshold worsened tactile sensation for both thumb and index fingertip pads. Interestingly, these effects of remote vibration of varying intensities on fingertip tactile sensation were found for all four locations to which the white-noise vibration was applied and for two fingertip pads for which tactile sensation was assessed. The way the thumb and index fingertip tactile sensation is influenced by white-noise vibration at the wrist, base of the palm, and back of the hand is postulated below.

2.4.2 Potential mechanism of remote white-noise vibration affecting fingertip tactile sensation

At the receptor level, it is postulated that not only perceptible but also imperceptible white-noise vibration activated mechanoreceptors in the skin site to which the remote vibration was applied. The minimum intensity of tactile stimuli on the palm to activate sensory neurons (neuronal threshold) was shown to be lower than the minimum intensity of tactile stimuli on the palm that is perceptible to a person (perceptual threshold) [33]. Thus, it is likely that the imperceptible vibration activated the skin mechanoreceptors and sensory afferents innervating the wrist, base of the palm, and back of the hand, while not perceived by the persons [34]. Since the remote vibration had white-noise low pass filtered at 500 Hz, all four mechanoreceptors could be stimulated, with pacinian corpuscle likely stimulated the most for its sensitivity to vibration. No definitive evidence exists as to if this weak vibration could reach tendon or muscle and stimulate spindles, although tendon vibration is typically performed with substantially suprathreshold

vibration intensity with a vibrator pushed into the skin overlaying the tendon unlike the preparation used here with the vibrator lightly placed on the skin.

Similar effects of all four remote vibration locations on fingertip sensation suggest that vibration affects fingertip sensing centrally, as opposed to peripherally. Specifically, the likelihood that the vibration may have traveled along the skin over the 10cm to 20cm distance to reach and affect the fingertip's mechanoreceptors is slim, given that vibration loses approximately 90% of its power as it travels 1cm to 2cm along the skin due to the skin's viscoelastic properties [35]. Also, the effect of vibration found in the results of this study was not related to the distance between the vibration location and the fingertips. Furthermore, vibration is unlikely to have led to direct mechano-electrical stimulation of the median nerve (responsible for fingertip sensation), since stimulation of the dorsum hand or hypothenar area, not overlapping the median nerve, led to the same result. Direct facilitation of the median nerve through action potential propagation within the nerve is also unlikely, since only one vibration location (thenar eminence) shared the median nerve with the fingertips and the other three vibration locations did not involve the median nerve in their pathways.

Centrally, neuronal activity induced by the remote white-noise vibration at the wrist, palm, and back of the hand could influence fingertip tactile sensing through the complex dynamics of the brain. Specifically, application of low-level noise to a neural system has been shown to increase phase synchronization between brain areas assessed by techniques such as the EEG [36, 37]. Facilitation in neural synchronization is indicative of enhanced transient communication networks for perception [37]. As such, when

application of low-level sensory noise to one body part facilitates neural synchronization in the brain, another body part's ability to detect sensory signals can improve: Visual noise to one eye or auditory noise to one ear led to phase synchronization of EEG signals among brain areas and enhanced signal detection with the other eye [38, 39, 40] or with the other ear [37]. In addition, crossmodal effects such as enhanced finger tactile and visual sensory threshold with auditory noise was also reported, potentially via the same noise-induced neural synchronization mechanism representative of establishment of transient networks for improved perception [41]. Likewise, the remote tactile noise-induced changes in fingertip tactile sensation shown in the present study along with the previous studies [17, 23] may have been mediated by noise-induced changes in neural synchronization involving brain networks for sensory perception.

As for the effect of white-noise intensity, remote white-noise vibration affected fingertip tactile sensation in a manner similar to stochastic resonance: Low-level imperceptible noise improved tactile signal detection, while perceptible (suprathreshold) noise degraded tactile signal detection [19, 21]. Optimal noise intensity of 60% of the sensory threshold, less effective intensity of 80%, and degrading intensity of 120% found in this study coincide with optimal noise range, less effective noise range, and degrading noise range, respectively, from previous studies [19, 21], although the present study delivered the noise and signal to two different skin sites within the upper extremity as opposed to a single skin site as in the previous studies. The postulated involvement of neural synchronization is not contradicted by the noise intensity effect: In fact, it was found that there was an optimal noise intensity that facilitated neural synchronization

whereas too high a noise intensity disrupted neural synchronization (i.e., stochastic resonance in neural synchronization) [36]. Thus, white-noise vibration at 60% of the sensory threshold at the remote locations may have facilitated neural synchronization, whereas 120% disrupted neural synchronization in the present study. Perceptible vibration at remote locations could also have reduced available attentional resources for fingertips.

In summary, it appears that the remote white-noise vibration may have affected neural synchronization for perceptual sensing thereby changing fingertip tactile sensation, although direct electrophysiologic evidence is warranted to test this viewpoint. In that respect, the neurobiological basis of this sensory manipulation method using remote sensory noise appears to be different from sensory noise applied directly to the fingertip that affects thresholds at the mechanoreceptor level [19, 27, 22]. In addition, the neurobiological basis of this sensory manipulation method appears to be different from the co-activation paradigm in which the two-point discrimination threshold of a fingertip pad improves after the fingertip pad receives suprathreshold vibration for 20 minutes or 3 hours, potentially via synaptic plasticity induced by co-activation of neighboring mechanoreceptors within the fingertip pad [42, 43].

2.4.3 Practical implications

This study suggests a new sensory manipulation paradigm for fingertip tactile sensation using white-noise vibration applied to different skin areas in the distal upper extremity. Specifically, imperceptible or perceptible white-noise vibration could be used to improve or degrade fingertip tactile sensory threshold, respectively, depending on

particular applications. For instance, since finger tactile sensation is essential for dexterous hand function [1], imperceptible white-noise vibration at the wrist or other parts of the upper extremity may be used to facilitate hand dexterity for high precision manual dexterity tasks [22] or to improve hand function for those with finger sensory deficit and subsequent hand impairment [44]. Such fingertip sensory manipulation is achievable with a relatively low-cost vibrator generating low-risk small vibration. In addition, the vibration does not have to be applied directly to the tactile signal source, but rather to a distant skin site such as the wrist or the back of the hand, which offers an advantage of placing a vibrator away from the fingers so as not to physically interfere with finger movement, finger sensing, and function.

Only tactile sensory threshold for vibratory stimuli was examined in this study. While improved performance on the two-point discrimination and texture discrimination tests was observed with imperceptible white-noise vibration applied to the side of the fingertip in healthy adults [22], such an effect lacked for the two-point discrimination test in chronic stroke patients with white-noise vibration applied to other upper extremity sites [17]. The way remote white-noise vibration affects other aspects of tactile sensation such as discrimination and resolution in healthy adults needs to be further investigated.

2.5 Conclusions

Remote white-noise vibration affected perceptual detection of fingertip tactile signal in healthy adults. Specifically, white-noise vibration at the intensity of 60% of sensory threshold improved fingertip tactile sensation while vibration at 120% of sensory threshold degraded fingertip tactile sensation. This effect of remote white-noise vibration

was found for all four remote locations in the hand and wrist to which the vibration was applied as well as for the two fingertips for which tactile sensation was measured. These results suggest that remote white-noise vibration exhibits stochastic resonance type behavior in affecting fingertip tactile sensation.

In the next chapter, we examined the effect of imperceptible white-noise vibration while sensing a touch stimuli, on the brain cortical activity for sensing.

CHAPTER 3

EFFECT OF IMPERCEPTIBLE VIBRATORY NOISE APPLIED TO WRIST SKIN ON FINGERTIP TOUCH EVOKED POTENTIALS

The objective of this study in the dissertation was to investigate if cortical activity for sensing touch stimuli on the fingertip is affected by imperceptible white-noise vibration applied to wrist skin. Recent studies have demonstrated that fingertip tactile sensation changes with white-noise vibration applied to different locations in the upper extremity such as wrist, forearm, dorsum of the hand, or base of the palm [17, 23, 45, 46]. Continuous, imperceptible, white-noise vibration applied to wrist skin resulted in decreased tactile sensory threshold of fingertips, indicating improved fingertip touch sensation [17, 45, 46].

3.1 Introduction

Sensation is important as a prerequisite for dexterous hand function including fine finger movements, gripping, and object manipulation [3, 2, 4, 1]. Therefore, improved fingertip touch sensation with vibration has direct implications for a wearable sensory enhancer wristband to assist human performance in high precision manual dexterity tasks as well as rehabilitation for those with a sensory deficit and impaired dexterity due to neurological problems [44].

Previous studies using imperceptible white-noise vibration have applied vibration directly to the fingertip to improve fingertip sensation [27, 22] or directly to the foot sole to improve foot sole sensation [27, 21]. However, the advantage of applying vibration to the wrist as opposed to the fingertips is that it exposes the entire finger/hand skin for

relevant tactile stimuli during dexterous manual tasks and also does not interfere with object manipulation using fingers.

The neurobiological bases for this remote vibration enhanced sensory feedback are yet poorly understood. It is thought that this effect is mediated by the central nervous system, since imperceptible vibration applied to the wrist is unlikely to have reached the fingertip and increased the sensitivity of mechanoreceptors in the fingertip pad skin: Vibration loses more than 90% of its power as it travels 1cm-2cm on the skin and approximately 99% of the power with a 6 cm travel due to the skin's viscoelastic properties [35]. While suprathreshold vibration may travel between the fingertip and wrist and activate remote mechanoreceptors [47, 48], the likelihood of activating remote mechanoreceptors becomes slim with subthreshold vibration, especially when the vibrating probe is surrounded by a ring, thus blocking the spread of vibration [49] in the previous studies [17, 23, 45]. In addition, manipulating the distance between fingertip and vibration location (e.g., fingertip-palm vs. fingertip-forearm) did not influence the results [17, 23, 45]. Furthermore, increasing the vibration intensity to a suprathreshold level at remote locations only degraded fingertip tactile sensation [45], indicating that transmission of vibration from the wrist to fingertip could not have improved fingertip tactile sensation. Also, vibration is unlikely to directly lead to stimulation of the median nerve (responsible for fingertip sensation), since stimulation of skin areas innervated by the radial or ulnar nerve, not overlapping the median nerve, can lead to the same results [17, 23, 45].

In this study, we aimed to evaluate whether vibration enhanced tactile perception is mediated by cortical-level processing. We examined if imperceptible white-noise wrist vibration affects somatosensory evoked potential for fingertip touch. Specifically, we hypothesized that the peak-to-peak amplitude of the somatosensory evoked potential in response to suprathreshold fingertip touch would increase when imperceptible white-noise vibration is applied to the wrist.

3.2 Methods

3.2.1 Participants

We studied 20 self-reported right-handed healthy adults (ten males) with no neurological or psychiatric history, and no history of upper limb trauma. The mean age of the participants was 25 ± 5 years. The protocol was approved by the Institutional Review Board (Study: 13.367-UWM). Participants read and signed a written informed consent form before participating in the experiment.

3.2.2 Procedure

The EEG somatosensory evoked potential in response to monofilament touch of the index fingertip was compared with vs. without imperceptible white-noise vibration applied to the volar wrist.

3.2.2.1 Imperceptible wrist vibration

Imperceptible vibration was applied to the volar aspect of the left wrist using a vibrator, C-3 Tactor (Engineering Acoustics, Inc., Casselberry, FL, USA). The vibrator was driven by white-noise signal low-pass filtered at 500Hz, as previously described [17]. The vibration intensity was adjusted to 60% of individual subjects' sensory

threshold at the wrist location determined at the beginning of the experiment. The sensory threshold is the minimum vibration intensity that a person can perceive and was determined using the method of ascending and descending limits [31]. All subjects reported that they could not feel the wrist vibration during the course of the EEG experiment.

3.2.2.2 Fingertip touch stimulation

The left index fingertip pad received touch stimulation by a monofilament delivered by a stepper motor triggered by a computer. The distance between the tip of the monofilament and the fingertip skin was adjusted so that the monofilament touches and bends slightly against the fingertip skin, in a similar manner compared with the clinical sensory assessment using the Semmes-Weinstein monofilament test [50]. The monofilament used here was similar to the 3.61 Semmes-Weinstein monofilament, which represents a light touch with 0.2g-force that healthy adults should be able to perceive [51]. The reason that this study did not test a stimulus that becomes perceivable only with vibration is that somatosensory evoked potentials for perceived vs. unperceived stimuli are known to be different [52, 34] and the difference in the evoked potential would be attributable not only to vibration but also to perception (confounding). Thus, this study examined changes in the somatosensory evoked potential of a perceivable stimulus with vibration. The rationale is that vibration affects not only the tactile threshold but also manual dexterity [44] suggesting changes in processing of perceived stimuli with vibration.

3.2.2.3 EEG acquisition

EEG signals were continuously recorded at 1kHz using a 64 channel active electrode system (actiCAP, Brain Products GmbH, Gilching, Germany) and a Synamps2 amplifier system (Neuroscan, Charlotte, NC). The electrode position followed the international 10-20 system with an average reference and a ground at AFz. The EEG cap was placed on the subject's head so that the Cz electrode was at the vertex. Each electrode site was hydrated using SuperVisc gel (Brain Products GmbH, Gilching, Germany). All electrodes' impedance was below 20k Ω . EEG signals were amplified, bandwidth filtered at 0.10Hz to 200Hz, and recorded at 1kHz using the Neuroscan software, SCAN 4.5.

A total of 200 fingertip touch stimulations were presented with a random interstimulus interval of 4s-5s through two continuous recordings of 9 minutes each. Each recording of 100 trials was composed of 4 blocks of 25 trials each. The imperceptible wrist vibration was on for two blocks, and off for the other two blocks. For vibration-on blocks, vibration was turned on 4s-5s prior to the first touch stimulation and continued on throughout the block. Similarly, for vibration-off blocks, vibration was turned off 4s-5s prior to the first touch stimulation and continued off throughout the block. The order of vibration blocks was randomized. Thus, each subject received 100 fingertip touch stimulations while wrist vibration was on and 100 fingertip touch stimulations while the wrist vibration was off. All subjects were able to perceive the monofilament touch of the fingertip. However, since the vibration was imperceptible, subjects did not know for which trials the wrist vibration was on.

