EFFECT OF REMOTE VIBROTACTILE NOISE ON PINCH FORCE MAINTENANCE ABILITY AND BRAIN ACTIVITY

by

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Noise has been used to enhance detection of signals thereby improving performance of nonlinear systems (referred to as “stochastic resonance”). In biological systems, the noise and signal integration may occur not only at the receptor level but also in the central nervous system, thereby allowing noise remotely applied from a signal to enhance the system’s response to the signal. However, integration of tactile signal and noise within the central nervous system has not been demonstrated in humans. In addition, whether the enhanced detection of tactile signals with remote noise results in changes in motor behavior is unknown.

The objectives of this thesis were to elucidate the effect of remote vibrotactile noise on hand motor control (Aim 1) and to demonstrate feasibility for quantifying the effect of remote vibrotactile noise on electroencephalography (EEG) activity (Aim 2). Aim 1 found that remote vibrotactile noise had little effect on young, healthy persons’ ability to maintain a target pinch force level. While remote noise may have enhanced people’s ability to detect very weak signals such as the monofilament stimulation in a previous study, it appears that remote noise was not effective during pinching activity involving strong tactile signals in this thesis.

Aim 2 developed methods for quantifying the effect of remote vibrotactile noise on the somatosensory cortex EEG activity in response to monofilament stimulation at the fingertip. A pilot data from one subject showed a trend for strengthened sensation/sensory feedback and sensorimotor information processing, as evidenced by increased peak-to-peak amplitude of event-related potentials and changes in power spectral densities with remote vibrotactile noise at 60% of sensory threshold, but not at 80% and 120% of the sensory threshold.

In conclusion, this thesis demonstrated that remote vibrotactile noise did not influence young healthy adults' ability to maintain pinch force. This thesis also demonstrated the ability for quantifying the effect of remote vibrotactile noise on EEG activity in response to fingertip stimulation, with a trend for improved sensory information processing. The results of this thesis may guide future investigation regarding the use of remote vibrotactile noise to influence brain activity, tactile sensing, and motor control.

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INTRODUCTION

Vibrotactile noise has been shown to improve people's tactile sensation via the mechanism called stochastic resonance (Collins et al., 2003; Enders et al., 2012; Kurita et al., 2011; Wells et al., 2005). Stochastic resonance is a phenomenon where presence of noise maximizes the detection and transmission of a weak signal, thereby enhancing performance of nonlinear systems. For instance, a bidirectional ring laser device can have a greater signal-to-noise ratio and change its laser direction more appropriately depending on the acoustic frequency of the modulator, when random noise is added to the modulator acoustic frequency output, compared to when no noise is added (McNamara et al., 1988). Such performance enhancement was mathematically explained by Duan et al. (2013) with analytical computation demonstrating that weak signals corrupted by white noise are detected with higher accuracy in a generalized correlation detector.

Stochastic resonance has been observed in biological systems as well. For example, the crayfish's single mechanoreceptor responded to a weak periodic signal (water flow) more coherently when the signal was accompanied by noise, compared to when the signal was not added by noise (Douglass et al., 1993). Additionally, in rats, the stimulus-response coherence of rats' slowly adapting type I afferents increased when the weak tactile stimulus was added with noise than when it was not added with noise (Collins et al., 1996).

Stochastic resonance also affects human sensory systems. For instance, Collins et al. (1997) have shown that healthy young adults' detection of a weak tactile stimulus applied to the fingertip improved when the tactile stimulus was added with low-level noise. Vibrotactile noise at the fingertip pad was also shown to enhance fingertip tactile sensation not only in young healthy adults, but also in older adults and stroke survivors and patients with diabetic neuropathy who have sensory deficit (assessed by monofilament test) (Liu et al., 2002).

However, not all noise improves the system's performance. There appears to be an optimal level of noise that improves the system's performance the most, and when the noise intensity deviates from the optimal level, the system's performance can worsen. For instance, Collins et al. (1997) showed that healthy young adults' detection of a weak tactile stimulus applied to the fingertip improved when the tactile stimulus was added with low-level noise, while the detection worsened with high-level noise masking the original signal. Healthy young adults' ability to hold their finger still (with as little position variation as possible) improved with a certain level of noise compared to no noise, and when the noise intensity increased further, the performance worsened with increased position variation (Mendez-Balbuena et al., 2012). In addition, Wells et al. (2005) demonstrated that both healthy young and old adults could detect tactile stimulation on the sole of the foot better when the tactile stimulation was added with noise whose intensity was either 33%, 50%, or 67% of the sensory threshold, compared to noise intensity with 0% (no noise), 83% or 100% of the sensory threshold. In other words, the detection accuracy and the noise intensity had a bell-shape curve. Furthermore, Manjarrez et al. (2002) showed that the signal-to-noise ratio in the electroencephalography (EEG) signals of the somatosensory cortex (C4 electrode) in response to vibrotactile stimulation of the fingertip increased when a certain level of noise was added to the vibrotactile stimulation, compared to no or lower-level noise, and then decreased when the noise level increased further from the optimal level in healthy young adults.