During EEG recording, subjects gazed at a fixation spot, wore ear plugs and a headphone to block sounds, and stayed relaxed (Figure 5). The motor moving the monofilament was contained in a foam structure to block the transmission of sound from the motor to the subject. All subjects reported that they could not hear the sound from the motor moving the monofilament. Subjects were seated with the left arm resting and left index fingernail fixed to stabilize the fingertip pad for the monofilament touch. The motor driving the monofilament and the finger receiving the touch were located behind a screen so that subjects could not see the monofilament's movement relative to the fingertip.

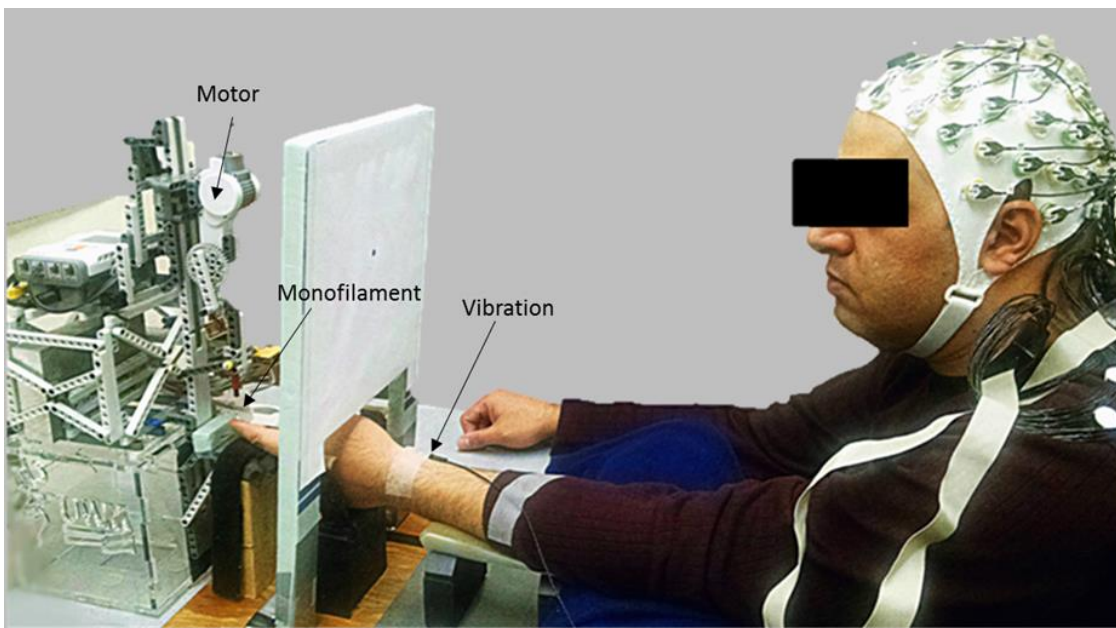


Figure 5: Experimental setup.

3.2.3 EEG analysis

The EEG data were analyzed using MATLAB (The MathWorks, Natick, MA) and EEGLAB toolbox [53]. The data were band-pass filtered at 0.5Hz to 50Hz to remove

drifts and line noise. Independent component analysis was performed on the data to remove sources of artifacts using the ADJUST algorithm [54]. Then, data were divided into epochs ranging from -100ms to 600ms relative to the stimulus onset (monofilament's touch of the fingertip). The time period before the fingertip touch (-100ms to 0ms) served as the baseline brain activity. To remove additional artefacts, a moving window peak to peak threshold method in ERPLAB [55] was used with a 200ms moving window, a 100ms window step, and a $100\mu\text{V}$ threshold, which resulted in rejection of an average 11% of trials (SD = 13%). The average somatosensory evoked potential was obtained by averaging remaining epochs for each subject for each condition.

The C4 electrode over the right primary sensorimotor area contralateral to the stimulation site [56, 57] was of primary interest. Thus, while evoked potentials for all electrodes were visually examined, primary statistical analysis was performed for C4 electrode to compare mean peak-to-peak somatosensory evoked potential amplitudes between the vibration-on and vibration-off conditions in the subject group using a paired t-test. We tested the hypothesis that the evoked potentials for the vibration-on condition would be greater than the evoked potentials for vibration-off. Significance level of 0.05 was used. After obtaining a significant result for the mean peak-to-peak evoked potential amplitudes, the increase in the positive peak and decrease in the negative peaks with vibration in the subject group were examined using paired t-tests with Bonferroni correction applied (with the significance level of 0.025).

As secondary analysis, the spread of the effect was examined for the C2, C4, C6, FC2, FC4, and FC6 electrodes representing the contralateral sensorimotor and premotor areas.

Involvement of these areas in the later phase of the evoked potential was shown in previous sensory perception literature [58, 52] as well as from visual inspection of our results (Figure 6). Repeated measures ANOVA was performed to determine if the factors of electrode, vibration (on/off), and their interaction affected the positive peak of the evoked potential.

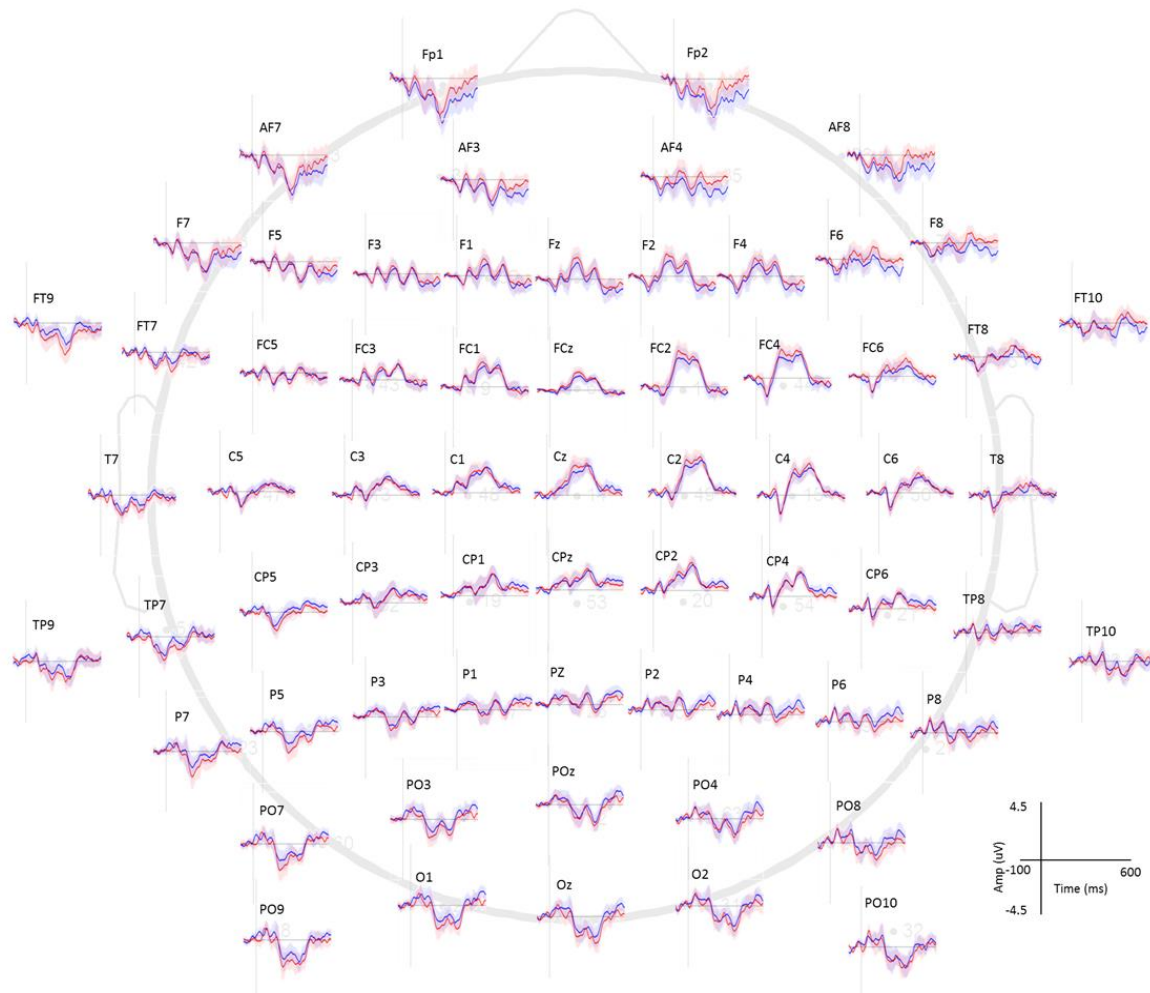


Figure 6: All electrodes' average potentials after touch on the index fingertip pad (time = 0 ms) while imperceptible white-noise vibration was applied to the volar wrist (red) as compared to vibration turned off (blue). Mean potentials averaged for all subjects with 95% confidence intervals are shown.

In addition, source reconstruction was performed to evaluate the anatomical location of the evoked potential generators. Cortical current sources were modeled using Brainstorm [59] on a standard 3-D brain model (Colin27: MNI brain with a 1 mm resolution) for the somatosensory evoked potential epoch period (-100ms to 600ms) for each subject and condition. Source reconstruction was performed on the evoked EEG data encompassing all channels (with the same filter settings 0.10Hz to 200Hz) with 1ms time bin. Forward modeling was conducted using OpenMEEG, which uses the symmetric boundary element method [60], and inverse modeling of the sources was constructed using a whitened and depth-weighted linear L2-minimum norm estimates (wMNE) algorithm [59]. Then, the average sources in the 10ms time bin around the negative and positive peaks (5ms before and after the peak) of the somatosensory evoked potential of the C4 electrode were obtained for each subject and condition. They were exported to SPM8, smoothed by 10mm, and averaged across subjects for each condition to visually compare between the two vibration conditions.

3.3 Results

Potentials after index fingertip touch with vs. without wrist vibration are shown for all electrodes in Figure 6. Specifically, evoked potentials for the C4 electrode averaged for all subjects are shown for the vibration on and off conditions (Figure 7). Peak-to-peak amplitudes of the somatosensory evoked potential after touch of the index fingertip pad averaged for all subjects are compared between the two vibration conditions in Figure 8A. The peak-to-peak evoked potential was significantly greater while the imperceptible white-noise vibration was applied to the volar wrist compared to while the vibration was

turned off ($p=0.003$, Figure 8A). The initial negative peak was not significantly larger with the vibration than without ($p=0.180$), whereas the late positive peak was significantly larger with the vibration than without ($p=0.024$, Figure 8B). The negative peak occurred at $85\text{ms} \pm 10\text{ms}$ (95% confidence interval) and $93\text{ms} \pm 16\text{ms}$ for the vibration on and off conditions, respectively ($p=0.113$), and the positive peak occurred at $277\text{ms} \pm 31\text{ms}$ and $274\text{ms} \pm 31\text{ms}$ for the vibration on and off conditions, respectively ($p=0.376$). The secondary analysis showed that the vibration significantly affected the positive peak of the evoked potential for all 6 electrodes encompassing the sensorimotor and premotor areas (Figure 9, $p=0.004$ for the vibration effect, $p=0.999$ for the vibration and electrode interaction).

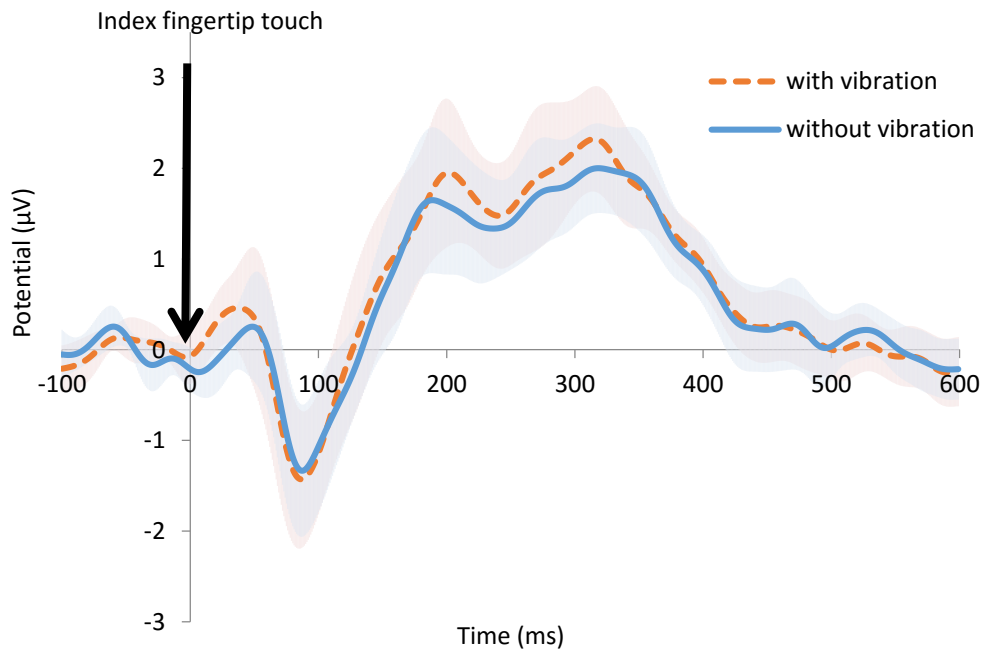


Figure 7: Somatosensory evoked potential after touch on the index fingertip pad while imperceptible white-noise vibration was applied to the volar wrist (red segmented line) as compared to vibration turned off (blue solid line). Mean potentials with an upper or lower bound 95% confidence interval at C4 electrode averaged for all subjects are shown.

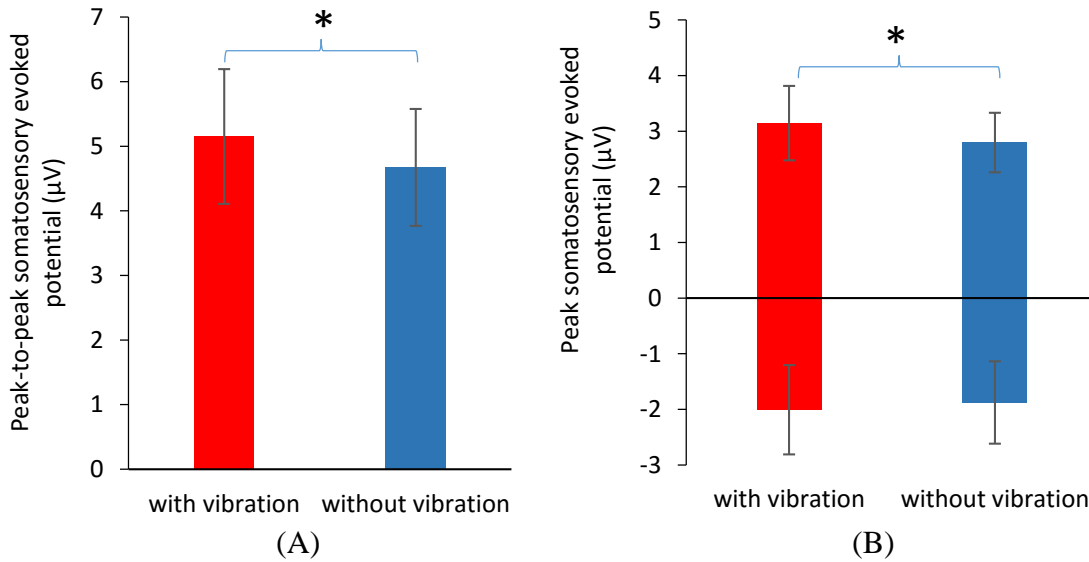


Figure 8: Mean peak-to-peak somatosensory evoked potential at C4 electrode after touch on the index fingertip pad while imperceptible white-noise vibration was applied to the volar wrist as compared to vibration turned off. (A): Mean of 20 subjects' mean peak-to-peak somatosensory evoked potentials are shown with 95% confidence intervals. (B) The mean positive and negative peaks for 20 subjects were compared separately.

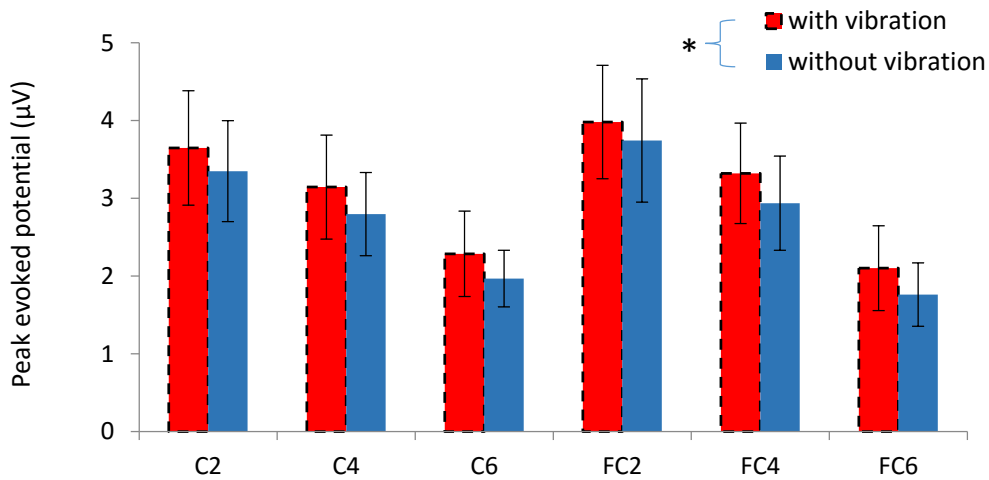


Figure 9: Peak somatosensory evoked potentials at C2, C4, C6, FC2, FC4, and FC6 electrodes after touch on the index fingertip pad while imperceptible white-noise vibration was applied to the volar wrist as compared to vibration turned off. Mean of 20 subjects' mean positive peak of the somatosensory evoked potentials are shown with 95% confidence intervals.

Source localization indicates activity on the sensorimotor area after fingertip touch (Figure 10). Specifically, changes in brain activity at the early negative peak and late positive peak of the C4 electrode somatosensory evoked potential after touch of the fingertip pad compared to the baseline (average across 100ms to 0ms before touch), averaged for all subjects, are shown for the vibration off and on conditions. A greater sensorimotor neural recruitment is observed in the vibration-on condition, especially during the late positive evoked potentials (Figure 10 right).

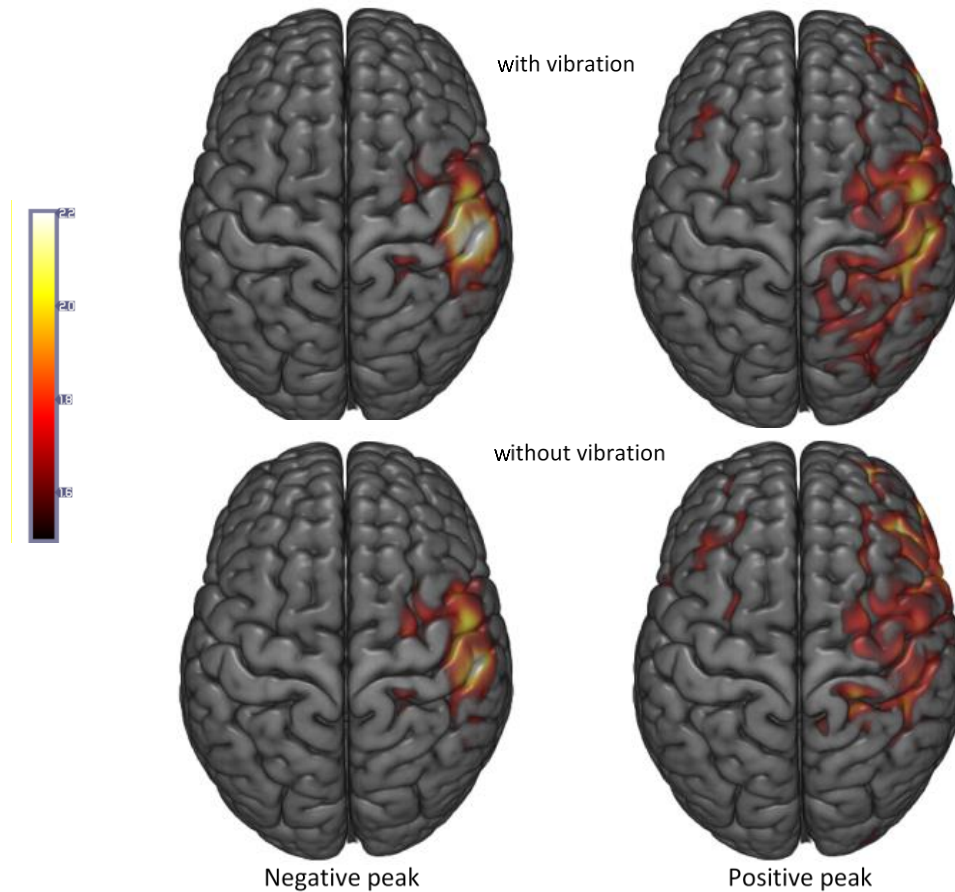


Figure 10: Source localization for the vibration-on condition (top) and vibration-off condition (bottom, control). Subject-averaged brain activity for the early negative peak (left) and the late positive peak (right) compared to the baseline (100 - 0 ms before touch) is shown for both vibration conditions.

3.4 Discussion

The result of this study provides evidence that imperceptible white-noise vibration applied to the volar aspect of the wrist affects cortical processing of fingertip tactile stimuli. Specifically, peak-to-peak somatosensory evoked potentials at the somatosensory cortex increased with wrist vibration. This increased peak-to-peak amplitude was due to increase in the positive peak in the later phase (after 200ms), not the negative peak in the earlier phase (~100ms) of the cortical sensory processing. This increased later phase positive peak was spread across the somatosensory, motor, and premotor cortex. Change in conscious attention could not have been involved because subjects did not feel the vibration throughout the EEG recordings and the order of vibration-off and vibration-on blocks were randomized.

This observation supports the modulation of cortical-level somatosensory processing during manipulation of vibratory feedback, providing the neurobiological basis for its use in rehabilitation. These findings challenge the typical assumption that imperceptible vibration at wrist, for instance from resting the hand on a table, has no influence on finger sensation. They also support the previous findings of remote vibration-induced changes in fingertip tactile perceptual sensory threshold [17, 46] and associated motor behavior [23, 44], supporting further investigation for use of wrist vibration to affect finger sensation for various applications.

The significant increase in the later component but not in the earlier component of the somatosensory evoked potential (Figure 8B) indicates that vibration affects conscious experience of the stimuli. The early component of the somatosensory evoked potential

originates from the arrival of the thalamo-cortical volley [61, 34] and is representative of stimulation strength which in this study was constant between the vibration on and off conditions. While perithreshold stimuli can evoke varying amplitudes of the early component potentially due to variability in neuronal firing and the amplitudes are associated with awareness [52], the present study used a suprathreshold stimulus that may be less affected by variability in neuronal firing. Similarities in the negative evoked potential at this time point suggest that the evoked signal reaching cortical levels is similar with or without vibration. On the other hand, the later components correlate with conscious experience and recurrent processing within the network of somatosensory and premotor cortices [58, 52]. The wrist vibration appears to have affected this conscious experience and recurrent processing of the finger tactile stimulus. With vibration, increased responses in the contralateral C and FC electrodes associated with the late component of the evoked potential support the idea that vibration has an effect on premotor areas of the cortex.

It is possible that the cortical modulation observed here is the result of the establishment of transient networks for recurrent processing and improved perception. Sensory noise has been shown to increase phase synchronization within and between EEG cortical sources [40, 41, 37], suggestive of establishment of networks [36, 37] for somatosensory processing. Such phase synchronization among brain areas is associated with improved sensory perception: Visual or auditory noise in one eye or one ear improves detection with the other eye or the other ear [40, 41, 37]. Even enhanced finger tactile sensory threshold was reported with auditory noise [41]. Thus, the wrist vibration

could have affected phase synchronization related to somatosensory processing of the finger stimuli.

In contrast to this body of literature describing the effect of background sensory noise on detection of other sensory signal, brief imperceptible sensory stimulation alone (without other sensory signal to detect) has been shown to transiently reduce BOLD signals suggesting focal deactivation or inhibition [62], reduce functional connectivity between the primary somatosensory area (SI) and frontoparietal areas and increase EEG alpha frequency power for the somatosensory area [34] indicative of “cortical idling” [63], resulting in impediment in sensory processing for the finger area receiving the imperceptible electrical stimulation [62]. The finding of the present study may not be in direct contradiction with these previous studies, as the imperceptible vibratory stimulation of the wrist could have induced a focal deactivation of the wrist area in the somatosensory cortex and spared neural resources for better sensing of other hand areas such as fingers, as in temporary deafferentation [64, 65, 66]. In previous deafferentation studies, numbing of forearm skin resulted in improved fingertip sensation assessed by the Grating orienting task and improved hand dexterity assessed by the Shape-sorter-drum task [65, 66] as well as increased evoked magnetic field for fingertip tactile stimulation and expansion of cortical representations for the fingers [66].

Taken together, our findings complement previous observations by corroborating that changes in sensory processing due to interfering stimuli occur as a result of modulation of cortical level networks. The recruitment of neural resources may depend on the underlying neural circuitry and anatomical distributions of cortical representations.

Disturbance affecting adjacent but overlapping cortical areas may lead to destructive interference. For example, across areas related to the index and middle fingers with a cortical overlap [67], impaired sensing for the index finger, either by constant frequency tactile stimulation [68] or imperceptible electrical stimulation [69], resulted in impaired sensing for the middle finger [68] and decreased BOLD signal in response to middle fingertip touch [69]. Conversely, when cortical areas are adjacent but separated such as between wrist and fingertip, it is possible that one area's deactivation leads to adjacent areas' increased activity [64]. However, it is also postulated that when the cortical areas are far away from each other (e.g., fingertip and upper arm or leg), the effect would not sustain.

3.5 Conclusions

In conclusion, the findings from this study indicate that enhanced sensory response motivated by vibratory sensory noise is related to cortical modulation, possibly as a result of the establishment of transient networks for improved perception. This mechanism could be explored for further use in neural rehabilitation. For instance, patients with impaired sensorimotor function who still have the two somatotopic areas adjacent to each other with residual tracts may use this sensory vibration to enhance their sensory experience and subsequent motor control. This study examined rather immediate effects of vibration, not the effects of long-term exposure to vibration. With long-term exposure of hours and days as in rehabilitation settings, dynamic changes may occur with sensitization or adaptation, which needs to be addressed before use of vibration in a long-term rehabilitation setting.

In the next chapter, we investigated if the cortical modulation of beta (β) band power was affected by imperceptible white-noise vibration while performing precision pinch.

CHAPTER 4

EFFECT OF IMPERCEPTIBLE VIBRATORY NOISE APPLIED TO WRIST SKIN ON CORTICAL CONTROL FOR PRECISION PINCH

The objective of this study in the dissertation was to investigate if the modulation of movement-based beta (β) band power during precision pinch is affected by imperceptible white-noise vibration applied to wrist skin. Recent studies have demonstrated improvement in hand tactile sensation with application of white-noise vibration away from the hand (e.g., wrist, forearm, dorsum of the hand, or base of the palm) [17, 23, 45, 46]. Continuous white-noise vibration application on the wrist skin resulted in faster reaction to hand perturbation and earlier stabilization of hand grip in healthy adults, and increased pinch grip strength in neurologically impaired patients [23, 44].

4.1 Introduction

Improvement in motor function was expected to result from improved sensation with subthreshold remote stimulation, because tactile sensation plays a key role in dexterous hand function [3, 2, 4, 1]. Tactile sensation through mechanoreceptors [3] and proprioception [70] is required in order to maintain a certain grip force without visual feedback [71]. Improving hand dexterity has implications in enhancing human performance in high dexterity tasks, helping aged people regain their hand functions, and serve as a rehabilitation tool for patients affected with neurological disorder.

The neurobiological bases for enhanced hand dexterity with improved hand tactile sensation via white-noise vibration is yet poorly understood. It has been demonstrated that the vibration enhanced tactile perception is mediated by cortical-level processing

[72], as opposed to the vibration applied to the wrist travelling to the fingertips, since vibration loses more than 90% of its power travelling 1cm-2cm on the skin [35]. The peak-to-peak somatosensory evoked potential increased with vibration and was spread across the somatosensory, motor, and premotor cortex [72]. The primary motor cortex (M1), responsible for voluntary hand movements, exhibited multiple, overlapping sites during individuated finger and wrist, suggesting interneuronal connections among various parts of the hand [73, 63], via which the vibration signal may reach high-order fingertip sensory afferents once it enters the central nervous system and affect both sensation and motor functions.