Based on the above observations, Wells et al. (2005) concluded that the noise intensity should be high enough for a weak signal to cross the sensory threshold but low enough not to swamp the signal. In other words, a weak signal that cannot reach the threshold may be able to reach the threshold when the signal is accompanied with a moderate level of noise. However, if noise is too large, the noise could dominate the signal, and the changes of the original signal may no longer be obvious for detection. Wells et al. (2005) showed a “∩” shape plot of detection accuracy as a function of noise intensity (Figure 1). Specifically, the detection accuracy increased as noise intensity increased from 0% to 33% of the sensory threshold, and the detection accuracy decreased as noise intensity increased from 67% to 100% in healthy young adults.

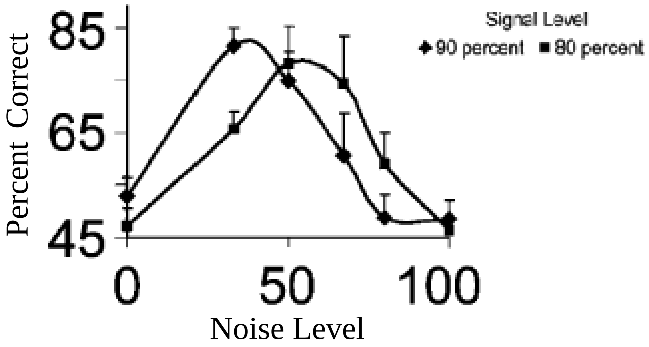


Figure 1: The plot of detection accuracy as a function of noise intensity (percent of the sensory threshold) (Wells et al., 2005).

Another characteristic of stochastic resonance is that noise does not have to be added directly to the external signal. Noise and signals can be applied to different parts of a system, with the noise and signal integration occurring at a higher level within the system. For instance, Hidaka et al. (2000) showed that the function of the baroreflex in response to the cardiopulmonary baroreceptor (signal) improved when noise was added to the arterial baroreceptor in healthy young adults. In other words, the cardiovascular system improved its response to the pressure signal in the heart (sensed by the cardiopulmonary baroreceptor) when noise was applied to the neck (sensed by the arterial baroreceptor). Such enhancement of sensation through application of remote noise (noise applied in a remote bodily location) has been observed not only in healthy young adults but also in patients. Enders et al. (2012) showed that subthreshold vibrotactile noise at the wrist or dorsal hand improved touch sensation of the index fingertip and thumb tip in stroke survivors as measured by the monofilament clinical test. The monofilament test is a clinical assessment of tactile sensation by examining whether a patient can feel a light touch by a single fishing line-like filament in different sizes on a specific body part (Winstein, 1991). Specifically, they applied subthreshold vibrotactile noise (at 40%, 60%, and 80% of the sensory threshold) at 4 different locations (dorsal wrist, volar wrist, the skin over dorsal 1st metacarpal bone, the skin over dorsal 2nd metacarpal bone) and recorded the monofilament score as an indicator for tactile sensation. They selected these four locations, because their study was concerned with development of a sensory assistive device to help people with dexterous hand function. Dexterous hand function requires physical interaction between the fingers and objects and an assistive device is desired to be away from the fingers to not interfere with the object manipulation. Therefore, the authors arbitrarily selected the four locations in the dorsal hand and wrist to be close to the fingers, but not to be in the way for object manipulation. They chose the three noise intensities of 40%, 60%, and 80% of the sensory threshold, since previous studies have shown the optimal vibrotactile noise intensity varied from 33% to 90% (Collins et al., 2003; Galica et al., 2009; Kurita et al., 2011; Priplata et al., 2002; Wells et al., 2005). The results indicated that stroke survivors' monofilament score improved with remote vibrotactile noise at all noise locations and all noise intensities. In other words, noise applied remotely from the fingertip could influence sensation at the fingertip.