β waves are neural oscillations due to brain activity in the frequency range 12-28 Hz [74]. The β -band power modulation have been shown to be in relation to voluntary movements [75]. An increase in β -band power is referred to as an event-related synchronization (ERS) and a decrease is referred to as an event-related desynchronization (ERD) [76]. A voluntary movement, is typically preceded by ERD, with power reaching a minimum during movement execution, followed by ERS after movement termination known as “beta rebound” [77, 63]. The β -band ERS/ERD are found mainly around the sensorimotor cortex, with a contralateral predominance [77, 78].

In this study, we aimed to evaluate whether vibration-enhanced motor function is mediated by β -band power modulation in the sensorimotor cortex. We evaluated the difference between β -band ERS and ERD. Specifically, we hypothesized that the peak-to-peak amplitude of the β -band event-related spectral perturbation (ERSP) during precision pinch would increase when imperceptible white-noise vibration is applied to the wrist.

4.2 Methods

4.2.1 Participants

Twenty healthy right-handed adults (eight females and twelve males) with a mean age of 25 ± 5 ranging from 19 to 40 years participated in the study. All subjects verbally disclosed that they had no history of upper limb injury or musculoskeletal or neurologic disorders. The protocol was approved by the Institutional Review Board (Study: 13.367-UWM). Subjects read and signed a written informed consent form before participating in the experiment.

4.2.2 Procedure

The EEG β -band modulation at the sensorimotor cortex during precision pinch grip was compared with vs. without imperceptible white-noise vibration applied to the volar wrist.

4.2.2.1 Imperceptible wrist vibration

Imperceptible vibration application was performed using the method described in the previous chapter [72]. The vibration was applied by attaching a C-3 Tactor (Engineering Acoustics, Inc. Casselberry, FL) on the left hand at the volar wrist. The C-3 Tactor generated white-noise vibration low pass filtered at 500Hz. The vibration was applied at an intensity of 60% of individual subjects' sensory threshold at the volar wrist. The sensory threshold, which is the minimum vibration intensity a person can perceive was determined at the beginning of the experiment using the ascending and descending limits [31].

4.2.2.2 Precision pinch

Subjects performed precision pinch using the left hand thumb and index fingers on two load cells (Mini40, ATI Industrial Automation, Apex, NC). The load cells were placed on a support facing each other as each load cell recorded pinch force from the thumb and index fingers separately when the fingers were placed on either sides of the two load cells. Subjects aimed at a pinch grip of 4N to prevent cutaneous receptors from being overloaded and becoming less relevant for grip control at high pinch force levels [79]. Two different types of pinches, namely a 2-sec sustained pinch and ballistic pinch were performed during the experiment both with and without imperceptible vibration applied at the wrist.

4.2.2.3 EEG acquisition

EEG signals were continuously recorded at 1kHz using a 64 channel active electrode system (actiCAP, Brain Products GmbH, Gilching, Germany) and a Synamps2 amplifier system (Neuroscan, Charlotte, NC). The electrode position followed the international 10-20 system with an average reference and a ground at AFz. The EEG cap was placed on the subject's head so that the Cz electrode was at the vertex. Each electrode site was hydrated using SuperVisc gel (Brain Products GmbH, Gilching, Germany). All electrodes' impedance was below 20k Ω . EEG signals were amplified, bandwidth filtered at 0.10Hz to 200Hz, and recorded at 1kHz using the Neuroscan software, SCAN 4.5.

A total of 250 pinches were performed, 125 pinches with remote sensory stimulation and 125 pinches without remote stimulation. Only 200 pinches without visual feedback

were used for analysis (see below). The pinches were performed by the subjects on seeing a cue displayed on a computer screen. During the experiment, subjects were seated with their left hand resting and left index and thumb fingers away from the load cells during rest, while a cue to rest was displayed on the screen as “REST”. Subjects were instructed to start pinching using their left index and thumb fingers at 4N once the cue changed to “PINCH”. During sustained pinch, subjects were instructed to maintain their pinch for the two seconds the pinch cue was displayed before relaxing and waiting for the next cue, whereas during ballistic pinch, subjects were instructed to try and pinch at 4N in a sudden and quick manner on seeing the cue to pinch and relax immediately. Subjects were instructed to perform the pinches in a swift motion without constant adjustments. The pinch cue was displayed for 2 seconds during sustained pinch and for 0.5 seconds during ballistic pinch. The time interval between the start of consecutive pinch cues were 7s-8s and 5s-6s for the sustained and ballistic pinch grips, respectively. Five runs of the experiment was performed for each pinch type. Each run with 50 pinch trials were composed of 2 blocks of 25 trials each with the imperceptible vibration on for one block and off for the other. At the beginning of each block the first 5 trials were presented with a visual feedback for subjects to practice pinching at 4N and for data analysis, the subjects aimed to perform pinch grips at 4N without visual feedback for the remaining 20 trials in each block. Subjects did not know which trials the vibration was on since the vibration was imperceptible.

During EEG recording, the subjects gazed at the screen and stayed relaxed with their left arm resting over the table (Figure 11).

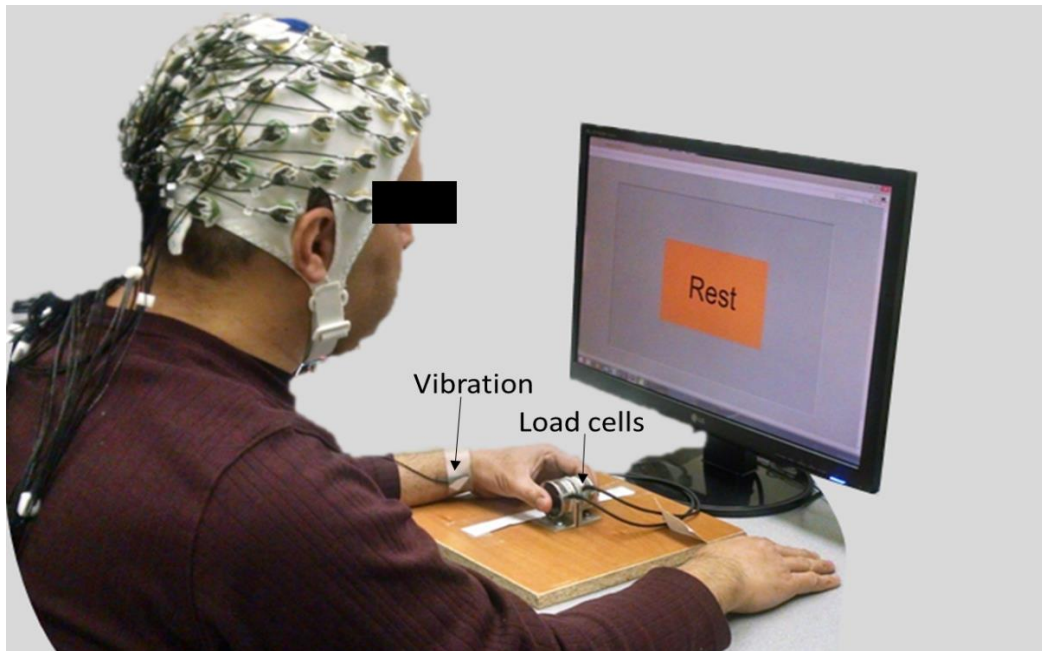


Figure 11: Experimental setup

4.2.3 Pinch force analysis

A force trace while the subjects pinched was constructed using the data from the two load cells which the subjects pinched. Only 98 files of force data out of 200 files for both pinches combined were available to us, with the rest lost due to a hard-disk crash. Using the available files, a force trace over time was constructed for each trial both sustained and ballistic pinches. The trials where subjects didn't perform a pinch, performed a pinch before the pinch cue, and ended a pinch before the pinch cue turned to rest were all removed. For sustained pinch, 0.6% of trials from the total number of trials (200 for each subject) were removed and 0.5% of trials were removed for ballistic pinch.

To examine whether pinch grip improved with noise, a t-test was performed separately for both pinch types. For sustained pinch, the mean force trace over a time period of 1000ms to 2000ms (pinch cue was presented at 0ms) was taken and compared

between with vs without remote sensory stimulation. The 1 second window was chosen to eliminate force initiation and termination and choose the time all subjects were performing a sustained pinch. For ballistic pinch, the peak force was compared. To examine if amount of force applied differed with pinch type and sensory condition, a repeated measures ANOVA was performed to examine the peak force during sustained pinch and ballistic pinch with and without remote sensory stimulation.

4.2.4 EEG analysis

The EEG data were analyzed using MATLAB (The MathWorks, Natick, MA) and EEGLAB toolbox [53]. The data were band-pass filtered at 0.5Hz to 50Hz to remove drifts and line noise. Independent component analysis was performed on the data to remove sources of artifacts using the ADJUST algorithm [54]. Then, data were divided into epochs ranging from -1000ms to 7000ms and -1000ms to 5000ms relative to the stimulus onset (when pinch cue was displayed) for sustained and ballistic pinch respectively, which is the minimum time length between consecutive pinch cues for the respective pinch types. The time period before the pinch cue (-1000ms to 0ms) served as the baseline brain activity and the epochs were baseline corrected. Artifacts were identified by visual inspection and rejected. Trials removed from force trace analysis were also removed from EEG data. For sustained pinch 21.2% of the total number of trials (200 for each subject) were rejected, and 27.4% of trials were rejected for ballistic pinch.

The primary interest was the C4 electrode located over the right primary sensorimotor area, contralateral to the left hand volar aspect where the white-noise vibration was applied [56, 57]. The C4 electrode was used for primary statistical analysis in both pinch conditions using a paired t-test to examine β -band amplitude change between ERD and ERS for each vibration condition. We tested the hypothesis that the β -band peak-to-peak amplitude would be greater for vibration-on condition compared to vibration-off condition at a significance level of 0.05.

Time-frequency analysis was performed for the C4 electrode using EEGLAB pop_newtimef function to find event-related perturbations (ERSP). ERSP is the average dynamic changes in amplitude of the EEG frequency spectrum as a function of time relative to the pinch cue. The epoch time length for each pinch condition was linearly spaced to 200 time points before and after the pinch cue combined. Frequency components for linearly spaced frequencies between 10Hz and 30Hz was obtained for these time points. ERSP was computed by calculating the baseline spectra from the time period preceding the pinch cue (-1000ms to 0ms). The epochs were divided into overlapping data windows, for which a moving average of the amplitude spectra were created. The spectral transforms of individual epochs were normalized by dividing by their respective mean baseline spectra. Finally, the normalized response transforms were averaged over all the trials to produce an average ERSP. The ERSP was calculated with respect to the pinch cue instructing the subject to pinch (-1000ms to 0ms, pinch cue being presented at 0ms) by a bootstrap algorithm [80], with the level of significance of $\alpha = 0.05$. The bootstrap algorithm was used to assess the significance of deviations from

baseline power. The significance levels were used to mask out the non-significant values in the ERSP plot. This was shown by the green areas (Figure 12: (A): Time-frequency plot for C4 electrode averaged over 20 subjects for both vibration-off and vibration-on conditions during sustained pinch. (B): Time-frequency plot for ballistic pinch. The time-frequency plot displays ERSP, the average dynamic changes in amplitude of the EEG frequency spectrum as a function of time relative to the pinch cue.). The bootstrap algorithm constructed a surrogate data distribution by randomly selecting latency windows in the specified epoch baseline, and then averaging these and selecting spectral estimates for each trial from the latency windows. The process was applied 200 times by default to produce a surrogate baseline amplitude distribution. The specified percentiles from the baseline were taken as significance thresholds. The pinch cue was used to align the epochs in both pinch conditions. β -band (12-28Hz) peak-to-peak amplitude was calculated from the ERSP. For instances where there are two negative peaks occurring at both pinch movement onset and offset, the largest peak was taken for calculation.

Having found significant results at the C4 electrode primary sensorimotor area site for just sustained pinch, the spread of β -band peak positive amplitude during ERS was examined. To determine the spread of the vibration effect, a repeated measures ANOVA was performed for the positive peaks at F4, FC1, FC2, C4, AF8, F2, F6, FC4, C6, CP4, and FCz electrodes representing the contralateral prefrontal areas (AF and F electrodes) [81], contralateral sensorimotor and primary motor areas (C and CP4 electrodes) [82], and premotor areas and the supplementary motor area (FC electrodes) (SMA) [83], to

determine if the factors of electrode, vibration condition, and their interactions affected the β -band positive peak while subjects performed sustained pinch.

A repeated measures ANOVA was also performed to evaluate beta bands' peak ERD and ERS values (ERSP(dB)) between the two pinch types only for the without vibration condition. This was done to examine whether ERD dip and/or ERS rebound was significantly different between the two pinch types.

4.3 Results

Peak-to-peak β -band amplitudes for both pinch conditions averaged for all subjects are compared between the vibration conditions in Figure 14: Peak-to-peak β -band amplitude after pinch cue was displayed while imperceptible white-noise vibration was off compared to vibration turned on (A): Mean peak-to-peak β -band amplitude at C4 electrode for all subjects are shown with 95% confidence intervals for sustained pinch. (B) Mean peak-to-peak β -band amplitude at C4 electrode for ballistic pinch.A and Figure 14: Peak-to-peak β -band amplitude after pinch cue was displayed while imperceptible white-noise vibration was off compared to vibration turned on (A): Mean peak-to-peak β -band amplitude at C4 electrode for all subjects are shown with 95% confidence intervals for sustained pinch. (B) Mean peak-to-peak β -band amplitude at C4 electrode for ballistic pinch.B. The peak-to-peak β -band amplitude for sustained pinch was significantly larger for vibration-on condition compared to vibration-off ($p=0.011$, Figure 14: Peak-to-peak β -band amplitude after pinch cue was displayed while imperceptible white-noise vibration was off compared to vibration turned on (A): Mean peak-to-peak β -band amplitude at C4 electrode for all subjects are shown with 95% confidence intervals for

sustained pinch. (B) Mean peak-to-peak β -band amplitude at C4 electrode for ballistic pinch.A), whereas β -band amplitude for ballistic pinch had no significant difference ($p=0.470$, Figure 14: Peak-to-peak β -band amplitude after pinch cue was displayed while imperceptible white-noise vibration was off compared to vibration turned on (A): Mean peak-to-peak β -band amplitude at C4 electrode for all subjects are shown with 95% confidence intervals for sustained pinch. (B) Mean peak-to-peak β -band amplitude at C4 electrode for ballistic pinch.B). β -band negative peak for sustained pinch was not significantly different between the two vibration conditions ($p=0.236$), whereas the β -band positive peak for sustained pinch was significantly larger with vibration on compared to vibration off ($p=0.012$, Figure 15: Mean β -band amplitude positive and negative peaks at C4 electrode for all subjects with 95% confidence intervals were compared for sustained pinch). The mean and standard deviation times for positive and negative peaks with and without vibration for both pinches are shown in Table 1. The β -band peak-to-peak amplitude for sustained pinch with vs. without vibration for all electrodes are shown in Figure 16: All electrodes' peak-to-peak β -band amplitude (dB) while imperceptible white-noise vibration was turned off (blue) as compared to when vibration was turned on (red). Mean peak-to-peak β -band amplitude for all subjects are shown with 95% confidence intervals for sustained pinch.. β -band positive peak for sustained pinch was significantly affected by vibration for all 11 electrodes (Figure 17: Positive peak β -band amplitude at F4, FC1, FC2, C4, AF8, F2, F6, FC4, C6, CP4, and FCz electrodes while imperceptible white-noise vibration was off compared to vibration turned on. Mean of all 20 subjects' mean positive peak of β -band amplitude are shown

with 95% confidence intervals., $p=0.000$ for the vibration effect, $p=0.996$ for electrode and vibration interaction). ERD and ERS did not show any statistical difference between the two pinch types for without remote stimulation condition ($p=0.208$).

The force trace analysis did not yield a significantly different mean force between with and without remote sensory stimulation during sustained pinch ($p=0.071$) (Figure 18: (A) Mean of the average force for a 1 sec window during sustained pinch with standard deviation compared with vibration turned off and on (B) Mean peak force with standard deviation for ballistic pinch compared with vibration turned off and onA). The ballistic pinch peak force did not show any significant difference between with and without remote sensory stimulation ($p=0.874$) (Figure 18: (A) Mean of the average force for a 1 sec window during sustained pinch with standard deviation compared with vibration turned off and on (B) Mean peak force with standard deviation for ballistic pinch compared with vibration turned off and onB). The peak force during sustained and ballistic pinch did not vary significantly from each other for both with and without sensory stimulation ($p=0.349$).

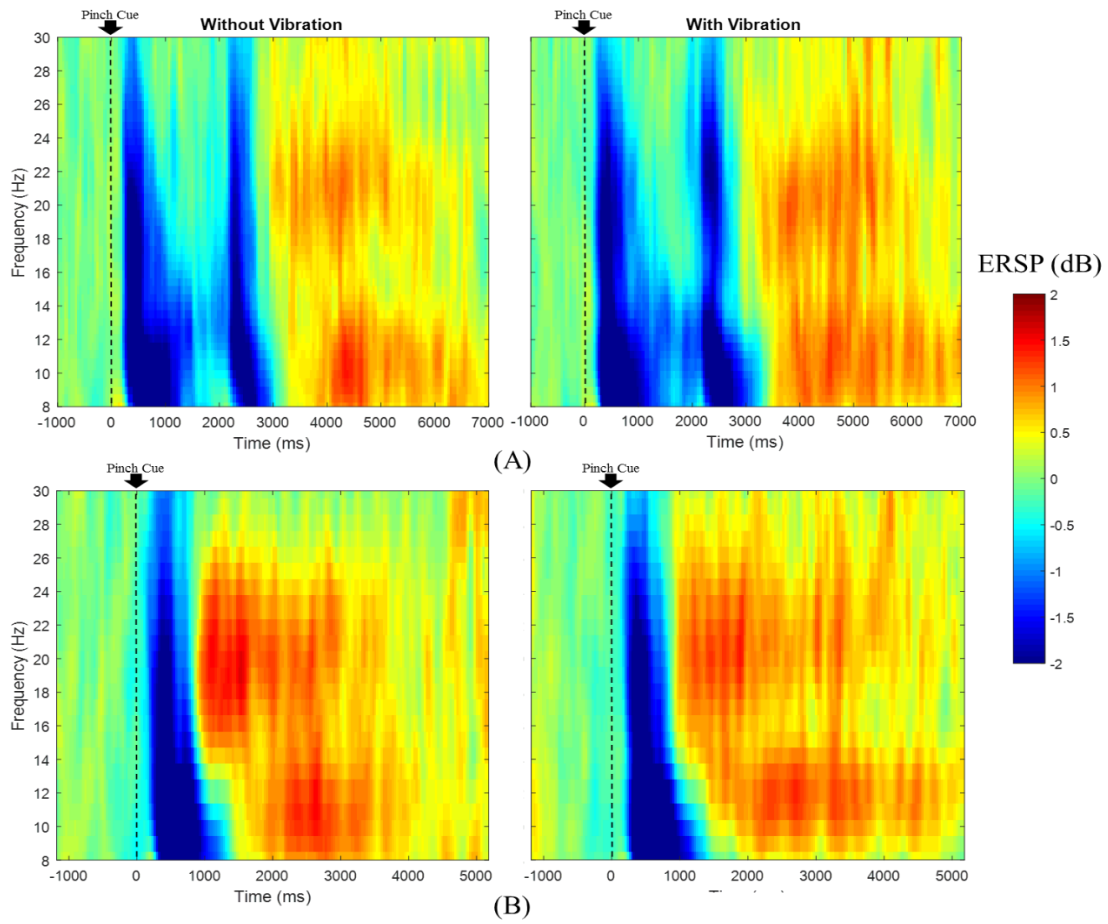


Figure 12: (A): Time-frequency plot for C4 electrode averaged over 20 subjects for both vibration-off and vibration-on conditions during sustained pinch. (B): Time-frequency plot for ballistic pinch. The time-frequency plot displays ERSP, the average dynamic changes in amplitude of the EEG frequency spectrum as a function of time relative to the pinch cue.

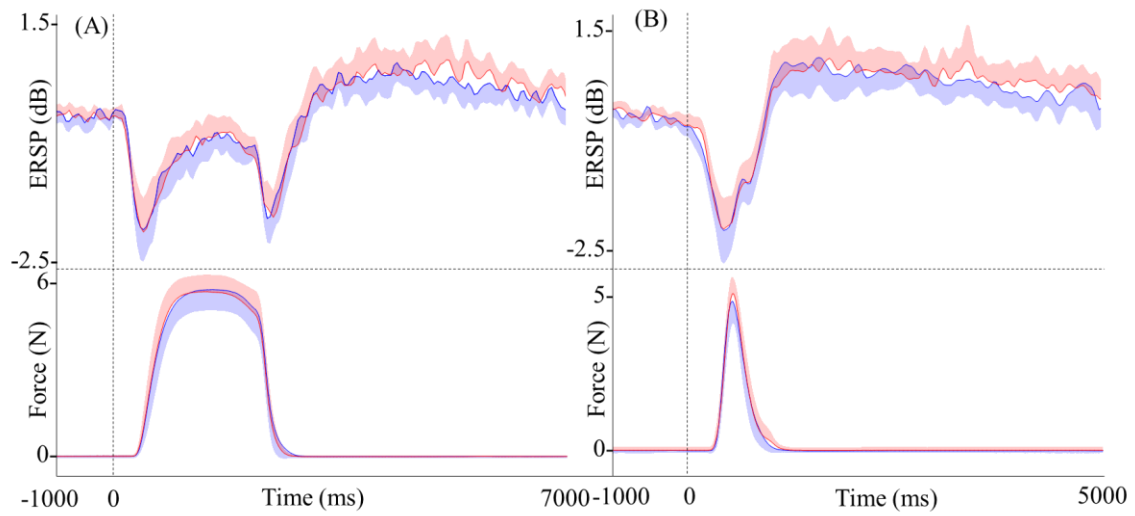


Figure 13: Mean ERSP for β -band (12-28 Hz) at C4 electrode averaged for all subjects and mean force over time, with an upper or lower bound 95% confidence interval are shown while imperceptible white-noise vibration was applied to the volar wrist (red segmented line) as compared to vibration turned off (blue solid line). (A): Time-ERSP plot force trace over time during sustained pinch. (B): Time-ERSP plot and force trace for ballistic pinch. Both plots are shown as a function of time relative to the pinch cue at 0 ms.

		Sustained pinch (mean \pm sd)	Ballistic pinch (mean \pm sd)
Without vibration	Positive peak	4322ms \pm 1232ms	2259ms \pm 1121ms
	Negative peak	1094ms \pm 954ms	465ms \pm 164ms
With vibration	Positive peak	4653ms \pm 925ms	2962ms \pm 1220ms
	Negative peak	1289ms \pm 929ms	541ms \pm 162ms

Table 1: Mean \pm sd times for the positive and negative peaks during sustained and ballistic pinch for both with and without vibration conditions.

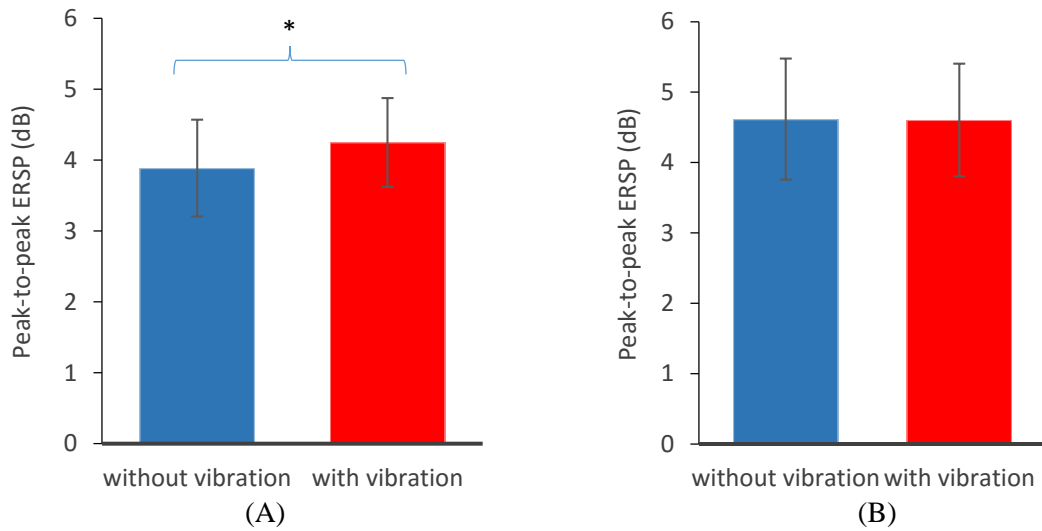


Figure 14: Peak-to-peak β -band amplitude after pinch cue was displayed while imperceptible white-noise vibration was off compared to vibration turned on (A): Mean peak-to-peak β -band amplitude at C4 electrode for all subjects are shown with 95% confidence intervals for sustained pinch. (B) Mean peak-to-peak β -band amplitude at C4 electrode for ballistic pinch.

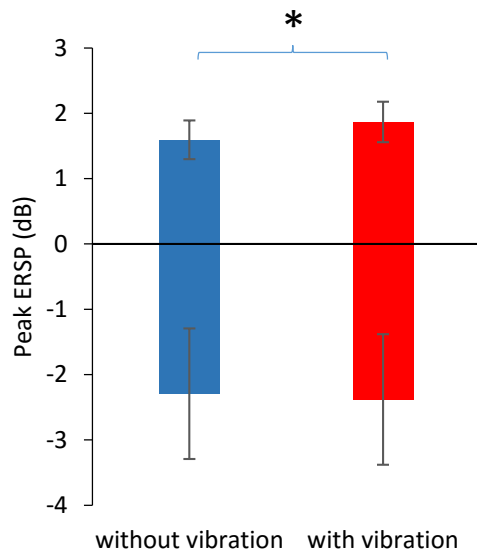


Figure 15: Mean β -band amplitude positive and negative peaks at C4 electrode for all subjects with 95% confidence intervals were compared for sustained pinch

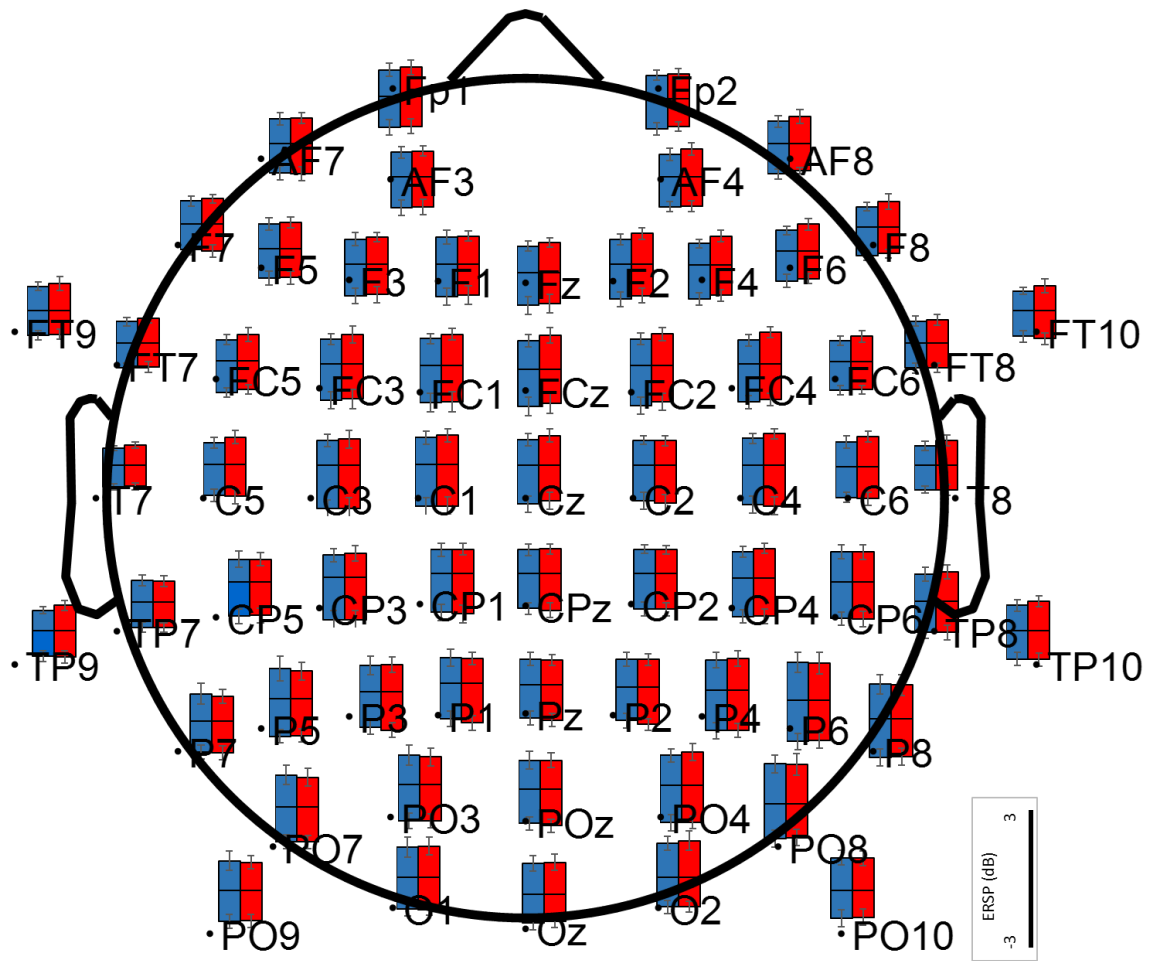


Figure 16: All electrodes' peak-to-peak β -band amplitude (dB) while imperceptible white-noise vibration was turned off (blue) as compared to when vibration was turned on (red). Mean peak-to-peak β -band amplitude for all subjects are shown with 95% confidence intervals for sustained pinch.