The mechanism by which remote noise affects a function (baroreflex function or fingertip tactile sensation) is unclear. Hidaka et al. (2000) postulated that the enhanced baroreflex function with remote noise may have been achieved through signal and noise integration at the brainstem level, because the baroreflex is controlled by the brainstem and both sensory information merge at the brainstem. In Enders et al. (2012), the authors first suspected that the vibrotactile noise at the wrist or dorsal hand may have travelled to the fingertip pads. However, it has been shown that vibrotactile noise loses 90% of its original power when it travels 1 to 2 cm on the skin and thus it is unlikely that vibrotactile noise can propagate more than 1 to 2 cm on the skin (Kurita et al., 2011). Therefore, the mechanical propagation of the vibrotactile noise from a remote location (wrist or dorsal hand) to the mechanoreceptors in the fingertip pads was considered an unlikely reason for the tactile sensory enhancement seen in the study. Thus, the authors postulated that a more likely mechanism for enhanced tactile sensation at the fingertip with the remote vibrotactile noise may be the noise and signal integration through interneuronal connections either in the spinal or supraspinal level such as the dorsal horn area in the spinal cord, medial lemniscus, thalamus, or somatosensory cortex.

Interneuronal connections between different parts of the hand have been suggested in the literature. For instance, Merzenich et al. (1983) have shown that the median and radial nerves may be directly connected in the central nervous system. In particular, Merzenich et al. (1983) found that immediately after the median nerve transection, the radial nerve had significant inputs to the somatosensory cortex area previously innervated by the median nerve in monkeys, suggesting integration of the median and radial nerves in the central nervous system. In addition, Manjarrez et al. (2003) showed that electrical recordings from the spinal cord and somatosensory cortex in response to tactile stimulation of the central pad of the hindpaw enhanced signal-to-noise ratios not only when tactile noise was added to the signal in the central pad of the hindpaw, but also when tactile noise was applied to the third hindpaw digit (remote noise) in cats. With the remote noise, when the spinal cord and brainstem were sectioned, such enhancement of the signal-to-noise ratio was still observed in the spinal level below the section, but not in the cortical level, suggesting that signal and noise integration occurs even at the spinal level (Manjarrez et al., 2003). These previous studies suggest 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 (Manjarrez et al., 2003). Hidaka et al. (2000) and (Enders et al., 2012) 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. Towards this end, Aim 2 was designed to examine if the noise and signal integration can be detected in the cortical level in humans. The noise and signal integration reflected in the cortical level does not necessarily mean that the integration occurs at the cortical level, but rather indicates the integration occurred somewhere in the human body either at the spinal level, cortical level, or at multiple places. Specifically, whether EEG can be used to detect the impact of remote vibrotactile noise on somatosensory brain activity in response to the fingertip tactile stimulation was investigated in Aim 2.

Another knowledge gap is whether remote noise enhancing sensation can be used to affect motor performance. Previous studies so far only demonstrated benefits of noise directly applied to the receptor of interest to enhance motor performance that utilizes the sensation involving the particular receptor. For instance, Kurita et al. (2011) applied subthreshold vibrotactile noise to the fingertip pad to improve healthy adults' fingertip tactile sensation as assessed by the monofilament test. In that study, with noise-induced improved tactile sensation, healthy adults' motor performance also improved, as quantified by the reduced magnitude of safety margin during grip-and-hold tasks. In another study, electrical noise was applied to the feet, which resulted in enhanced somatosensation of the feet as assessed by the improved monofilament test score, as well as improved balance control as quantified by the reduced postural sway in both healthy young and old adults (Collins et al., 2003). Details on the importance of tactile sensation in motor performance are described in Aim 1 Introduction. These previous studies illustrate the examples for how enhanced tactile sensation with noise can improve relevant motor performance.

However, these studies used noise directly injected to the signal around the target receptors, not remote noise. Recently, within the laboratory, the effect of remote noise applied to the wrist and the dorsal hand (that has been shown to improve the fingertip tactile sensation) on control of digit force direction during grip among stroke survivors was investigated. The remote noise did not appear to immediately improve the grip control among stroke survivors (unpublished data). However, whether the lack of improvement in motor performance is due to stroke survivors’ motor deficit, impaired sensorimotor integration, or ineffectiveness of the remote noise for motor performance is unclear. Therefore, Study 1 examine if remote vibrotactile noise could improve young healthy adults’ motor control. In Aim 1, in addition to examining the effect of remote noise on motor control, the effect of bandage was examined, because the bandage is known to deteriorate the tactile sensation in healthy adults (Griffin, 1995) and thus, the observed effect of bandage would confirm the role of tactile sensation in the particular motor control. Since the benefit of the particular remote vibrotactile noise on healthy adults has not been established yet, addition of the bandage in the protocol was deemed necessary to demonstrate the influence of tactile sensation manipulation on the motor performance of choice.

In summary, this thesis aimed at investigating the effect of remote noise on the underlying neural mechanism and motor control in humans. Specifically, the objectives of this thesis were to elucidate the effect of remote vibrotactile noise on hand motor control in healthy young adults (Aim 1) and to demonstrate feasibility for quantifying the effect of remote vibrotactile noise on somatosensory electroencephalography (EEG) activity in one healthy young adult as a pilot study (Aim 2). To achieve these objectives, the following two phases were carried out. The aims of these phases are as follows:

Aim 1: The effect of sensory manipulation on the ability to maintain pinch force

> **Objective 1:** To examine the effects of remote vibrotactile noise (aimed at enhancing tactile sensation) and bandaged fingertip pads (simulating tactile sensation loss) on people’s ability to maintain pinch force without visual feedback.

Hypothesis: People will reduce pinch force error with remote subthreshold vibrotactile noise and increase pinch force error when the fingertips are wrapped in bandages.

Aim 2: The effect of remote vibrotactile noise on the somatosensory cortex activity

Objective 2: To demonstrate the feasibility for quantifying the effect of remote vibrotactile noise on electroencephalography (EEG) activity in response to monofilament stimulation of the index fingertip.

Although this thesis involved healthy young adults only as the subject population, the knowledge obtained from this work can have an impact in rehabilitation applications. For instance, Kurita et al. (2011) developed a wearable device applying vibrotactile noise to the fingertip pad to improve people’s tactile sensation and grip performance. They projected that such a wearable device could assist older adults with fingertip sensation and grip performance. However, having a noise-generating device at the fingertip as in Kurita et al. (2011) interferes with object manipulation and dexterous finger movement and thus can be impractical. Thus, if this thesis would show that remote vibrotactile noise (such as at the wrist or back of the hand) could enhance hand grip performance such as the ability to maintain force accurately in healthy young adults in Aim 1, the remote noise technique could be adopted by Kurita et al. (2011) or others to assist the elderly with hand grip performance without having the wearable device interfering with the hand-object interaction at the fingertips.

In addition, if Aim 2 would show the integration of the signal and noise in the central nervous system in healthy young adults, this knowledge could be applied to help people who have reduced sensation due to injury to the peripheral nerve or receptors to sense better by applying remote vibrotactile noise. Again, having the noise-generating device away from the fingertips is more practical than having the device right by the fingertips to not interfere with typical daily activities with the hands.

AIM 1:

EFFECT OF SENSORY MANIPULATION ON THE ABILITY TO MAINTAIN PINCH FORCE

1.1 Introduction

This study examined if remote vibrotactile noise could improve young healthy adults' motor control, as described in the thesis Introduction section. The effect of *remote* noise on motor control in *healthy* young adults was tested in this study because previous studies only demonstrated the benefit of noise *directly* applied to tactile signals on motor control in *healthy* adults (Collins et al., 2003; Galica et al., 2009; Kurita et al., 2011; Priplata et al., 2002). In our laboratory, the effect of remote noise on stroke survivors' grip control was examined, although immediately improvement was not seen (unpublished data), which could be due to stroke survivors' motor deficit or impaired sensorimotor integration. Therefore, this study examined the effect of remote noise on motor control in healthy young adults. The similar remote noise as in Enders et al. (2012) were used, because Enders et al. (2012) showed improved tactile sensation with remote noise.

Noise typically enhances detection of sensory signals via stochastic resonance. However, once sensation improves with noise, improvement in motor control can be expected in humans, because human motor behavior utilizes feedback control using sensory signals. For instance, *direct* vibrotactile noise to the fingertip (presumably enhancing the fingertip tactile sensation) reduced safety margin, implying improved hand grip control among healthy adults in Kurita et al. (2011). *Direct* vibrotactile noise applied to the feet (presumably enhancing feet tactile sensation) reduced postural sway in healthy young and old adults, implying improved balance control (Collins et al., 2003; Priplata et al., 2002). *Direct* vibrotactile noise to the feet also reduced the stride, stance, and swing time variability during gait in healthy old adults (Galica et al., 2009). Thus, this study examined if *remote* vibrotactile noise (presumably enhancing the fingertip tactile sensation) could enhance hand grip control.