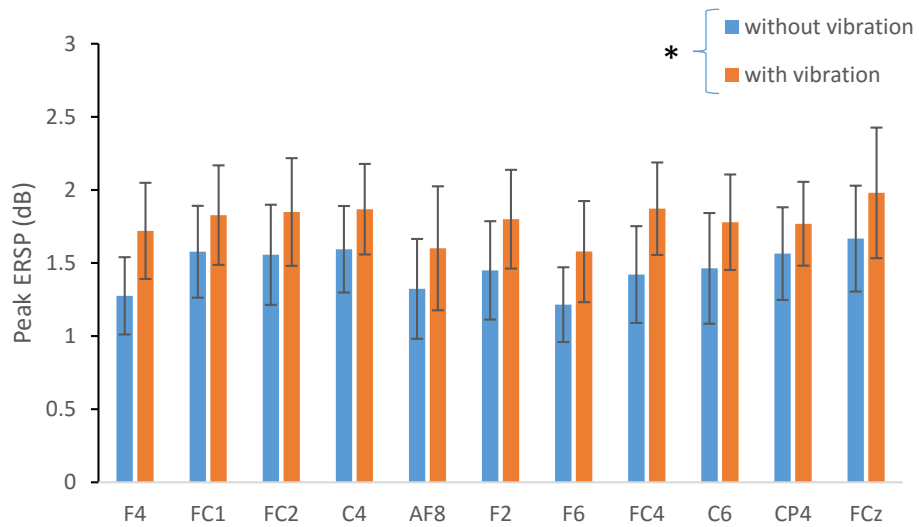


Figure 17: Positive peak β -band amplitude at F4, FC1, FC2, C4, AF8, F2, F6, FC4, C6, CP4, and FCz electrodes while imperceptible white-noise vibration was off compared to vibration turned on. Mean of all 20 subjects' mean positive peak of β -band amplitude are shown with 95% confidence intervals.

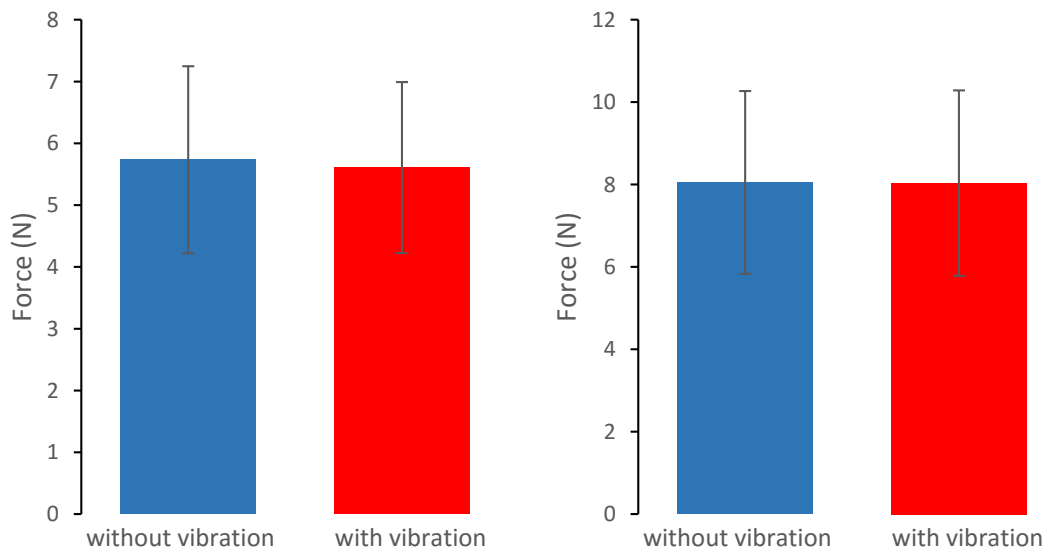


Figure 18: (A) Mean of the average force for a 1 sec window during sustained pinch with standard deviation compared with vibration turned off and on (B) Mean peak force with standard deviation for ballistic pinch compared with vibration turned off and on

4.4 Discussions

The result provides evidence that imperceptible white-noise vibration applied to the volar aspect of the wrist affects movement-related β -band power modulation.

Specifically, the peak-to-peak β -band amplitude increased with white-noise vibration.

The increased peak-to-peak β -band amplitude was due to increase in the positive peak event-related synchronization activity, not the negative event-related desynchronization activity. This increased positive peak was spread across the prefrontal, sensorimotor, primary motor, premotor areas, and the supplementary motor area (SMA). This effect was not due to change in conscious attention since during the EEG recordings, the subjects did not feel the vibration and the vibration-off and vibration-on blocks were randomized.

The observation supports the hypothesis that β -band power modulation is affected by white-noise vibration. Thus, providing the neurological basis for the use of this technique in rehabilitation. These findings support previous behavioral changes induced by remote white-noise vibration on finger tactile sensation [17, 46, 45], motor function [23, 44], and neurological evidence of vibration induced changes in cortical processing of touch stimulation [72]. These findings support further investigation for use of vibration applied to the wrist to affect motor function for various applications.

β -band ERS positive peak showed a significant increase with remote sensory stimulation compared to without stimulation during sustained pinch. β -band ERD did not show any significant difference between vibration-on and vibration-off conditions during both pinches. Desynchronization of β -band signals occurs in motor-related brain regions

during preparation and execution of voluntary movements [75]. β -band ERD have been shown to be not affected by parameters of a motor task such as movement direction [86], movement time [87, 88], speed of movement [89, 88], and force [90, 88], suggesting that ERD is not affected by sensory afferents. Thus, β -band ERD is an undifferentiated reflection of neuronal activity [89] and is also observed in the present study in the mean β -band ERD for sustained pinch in Figure 13A where there are two instances of ERD peaks, both at movement onset and offset. Comparing the ERD with the force trace below shows that β -band ERD peaks happened both during pinch movement planning and execution but not during sustained muscular contraction. This further supports the idea β -band ERD is unaffected by sensory inputs. Synchronized β -band signals has been shown to increase following movement termination [63] or in response to somatosensory stimulation [91]. ERS has been postulated to represent deactivated cortical networks involved in motor program execution leading to an idle state of the motor system [76] or a sensory reafference [92]. Impairment of post movement beta rebound have been found in several sensorimotor-related diseases [93] [94]. The influence of sensory feedback on ERS can also be seen in a study by Cassim et al., where β -band ERS was suppressed following passive movement termination performed after ischemia induced anesthesia [92]. The significantly higher β -band ERS rebound with remote sensory stimulation in the present study, suggests that the ERS is not simply due to a rebound following a period of suppression of β -band activity, but rather implies β -band ERS as an active process that necessitates peripheral feedback following movement termination for its complete development [95].

β -band ERS showed significant increase with improved tactile sensation via remote sensory stimulation compared to without remote sensory stimulation only for sustained pinch and not ballistic pinch. Conversely, the ERS rebound was slightly higher in ballistic pinch in general compared to sustained pinch, which is in agreement with previous studies showing that sustained movements elicit a weaker rebound compared to ballistic movements [96] [97], but the difference was not statistically significant ($p=0.208$). The different behavior in the β -band ERS rebound with remote sensory stimulation found between sustained and ballistic pinches might be explained by differences in the sensory input in each pinch type [96]. Sustained pinch requires a larger tactile sensory feedback compared to ballistic pinch, in order to maintain a steady pinch grip. Steady motor state maintenance is facilitated by an increase in tactile perception [98]. Thus, the reliance on tactile sensory feedback during sustained pinch might have led to the significant increase in the ERS rebound following sustained pinch termination with remote sensory stimulation compared to without stimulation.

The spread of β -band ERS was seen at the contralateral prefrontal areas (AF and F electrodes) [81], contralateral sensorimotor and primary motor areas (C and CP4 electrodes) [82], and premotor areas and the supplementary motor area (FC electrodes) (SMA) [83]. The prefrontal cortex is involved in organization of goal-directed behavioral sequences [84], such as the pinch on cue command in our current study. The premotor and motor areas have been shown to be involved in planning and execution of voluntary arm and hand movements [85] such as pinching.

The present findings suggest that β -band oscillations perform sensorimotor ‘recalibration’ following a movement. Analogous with a radar or sonar system, the motor cortex sends out oscillatory signal pulse to the peripheral and the somatosensory cortex, using the response pulse, determines the system state (position, contraction strength). Since imperceptible white-noise vibration have been shown to improve sensory signal transmission to the somatosensory cortex [72], it explains a larger β -band oscillations with vibration induced enhancement in finger tactile sensation. Sensory feedback following a movement might be of use in trial-to-trial motor learning [95] and enhanced sensory feedback via remote sensory stimulation can lead to increased motor learning enabling subjects to perform a motor task better.

4.5 Conclusions

In conclusion, the present findings indicate that enhanced motor function with vibratory noise is related to β -band power modulation. The recalibration mechanism can be used in rehabilitation by elevating the cortico-muscular coherence during training and rehabilitative exercises. The elevated coherence might lead to longer consolidation of the training in its proprioceptive context. However, only the immediate effect of vibration was studied and long-term use in a rehabilitation setting might need addressing long-term effects of exposure to vibration.

The next chapter is a summary of our findings from all the individual studies in this dissertation.

CHAPTER 5

SUMMARY

The dissertation was significant by creating new knowledge on cortical control of hand sensory and motor functions. This new knowledge on the brain mechanism that underlies sensory input-dependent changes in the brain activity and resulting hand function could lead to the application of remote sensory noise to enhance human performance in high precision manual dexterity tasks. The dissertation developed a novel way to demonstrate brain mechanisms of enhanced or deteriorated hand function using EEG.

One of the main findings of this dissertation was that the remote white-noise vibration affected detection of fingertip tactile signal in healthy adults. Investigation of fingertip tactile sensation in healthy adults in Chapter 2 revealed that subthreshold white-noise vibration at 60% sensory threshold improved the thumb and index fingertip tactile sensation in healthy individuals, while suprathreshold 120% noise degraded fingertip tactile sensation. The effects of remote white-noise vibration were found across all four remote locations in the hand and wrist used in the study.

The findings from Chapter 1 led to an EEG study on healthy young adults in Chapter 3 to investigate the cortical mechanism of vibration-enhanced tactile sensation. The study revealed that the imperceptible white-noise vibration affected cortical modulation for touch stimuli to the fingertip. The cortical modulation expressed itself with larger event-related evoked potentials in the somatosensory cortex with white-noise vibration applied

at the volar aspect of the wrist. It is possible that the cortical modulation is a result of the establishment of transient networks for improved perception.

White-noise vibration was also found to enhance motor functions in previous studies by our research group [23, 44]. Building on Chapter 3, further investigations were made using EEG in healthy young adults performing pinching tasks. The findings revealed that the enhanced motor function with vibratory noise is related to β -band power modulation. β -band power showed an increase in amplitude when white-noise vibration was applied at the volar aspect of the wrist. The enhanced motor function may be a result of stronger recalibration and enhanced motor learning with enhanced sensory feedback via remote sensory stimulation.

In summary, this dissertation showed that remote white-noise vibration affects fingertip tactile sensation in healthy young adults. The white-noise vibration affected tactile sensitivity through evoked potentials and motor function by β -band power modulation. The dissertation demonstrated the possibility for a remote white-noise vibration device that can be worn around the wrist and remotely improve fingertip tactile sensation while not impeding manual dexterity. The mechanism by which white-noise affects sensation at fingertips and motor function can be further explored for use in neural rehabilitation.

5.1 Future directions

Future research may possibly explore how remote white-noise vibration affects other aspects of tactile sensation such as discrimination and resolution in healthy adults and the long-term effects of vibration on sensation and hand function. This may be required

before adopting white-noise vibration technology as a long-term rehabilitation tool or to enhance human performance. In addition, the stimulation parameters such as vibration intensity and locations to apply the vibration needs to be optimized before the technology is implemented in a wrist-worn device.