Fingertip tactile sensation is important for proper hand grip control. For instance, when the cutaneous feedback was removed from healthy individuals’ index finger and thumb while the motor system was unaffected, they dropped a grasped object on 36% of the grip and lift trials, compared to no drops without anesthesia (Augurelle et al., 2003). Anesthesia of the fingertips also led to inappropriate safety margin and lack of proper modulation of safety margin in healthy young adults in Westling and Johansson (1984). When healthy young adults’ index finger and thumb were covered with bandages (DuoDERM, 3M Medical-Surgical Division, St. Paul, MN, USA), degrading tactile sensation (assessed by monofilament test), safety margin increased during grip and lift tasks, indicating worsened hand grip motor control (Griffin, 1995).

This observation of impaired motor control in the presence of altered sensation is also seen in people who develop the sensory impairment. Older adults with reduced tactile sensation (larger two-point discrimination score) had greater force fluctuation during submaximal pinch force production compared to young adults (Ranganathan et al., 2001). Furthermore, people with reduced tactile sensation such as patients with stroke (Blennerhassett et al., 2006) and patients with neuropathy (Thonnard et al., 1997) displayed inefficient safety margins. Therefore, the fingertip tactile sensation is important for proper hand grip control.

Hand grip control can be quantified by multiple different ways such as safety margin, grip force variability, and grip force maintenance. Grip force maintenance was chosen as the task of this study, because young healthy adults are shown to have drifts in the grip force when the visual feedback of their grip force disappears (Vaillancourt & Russell, 2002), suggesting room for improvement with noise. In order to maintain a certain grip force without visual feedback, people need to obtain information regarding their current grip force level from tactile sensation through mechanoreceptors (Johansson & Westling, 1984) and proprioception (Gentilucci et al., 1994). Among the two senses, noise is expected to affect tactile sensation, based on Enders et al. (2012). It is thought that the changes in tactile sensation may influence the force maintenance accuracy. To ensure that changes in tactile sensation influence the force maintenance accuracy, we added a DuoDERM bandage condition that is known to deteriorate tactile sensation (Griffin, 1995).

The importance of tactile sensation on pinch force accuracy may depend on pinch force level. For instance, Vaillancourt and Russell (2002) showed that the extent of pinch force drift after the removal of visual feedback for pinch force was greater when people had to maintain a high pinch force (approximately 25% of the maximum pinch force or higher) than a low pinch force at 5% of the maximum pinch force. De Serres and Fang (2004) showed that pinch force error in force matching tasks (between the two hands and between consecutive pinches) was greater for older adults with sensory deficit (assessed by the monofilament test) than young adults only at 5% maximum pinch force, but not at 20% and 40% maximum pinch force. However, these studies could not pinpoint why pinch force accuracy differed depending on the pinch force levels, and why aging-related deterioration in tactile sensation affected pinch force accuracy differently depending on the pinch force levels. Thus, inclusion of the DuoDERM bandage was expected to reveal whether tactile sensation affects pinch force accuracy or not in our study.

The objective of this study was to determine the effect of tactile sensory manipulation on persons' ability to maintain pinch force in the absence of visual feedback. Specifically, this thesis examined the effect of vibrotactile noise (aiming for enhanced tactile sensation) as well as bandages on the fingertip pads (aiming for deterioration of tactile sensation) on the accuracy of pinch force maintenance in young health adults. In addition to the remote noise application to enhance fingertip tactile sensation, the DuoDERM bandage condition (to deteriorate tactile sensation) was added to serve as a negative control.

1.2 Methods

1.2.1 Subjects

Fifteen healthy young adults (19-36 years old) participated in this study (see the power analysis below). The inclusion criterion was the age between eighteen and forty. The lower limit was to ensure that no vulnerable minors were used for the study. The upper limit was to minimize the chance of age-related changes in either sensation or force production. It was shown that tactile sensation quantified by the vibration threshold remained unchanged for people under 45 years old, but deteriorated on average after the age of 45 (Whanger & Wang, 1974). Additionally, Mathiowetz et al.

(1985) found that the pinch strength was stable from 20 to 50 years old and then gradually declined for those older than 50 years old. The exclusion criterion was any history of neuromuscular disorders in the wrist or hand and any history of upper body orthopedic issues that would interfere with gripping.

The number of subjects was determined by power analysis. A conservative effect size of 0.2 was used (Cohen, 1988). In a previous study, an effect size of 0.28 was observed when pinch force control improved with an additional sensory modality (visual feedback) (Seo et al., 2011). For power of 0.8 for healthy young adults, G*Power (Faul et al., 2007) gave a sample size of 14 for a within-factors ANOVA design at alpha of 0.05. We collected 1 more subject than recommended by the power analysis to be conservative. All subjects signed a consent form and followed a protocol approved by the Institutional Review Board at the University of Wisconsin-Milwaukee.

1.2.2 Procedure

Subjects were instructed to maintain an isometric precision pinch grip at a prescribed target force level. Pinch force was measured using two 6-axis load cells (Mini40, ATI Industrial Automation Inc., Apex, NC, USA; Figure 2) with the sampling frequency of 500 Hz. Visual feedback for the target and actual pinch forces was given only for the first 8 seconds and then actual pinch force feedback was taken away for the next 12 seconds, similar to the protocol in a previous study quantifying pinch force accuracy (Vaillancourt & Russell, 2002). Vaillancourt and Russell (2002) surmised that in pinch force maintenance task, it may take as long as 8 seconds for young healthy adults to process the visual force feedback (including time for the nervous system to detect the visual information, send the afferent signal to the cortical structure, calculate a necessary motor response, and send the motor signal to the motor neuron pool). In addition, the 12 second period provides sufficient time for the pinch force to drift as well as for subjects to correct their pinch force if they could. After the 20 seconds of pinch, subjects were instructed to rest.

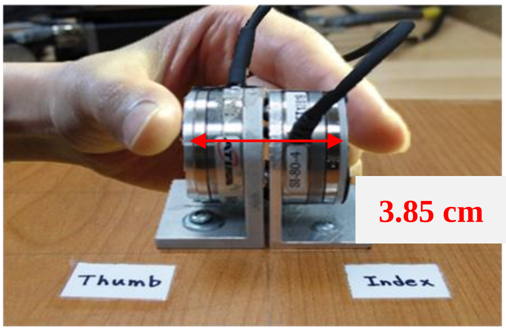


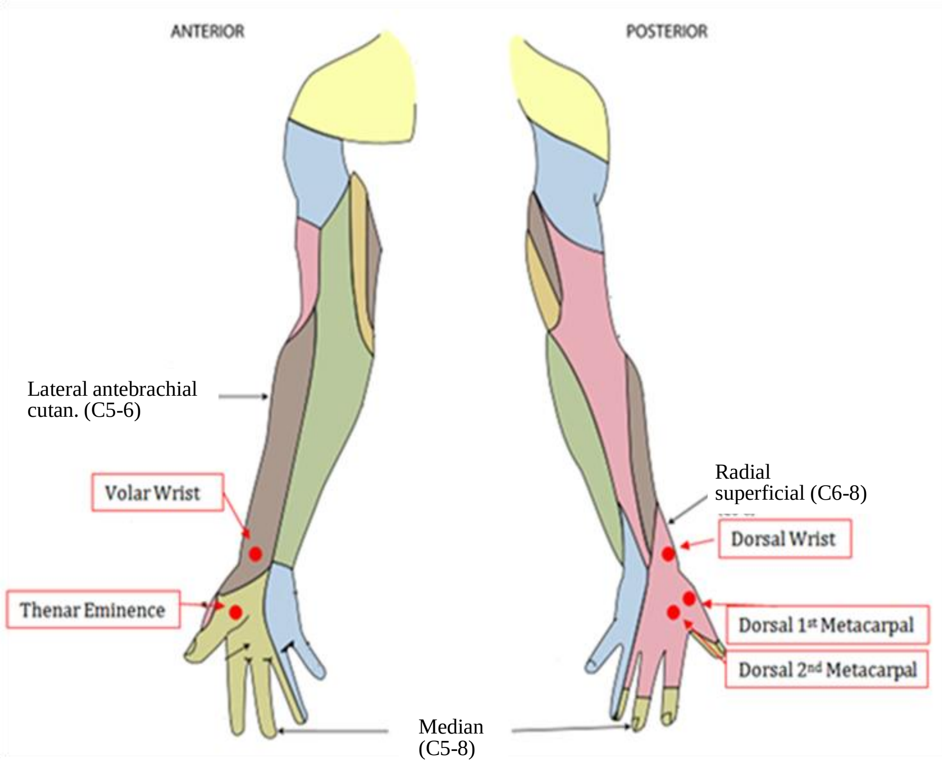
Figure 2: The pinch force measurement device and its size.