REFERENCES

- [1] V. M. Zatsiorsky and M. L. Latash, "Prehension synergies," *Exerc Sport Sci Rev.*, vol. 32, pp. 75-80, 2004.
- [2] A. S. Augurelle, A. M. Smith, T. Lejeune and J. L. Thonnard, "Importance of cutaneous feedback in maintaining a secure grip during manipulation of hand-held objects," *J Neurophysiol.*, vol. 89, pp. 665-671, 2003.
- [3] R. S. Johansson and G. Westling, "Roles of glabrous skin receptors and sensorimotor memory in automatic control of precision grip when lifting rougher or more slippery objects," *Exp Brain Res.*, vol. 56, pp. 550-564, 1984.
- [4] J. Monzee, Y. Lamarre and A. M. Smith, "The effects of digital anesthesia on force control using a precision grip," *J Neurophysiol.*, vol. 89, pp. 672-683, 2003.
- [5] T. Kalisch, P. Ragert, P. Schwenkreis, H. R. Dinse and M. Tegenthoff, "Impaired tactile acuity in old age is accompanied by enlarged hand representations in somatosensory cortex," *Cereb Cortex*, vol. 19, pp. 1530-1538, 2009.
- [6] J. L. Leveque, J. Dresler, E. Ribot-Ciscar, J. P. Roll and C. Poelman, "Changes in tactile spatial discrimination and cutaneous coding properties by skin hydration in the elderly," *J Invest Dermatol.*, vol. 115, pp. 454-458, 2000.
- [7] J. C. Stevens and M. Q. Patterson, "Dimensions of spatial acuity in the touch sense: changes over the life span," *Somatosens Mot Res.*, vol. 12, pp. 29-47, 1995.
- [8] L. M. Carey, "Somatosensory loss after stroke," *Critical Rev Phys Rehab Med.*, vol. 7, pp. 51-91, 1995.
- [9] A. J. Turton and S. R. Butler, "Referred sensations following stroke," *Neurocase*, vol. 7, pp. 397-405, 2001.
- [10] A. I. Vinik, T. S. Park, K. B. Stansberry and G. L. Pittenger, "Diabetic neuropathies," *Diabetologia*, vol. 43, no. 8, pp. 957-973, 2000.
- [11] J. M. Blennerhassett, L. M. Carey and T. A. Matyas, "Grip force regulation during pinch grip lifts under somatosensory guidance: comparison between people with stroke and healthy controls," *Arch Phys Med Rehabil.*, vol. 87, pp. 418-429, 2006.
- [12] J. M. Blennerhassett, T. A. Matyas and L. M. Carey, "Impaired discrimination of surface friction contributes to pinch grip deficit after stroke," *Neurorehabil Neural Repair*, vol. 21, pp. 263-272, 2007.
- [13] R. M. Dannenbaum and L. A. Jones, "The assessment and treatment of patients who have sensory loss following cortical lesions," *J Hand Ther.*, vol. 6, pp. 130-138, 1993.
- [14] F. Tremblay, K. Wong, R. Sanderson and L. Cote, "Tactile spatial acuity in elderly persons: assessment with grating domes and relationship with manual dexterity," *Somatosens Mot Res.*, vol. 20, pp. 127-132, 2003.
- [15] N. J. Seo, W. Z. Rymer and D. G. Kamper, "Altered digit force direction during

- pinch grip following stroke," *Exp Brain Res.*, vol. 202, pp. 891-901, 2010.
- [16] C. Pazzaglia, P. Caliandro, G. Granata, P. Tonali and L. Padua, "'Dropping objects": a potential index of severe carpal tunnel syndrome," *Neurol Sci.*, vol. 31, pp. 437-439, 2010.
- [17] L. R. Enders, P. Hur, M. J. Johnson and N. J. Seo, "Remote vibrotactile noise improves light touch sensation in stroke survivors' fingertips via stochastic resonance," *J Neuroeng Rehabil.*, vol. 10, p. 105, 2013.
- [18] J. M. Hijmans, J. H. B. Geertzen, W. Zijlstra, A. L. Hof and K. Postema, "Effects of vibrating insoles on standing balance in diabetic neuropathy," *JRRD*, vol. 45, pp. 1441-1450, 2008.
- [19] J. J. Collins, T. T. Imhoff and P. Grigg, "Noise-mediated enhancements and decrements in human tactile sensation," *Physical Review E*, vol. 56, p. 923, 1997.
- [20] F. Moss, L. M. Ward and W. G. Sannita, "Stochastic resonance and sensory information processing: a tutorial and review of application," *Clin Neurophysiol.*, vol. 115, pp. 267-281, 2004.
- [21] C. Wells, L. M. Ward, R. Chua and J. T. Inglis, "Touch noise increases vibrotactile sensitivity in old and young.," *Psychol Sci.*, vol. 16, no. 4, pp. 313-320, 2005.
- [22] Y. Kurita, M. Shinohara and J. Ueda, "Wearable Sensorimotor Enhancer for Fingertip Based on Stochastic Resonance Effect," *IEEE Transactions on Human-Machine Systems*, vol. 43, pp. 333-337, 2013.
- [23] P. Hur, Y.-H. Wan and N. J. Seo, "Investigating the Role of Vibrotactile Noise in Early Response to Perturbation," *IEEE Transactions on Biomedical Engineering*, vol. 61, pp. 1628-1633, 2014.
- [24] Y. L. Tseng, "Effect of remote vibrotactile noise on pinch force maintenance ability and brain activity," University of Wisconsin-Milwaukee, Milwaukee, 2013.
- [25] E. Manjarrez, O. Diez-Martinez, I. Mendez and A. Flores, "Stochastic resonance in human electroencephalographic activity elicited by mechanical tactile stimuli," *Neurosci Lett.*, vol. 324, pp. 213-216, 2002.
- [26] L. M. Carey and T. A. Matyas, "Frequency of discriminative sensory loss in the hand after stroke in a rehabilitation setting.," *J Rehabil Med.*, vol. 43, pp. 257-263, 2011.
- [27] W. Liu, L. A. Lipsitz, M. Montero-Odasso, J. Bean, D. C. Kerrigan and J. J. Collins, "Noise-enhanced vibrotactile sensitivity in older adults, patients with stroke, and patients with diabetic neuropathy," *Arch Phys Med Rehabil.*, vol. 83, pp. 171-176, 2002.
- [28] K. Y. Haaland and D. L. Harrington, "Hemispheric asymmetry of movement," *Curr Opin Neurobiol.*, vol. 6, pp. 796-800, 1996.
- [29] L. B. Bagesteiro and R. L. Sainburg, "Nondominant arm advantages in load compensation during rapid elbow joint movements," *J Neurophysiol.*, vol. 90, pp. 1503-1513, 2003.

- [30] R. L. Sainburg and S. Y. Schaefer, "Interlimb differences in control of movement extent," *J Neurophysiol.*, vol. 92, pp. 1374-1383, 2004.
- [31] W. H. Ehrenstein and A. Ehrenstein, "Psychophysical methods," in *Modern techniques in neuroscience research*, Springer, 1999, pp. 1211-1241.
- [32] B. G. Tabachnick and L. S. Fidell, *Using multivariate statistics 5th Ed*, New York: Ally and Bacon, 2007.
- [33] A. B. Vallbo and R. S. Johansson, "Properties of cutaneous mechanoreceptors in the human hand related to touch sensation," *Hum Neurobiol.*, vol. 3, pp. 3-14, 1984.
- [34] T. Nierhaus, N. Forschack, S. K. Piper, S. Holtze, T. Krause, B. Taskin, X. Long, J. Stelzer, D. S. Margulies, J. Steinbrink and A. Villringer, "Imperceptible somatosensory stimulation alters sensorimotor background rhythm and connectivity," *J Neurosci.*, vol. 35, pp. 5917-5925, 2015.
- [35] L. R. Manfredi, A. T. Baker, D. O. Elias, J. F. Dammann 3rd, M. C. Zielinski, V. S. Polashock and S. J. Bensmaia, "The effect of surface wave propagation on neural responses to vibration in primate glabrous skin," *PLoS One*, vol. 7, p. e31203, 2012.
- [36] L. M. Ward, "Physics of neural synchronisation mediated by stochastic resonance," *Contemporary Physics.*, vol. 50, pp. 563-574, 2009.
- [37] L. M. Ward, S. E. MacLean and A. Kirschner, "Stochastic resonance modulates neural synchronization within and between cortical sources," *PLoS One*, vol. 5, p. e14371, 2010.
- [38] T. Mori and S. Kai, "Noise-induced entrainment and stochastic resonance in human brain waves," *Physical Review Letters*, vol. 88, p. 218101, 2002.
- [39] K. Kitajo, D. Nozaki, L. M. Ward and Y. Yamamoto, "Behavioral stochastic resonance within the human brain," *Phys Rev Lett.*, vol. 90, p. 218103, 2003.
- [40] K. Kitajo, S. Doesburg, K. Yamanaka, D. Nozaki, L. Ward and Y. Yamamoto, "Noise-induced large-scale phase synchronization of human-brain activity associated with behavioural stochastic resonance," *EPL (Europhysics Letters)*, vol. 80, p. 40009, 2007.
- [41] E. Lugo, R. Doti and J. Faubert, "Ubiquitous crossmodal Stochastic Resonance in humans: auditory noise facilitates tactile, visual and proprioceptive sensations," *PLoS One*, vol. 3, p. e2860, 2008.
- [42] H. R. Dinse, N. Kleibel, T. Kalisch, P. Ragert, C. Wilimzig and M. Tegenthoff, "Tactile coactivation resets age-related decline of human tactile discrimination," *Ann Neurol.*, vol. 60, pp. 88-94, 2006.
- [43] H. R. Dinse and M. Tegenthoff, "Evoking plasticity through sensory stimulation: Implications for learning and rehabilitation," *e-Neuroforum*, vol. 6, pp. 11-20, 2015.
- [44] N. J. Seo, M. L. Kosmopoulos, L. R. Enders and P. Hur, "Effect of Remote Sensory

- Noise on Hand Function Post Stroke," *Front Hum Neurosci.*, vol. 8, p. 934, 2014.
- [45] K. Lakshminarayanan, A. W. Lauer, V. Ramakrishnan, J. G. Webster and S. N. J. "Application of Vibration to Wrist and Hand Skin Affects Fingertip Tactile Sensation," *Physiological Reports*, vol. 3, p. e12465, 2015.
- [46] F. Wang, K. Lakshminarayanan, G. P. Slota, N. J. Seo and J. G. Webster, "An MRI-compatible hand sensory vibrotactile system," *Physiol Meas.*, vol. 36, pp. 15-21, 2015.
- [47] B. Delhaye, V. Hayward, P. Lefevre and J. L. Thonnard, "Texture-induced vibrations in the forearm during tactile exploration," *Frontiers in behavioral neuroscience*, vol. 6, p. 37, 2012.
- [48] X. Libouton, O. Barbier, Y. Berger, L. Plaghki and J. L. Thonnard, "Tactile roughness discrimination of the finger pad relies primarily on vibration sensitive afferents not necessarily located in the hand.," *Behav Brain Res.*, vol. 229, pp. 273-279, 2012.
- [49] R. T. Verrillo, "Investigation of some parameters of the cutaneous threshold for vibration," *The Journal of the Acoustical Society of America*, vol. 34, pp. 1768-1773, 1962.
- [50] Y. Feng, F. J. Schlosser and B. E. Sumpio, "The Semmes Weinstein monofilament examination as a screening tool for diabetic peripheral neuropathy," *J Vasc Surg.*, vol. 50, pp. 675-682, 2009.
- [51] C. Cooper and J. D. Canyock, "Ch. 23 Evaluation of Sensation and Intervention for Sensory Dysfunction," in *Pedretti's Occupational Therapy: Practice Skills for Physical Dysfunction 7th ed*, St. Louis, Mosby/Elsevier, 2013, pp. 575-589.
- [52] R. Auksztulewicz and F. Blankenburg, "Subjective rating of weak tactile stimuli is parametrically encoded in event-related potentials," *J Neurosci.*, vol. 33, pp. 11878-11887, 2013.
- [53] A. Delorme and S. Makeig, "EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis," *J Neurosci Methods*, vol. 134, pp. 9-21, 2004.
- [54] A. Mognon, J. Jovicich, L. Bruzzone and M. Buiatti, "ADJUST: An automatic EEG artifact detector based on the joint use of spatial and temporal features," *Psychophysiology*, vol. 48, pp. 229-240, 2011.
- [55] J. Lopez-Calderon and S. J. Luck, "ERPLAB: an open-source toolbox for the analysis of event-related potentials," *Front Hum Neurosci.*, vol. 8, p. 213, 2014.
- [56] S. Hadjidimitriou, A. Zacharakis, P. Doulgeris, K. Panoulas, L. Hadjileontiadis and S. Panas, "Sensorimotor cortical response during motion reflecting audiovisual stimulation: evidence from fractal EEG analysis," *Medical & Biological Engineering & Computing*, vol. 48, p. 561-572, 2010.
- [57] C. Babiloni, E. Cassetta, G. Binetti, M. Tombini, C. Del Percio, F. Ferreri, R. Ferri, G. Frisoni, B. Lanuzza, F. Nobili and L. Parisi, "Resting EEG sources correlate

- with attentional span in mild cognitive impairment and Alzheimer's disease," *European Journal of Neuroscience*, pp. 3742-3757, 2007.
- [58] Y. Zhang and M. Ding, "Detection of a weak somatosensory stimulus: role of the prestimulus mu rhythm and its top-down modulation," *J Cogn Neurosci.*, vol. 22, pp. 307-322, 2010.
- [59] F. Tadel, S. Baillet, J. C. Mosher, D. Pantazis and R. M. Leahy, "Brainstorm: a user-friendly application for MEG/EEG analysis," *Comput Intell Neurosci.*, vol. 2011, p. 879716, 2011.
- [60] A. Gramfort, T. Papadopoulo, E. Olivi and M. Clerc, "OpenMEEG: opensource software for quasistatic bioelectromagnetics," *Biomed Eng Online*, vol. 9, p. 45, 2010.
- [61] T. Allison, G. McCarthy, C. C. Wood and S. J. Jones, "Potentials evoked in human and monkey cerebral cortex by stimulation of the median nerve. A review of scalp and intracranial recordings," *Brain*, vol. 114, no. 6, pp. 2465-2503, 1991.
- [62] F. Blankenburg, B. Taskin, J. Ruben, M. Moosmann, P. Ritter, G. Curio and A. Villringer, "Imperceptible stimuli and sensory processing impediment," *Science*, vol. 299, no. 5614, p. 1864, 2003.
- [63] G. Pfurtscheller, A. Stancak Jr and C. Neuper, "Event-related synchronization (ERS) in the alpha band--an electrophysiological correlate of cortical idling: a review," *Int J Psychophysiol.*, vol. 24, pp. 39-46, 1996.
- [64] T. Weiss, W. H. Miltner, J. Liepert, W. Meissner and E. Taub, "Rapid functional plasticity in the primary somatomotor cortex and perceptual changes after nerve block," *Eur J Neurosci.*, vol. 20, pp. 3413-3423, 2004.
- [65] T. Weiss, E. Sens, U. Teschner, W. Meissner, C. Preul, O. W. Witte and W. H. Miltner, "Deafferentation of the affected arm: a method to improve rehabilitation?," *Stroke*, vol. 42, pp. 1363-1370, 2011.
- [66] E. Sens, U. Teschner, W. Meissner, C. Preul, R. Huonker, O. W. Witte, W. H. Miltner and T. Weiss, "Effects of temporary functional deafferentation on the brain, sensation, and behavior of stroke patients," *J Neurosci.*, vol. 32, pp. 11773-11779, 2012.
- [67] T. Krause, R. Kurth, J. Ruben, J. Schwiemann, K. Villringer, M. Deuchert, M. Moosmann, S. Brandt, K. Wolf, G. Curio and A. Villringer, "Representational overlap of adjacent fingers in multiple areas of human primary somatosensory cortex depends on electrical stimulus intensity: an fMRI study," *Brain Res.*, vol. 899, pp. 36-46, 2001.
- [68] P. Ragert, T. Kalisch, B. Bliem, S. Franzkowiak and H. R. Dinse, "Differential effects of tactile high- and low-frequency stimulation on tactile discrimination in human subjects," *BMC Neurosci.*, vol. 9, p. 9, 2008.
- [69] B. Taskin, S. Holtze, T. Krause and A. Villringer, "Inhibitory impact of subliminal electrical finger stimulation on SI representation and perceptual sensitivity of an adjacent finger," *Neuroimage*, vol. 39, pp. 1307-1313, 2008.