Pinch force error was determined as the root mean square error between the target pinch force and actual pinch force (Park, 2012) during the 12 seconds of pinch without visual feedback, normalized by the target force (in % target force). The equation used is shown below:

$$\text{Pinch force error} = \sqrt{\frac{\Sigma(actual\ force - target\ force)^2}{number\ of\ data\ points}} \quad \text{(Eq. 1)}$$

Pinch force error was compared among different tactile sensory manipulation conditions. The sensory manipulations were: (i) normal pinching without vibrotactile noise; (ii) pinching with vibrotactile noise at one of three intensities (60%, 80% and 120% of sensory threshold) applied at one of five locations in the hand and wrist remote from the fingertips, intended to enhance tactile sensation at the fingertips (Enders et al., 2012); and (iii) bandaged thumb and index finger with DuoDERM CGF Extra Thin Dressings (ConvaTec Inc., Skillman, NJ, USA; Fig. 3a), simulating deteriorated tactile sensation.

The five locations of the remote vibrotactile noise were: dorsum hand over the 1st metacarpal bone, dorsum hand over the 2nd metacarpal bone, dorsal wrist, volar wrist and thenar eminence (Figure 3). The first four locations of the remote noise were based on the previous study that showed enhanced tactile sensation (Enders et al., 2012). In addition, one additional location at the thenar eminence was included in this study. It was anticipated that these five locations might provide a clue behind the neural mechanism for the effect of remote noise, in case some locations would work better than other locations. For instance, if application of noise to the thenar eminence would result in greater pinch force accuracy (or smallest pinch force error) compared to other locations, then it might be related to the thenar eminence sharing the median nerve with the index finger and thumb tip pads. If the three dorsal locations would result in greater pinch force accuracy compared to others, then it might suggest the neuronal connections between the radial and median nerves within the central nervous system, as suggested in Merzenich et al. (1983).



Source: http://healthpages.org/anatomy-function/spinal-nerves/

Figure 3: Five locations for vibrotactile noise

Three intensities tested for the remote noise were: 60%, 80% and 120% of sensory threshold. Two subthreshold noise intensities, 60% and 80% sensory threshold, were chosen based on Enders et al. (2012). These two noise intensities are within the range (33% to 90% of the sensory threshold) that has been previously shown to be optimal (Collins et al., 2003; Galica et al., 2009; Kurita et al., 2011; Priplata et al., 2002; Wells et al., 2005). Additionally, noise at 120% of the sensory threshold was added as a suprathreshold vibrotactile noise for comparison. The specific noise intensity for each location was set based on the sensory threshold at that location for each subject. To determine the sensory threshold, the noise intensity was increased and decreased until the subject was barely able to distinguish between an “off” and an “on” presentation of the vibrotactile noise.

The remote vibrotactile noise protocol followed the previous study with the remote noise (Enders et al., 2012). Specifically, white noise with frequencies between 0 to 500 Hz (Johansson & Westling, 1984), which cover the sensitive frequencies for all four cutaneous mechanoreceptors, was generated by an EAI C-3 Tactor (Engineering Acoustics Inc., Casselberry, FL, USA; Figure 4b-c).

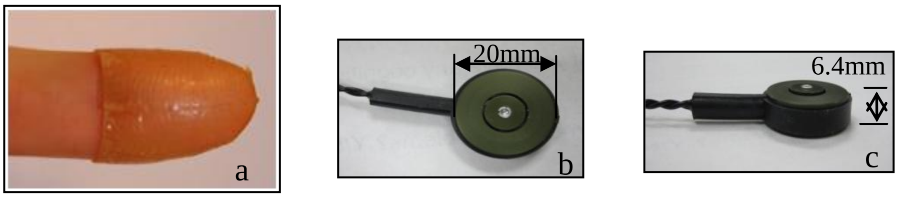


Figure 4: The sensory manipulations using the bandage (a) or vibrotactile stimulation (b, c).

Two target force levels were used. They were 5% and 20% of the maximum pinch force following a previous study (De Serres & Fang, 2004), estimated after subjects performed maximum voluntary pinch grip contractions. De Serres and Fang (2004) showed that older adults with sensory deficit (assessed by the monofilament test) had greater pinch force error than young adults only when they were pinching at 5% of the maximum pinch force, but not at 20% of the maximum pinch force. This could be either because tactile sensation does not play an important role in force accuracy during high pinch force exertion, or because older adults have greater difficulty in generating low pinch force due to loss of low-force motor units (Galganski et al., 1993). If the former is true, sensory manipulation would have an impact on the pinch force accuracy only during 5% pinch, not during 20% pinch in the present study.