- [70] M. Gentilucci, I. Toni, S. Chieffi and G. Pavesi, "The role of proprioception in the control of prehension movements: a kinematic study in a peripherally deafferented patient and in normal subjects," *Exp Brain Res*, pp. 99(3):483-500, 1994.
- [71] D. E. Vaillancourt and D. M. Russell, "Temporal capacity of short-term visuomotor memory in continuous force production.," *Exp Brain Res.*, vol. 145, no. 3, pp. 275-285, 2002.
- [72] N. J. Seo, K. Lakshminarayanan, L. Bonilha, A. W. Lauer and B. D. Schmit, "Effect of imperceptible vibratory noise applied to wrist skin on fingertip touch evoked potentials—an EEG study," *Physiological reports*, vol. 3, no. 11, p. e1262, 2015.
- [73] J. N. Sanes, J. P. Donoghue, V. Thangaraj, R. R. Edelman and S. Warach, "Shared neural substrates controlling hand movements in human motor cortex," *Science*, vol. 268, no. 5218, p. 1775, 1995.
- [74] M. Rangaswamy, B. Porjesz, D. B. Chorlian, K. Wang, K. A. Jones, S. Kuperman, J. Rohrbaugh, S. J. O'Connor, L. O. Bauer, T. Reich and H. Begleiter, "Resting EEG in offspring of male alcoholics: beta frequencies," *International Journal of Psychophysiology*, vol. 51, no. 3, pp. 239-251, 2004.
- [75] H. Jasper and W. Penfield, "Electrocorticograms in man: effect of voluntary movement upon the electrical activity of the precentral gyrus," *Archiv für Psychiatrie und Nervenkrankheiten*, vol. 183, pp. 163-174, 1949.
- [76] G. Pfurtscheller and F. L. Da Silva, "Event-related EEG/MEG synchronization and desynchronization: basic principles," *Clinical neurophysiology*, vol. 110, no. 11, pp. 1842-1857, 1999.
- [77] R. Salmelin, M. Hämäläinen, M. Kajola and R. Hari, "Functional segregation of movement-related rhythmic activity in the human brain," *Neuroimage*, vol. 2, no. 4, pp. 237-243, 1995.
- [78] M. Taniguchi, A. Kato, N. Fujita, M. Hirata, H. Tanaka, T. Kihara, H. Ninomiya, N. Hirabuki, H. Nakamura, S. E. Robinson, D. Cheyne and T. Yoshimine, "Movement-related desynchronization of the cerebral cortex studied with spatially filtered magnetoencephalography," *Neuroimage*, vol. 12, pp. 298-306, 2000.
- [79] S. J. De Serres and N. Z. Fang, "The accuracy of perception of a pinch grip force in older adults," *Can. J. Physiol. Pharmacol.*, vol. 82, p. 693-701, 2004.
- [80] B. Graimann, J. E. Huggins, S. P. Levine and G. Pfurtscheller, "Visualization of significant ERD/ERS patterns in multichannel EEG and ECoG data," *Clin Neurophysiol.*, vol. 113, p. 43-47, 2002.
- [81] L. Li and D. Zhao, "Age-Related Inter-Region EEG Coupling Changes During the Control of Bottom-Up and Top-Down Attention," *Frontiers in aging neuroscience*, vol. 7, 2015.
- [82] J. A. Wilson, G. Schalk, L. M. Walton and J. C. Williams, "Using an EEG-based brain-computer interface for virtual cursor movement with BCI2000," *J Vis Exp.*, vol. 29, 2009.

- [83] I. Puzzo, N. R. Cooper, P. Vetter and R. Russo, "EEG activation differences in the pre-motor cortex and supplementary motor area between normal individuals with high and low traits of autism," *Brain research*, vol. 1342, pp. 104-110, 2010.
- [84] J. M. Fuster, Prefrontal cortex., Birkhäuser Boston, 1988.
- [85] J. G. Colebatch, M. P. Deiber, R. E. Passingham, K. J. Friston and R. S. Frackowiak, "Regional cerebral blood flow during voluntary arm and hand movements in human subjects," *Journal of neurophysiology*, vol. 65, no. 6, pp. 1392-1401, 1991.
- [86] S. Waldert, H. Preissl, E. Demandt, C. Braun, N. Birbaumer, A. Aertsen and C. Mehring, "Hand movement direction decoded from MEG and EEG," *J Neurosci.*, vol. 28, p. 1000–1008, 2008.
- [87] F. Cassim, W. Szurhaj, H. Sediri, D. Devos, J. Bourriez, I. Poirot, P. Derambure, L. Defebvre and J. Guieu, "Brief and sustained movements: differences in event-related (de)synchronization (ERD/ERS) patterns," *Clin Neurophysiol.*, vol. 111, p. 2032–2039, 2000.
- [88] M. Tombini, F. Zappasodi, L. Zollo, G. Pellegrino, G. Cavallo, F. Tecchio, E. Guglielmelli and P. M. Rossini, "Brain activity preceding a 2D manual catching task," *Neuroimage*, vol. 47, p. 1735–1746, 2009.
- [89] A. Stancak Jr. and G. Pfurtscheller, "Event-related desynchronisation of central beta-rhythms during brisk and slow self-paced finger movements of dominant and nondominant hand," *Cogn Brain Res.*, vol. 4, p. 171–183, 1996.
- [90] T. Mima, N. Simpkins, T. Oluwatimilehin and M. Hallett, "Force level modulates human cortical oscillatory activities," *Neurosci Lett.*, vol. 275, p. 77–80, 1999.
- [91] G. Pfurtscheller, G. Krausz and C. Neuper, "Mechanical stimulation of the fingertip can induce bursts of beta oscillations in sensorimotor areas," *J Clin Neurophysiol*, vol. 18, p. 559–564, 2001.
- [92] F. Cassim, C. Monaca, W. Szurhaj, J. L. Bourriez, L. Defebvre, P. Derambure and J. D. Guieu, "Does post-movement beta synchronization reflect an idling motor cortex?," *Neuroreport*, vol. 12, p. 3859–3863, 2001.
- [93] G. Tamas, I. Szirmai, L. Palvolgyi, A. Takats and A. Kamondi, " Impairment of post-movement beta synchronisation in parkinson's disease is related to laterality of tremor," *Clin Neurophysiol*, vol. 114, p. 614–623, 2003.
- [94] N. Reyns, P. Derambure, A. Duhamel, J. Bourriez and S. Blond, "Motor cortex stimulation modulates defective central beta rhythms in patients with neuropathic pain.," *Clin Neurophysiol*, vol. 124, pp. 761-769, 2013.
- [95] D. L. P. A. Kühn AA, K. Yarrow, A. Kupsch, G. H. Schneider, M. I. Hariz, T. Trottenberg and P. Brown, "Modulation of beta oscillations in the subthalamic area during motor imagery in Parkinson's disease," *Brain*, vol. 129, no. 3, pp. 695-706, 2006.
- [96] M. Alegre, A. Labarga, I. G. Gurtubay, J. Iriarte, A. Malanda and e. al.,

- "Movement-related changes in cortical oscillatory activity in ballistic sustained and negative movements," *Exp Brain Res*, vol. 148, pp. 17-25, 2003.
- [97] F. Cassim, W. Szurhaj, H. Sediri, D. Devos, J. Bourriez and e. al., "Brief and sustained movements: differences in event-related (de)synchronization (ERD/ERS) patterns," *Clin Neurophysiol*, vol. 111, p. 2032–2039, 2000.
- [98] K. Gourab and B. D. Schmit, "Changes in movement-related β -band EEG signals in human spinal cord injury," *Clinical Neurophysiology*, vol. 121, no. 12, pp. 2017-2023, 2010.
- [99] A. G. Androulidakis, L. M. Doyle, T. P. Gilbertson and P. Brown, "Corrective movements in response to displacements in visual feedback are more effective during periods of 13–35 Hz oscillatory synchrony in the human corticospinal system," *Eur J Neurosci.*, vol. 24, no. 11, p. 3299–3304, 2006.
- [100] S. N. Baker, E. Olivier and R. N. Lemon, "Coherent oscillations in monkey motor cortex and hand muscle EMG show task-dependent modulation," *J Physiol.*, vol. 501, no. 1, p. 225–241, 1997.
- [101] S. N. Baker, C. Gabriel and R. N. Lemon, "EEG oscillations at 600 Hz are macroscopic markers for cortical spike bursts," *The Journal of physiology*, vol. 550, no. 2, pp. 529-534, 2003.
- [102] T. Gilbertson, E. Lalo, L. Doyle, V. Di Lazzaro, B. Cioni and P. Brown, "Existing motor state is favored at the expense of new movement during 13–35 Hz oscillatory synchrony in the human corticospinal system," *J Neurosci.*, vol. 25, p. 7771–7779, 2005.
- [103] R. Kristeva, L. Patino and W. Omlor, "Beta-range cortical motor spectral power and corticomuscular coherence as a mechanism for effective corticospinal interaction during steady-state motor output," *Neuroimage*, vol. 36, p. 785–792, 2007.
- [104] E. Lalo, T. Gilbertson, L. Doyle, V. Di Lazzaro, B. Cioni and P. Brown, "Phasic increases in cortical beta activity are associated with alterations in sensory processing in the human," *Exp Brain Res.*, vol. 177, p. 137–145, 2007.
- [105] R. Salmelin and R. Hari, "Spatiotemporal characteristics of sensorimotor neuromagnetic rhythms related to thumb movement," *Neuroscience*, vol. 60, p. 537–550, 1994.

CURRICULUM VITAE

NAME Kishor Lakshminarayanan	POSITION TITLE PhD Candidate
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EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	YEARS	FIELD OF STUDY
Pondicherry University, Pondicherry, India	B.S.	2006-2010	Biomedical Engineering
Arizona State University, AZ, USA	M.S.	2011-2013	Bioengineering
University of Wisconsin- Milwaukee, WI, USA	Ph.D.	2013- current	Mechanical Engineering

Positions

ACTIVITY/ OCCUPATION	BEGINNING DATE (mm/yy)	ENDING DATE (mm/yy)	FIELD	INSTITUTION/ COMPANY	SUPERVISOR / EMPLOYER
Biomedical Engineer	2010	2011	Bio- engineering	Mahatma Gandhi Hospital and Research Institute, India	
Graduate Research Assistant	2011	2013	Bio- engineering	Human Visuomotor Laboratory, Arizona State University	Christopher Buneo, Ph.D.
Graduate Research Assistant	2013	2015	Industrial Engineering	University of Wisconsin-Milwaukee	Na Jin Seo, Ph.D
Teaching Assistant	2015	2016	Mechanical Engineering	University of Wisconsin-Milwaukee	Dan Beller, Ph.D

Honors

2014	IEEE Larry House Student Poster Competition, Milwaukee School of Engineering, 3rd place award
2014	University of Wisconsin-Milwaukee Travel Award
2013- 2017	University of Wisconsin-Milwaukee Dean's Fellowship

Academic and Professional Membership/Activity

2015	Member, American Heart Association
2014	Member, American Society of Biomechanics
2007- Present	Member, Biomedical Engineering Society of India
2010	Volunteer at Billroth Hospitals in Chennai, India

C. Publications

Peer-reviewed Journal Publications

1. **K. Lakshminarayanan**, A. W. Lauer, V. Ramakrishnan, J. G. Webster and S. N. J, "Application of Vibration to Wrist and Hand Skin Affects Fingertip Tactile Sensation," *Physiological Reports*, p. 3:e12465, 2015.
2. F. Wang, **K. Lakshminarayanan**, G. P. Slota, N. J. Seo and J. G. Webster, "An MRI-compatible hand sensory vibrotactile system," *Physiol Meas*, pp. 36:N15-21, 2015.
3. N. J. Seo, **K. Lakshminarayanan**, L. Bonilha, A. W. Lauer and B. D. Schmit, "Effect of imperceptible vibratory noise applied to wrist skin on fingertip touch evoked potentials—an EEG study," *Physiological reports*, p. 3(11):e1262, 2015.
4. N. J. Seo, J. Kumar, P. Hur, V. Crocher, B. Motawar and **K. Lakshminarayanan**, "Development and usability evaluation of low-cost hand and arm virtual reality rehabilitation games," *Journal of Rehabilitation Research & Development*, 2015 accepted
5. **K. Lakshminarayanan**, F. Wang, J. G. Webster, N. J. Seo, "Feasibility and usability of a wearable orthotic for stroke survivors with hand impairment," *Disability and Rehabilitation: Assistive Technology*. pp. 29:1-9, 2015

Masters Thesis

1. **Lakshminarayanan K.** "The role of visual information about limb configuration in the planning of reaching movements in 3D space" Master's Thesis, Arizona State University, 2013.

Conference Proceedings

1. **Lakshminarayanan K**, Webster J.G., and Seo N.J. “Effects of Remote Vibrotactile Noise on Fingertip Tactile Sensation in Healthy Adults”. 2014 Meeting of The Milwaukee Chapter of the Society for Neuroscience, Milwaukee, WI
2. **Lakshminarayanan K**, Webster J.G., and Seo N.J. “Effects of Remote Vibrotactile Noise on Fingertip Tactile Sensation”. 2014 American Society of Biomechanics, Boston, MA