Pinch force error was measured for each sensory manipulation condition (for a total of 21, including noise with three intensities and five locations, the normal pinching while the noise generator was attached in the five locations despite zero noise, and the bandaged condition) at both 5% and 20% target pinch force levels, twice for a total of 84 trials. Only two repetitions were performed to minimize participant load (current protocol 2 hours). Testing of the five noise locations and the bandage condition was randomized. Within each noise location, the order of testing different noise intensities (0%, 60%, 80% and 120% sensory threshold) and target force were randomized. The non-dominant hand was used because the non-dominant hand typically maintains target force less accurately (Henningsen et al., 1995), and thus has more room to improve compared to the dominant hand.

1.2.3 Statistical analysis

First, repeated measures analysis of variance (ANOVA) determined if the pinch force error was affected by sensory manipulation (bandaged condition, normal pinching with 0% noise, pinching with 60% noise, pinching with 80% noise, and pinching with 120% noise), target force, and noise location (nested under sensory manipulation), and their interactions. Since there was a significant interaction between sensory manipulation and target force, indicating that the effect of sensory manipulation was different depending on the target force level, ANOVAs were performed for each target force level. In other words, two separate repeated measures ANOVAs determined if the pinch force error was affected by sensory manipulation, and noise location (nested under sensory manipulation), and their interaction. Tukey post hoc test were performed to further examine differences between different levels within significant factors. A significance level of 0.05 was used.

The distribution of the data was evaluated by Test for Skewness. A significant skew of $p<0.01$ was considered to be significant evidence for skewed data (Tabachnick & Fidell, 2007). Pinch force error data was found to be non-normal and so logarithmic transformation was applied to normalize the data set, following the studies which also examined pinch force error with logarithmic transformation (Nagasawa & Demura, 2009; Patten et al., 2003). The transformed data was used for all ANOVAs. ANOVA with transformed data was used, because interaction effects (e.g., between sensory manipulation and target force level) are difficult to determine with a nonparametric test (Sheskin, 2011). In addition, a high number of nonparametric tests among all individual conditions could increase the probability of Type I error (Sheskin, 2011).

1.3 Results

The force traces for individual trials for all subjects are shown in Figure 5. Subjects drifted their pinch force after the visual feedback was removed as seen in Figure 5. Noticeable is that after the removal of visual feedback, pinch force drift was larger during 20% pinch than 5% pinch. In addition, pinch force tended to decrease rather than increase after the removal of visual feedback during 20% pinch, more so compared to 5% pinch.

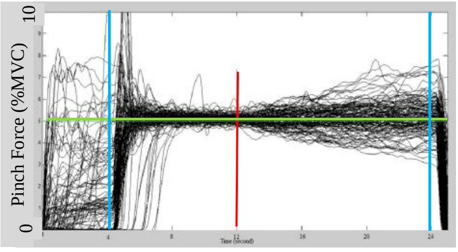
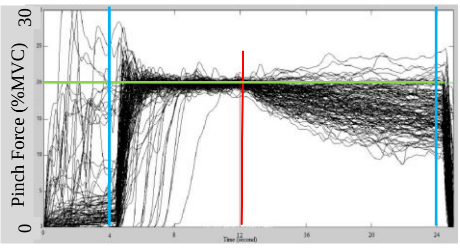
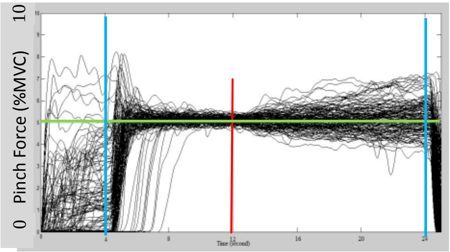
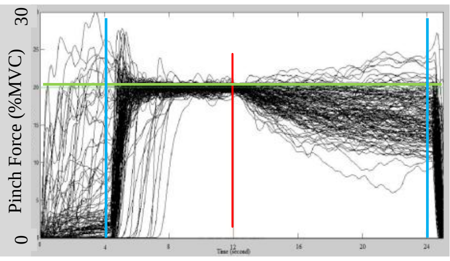
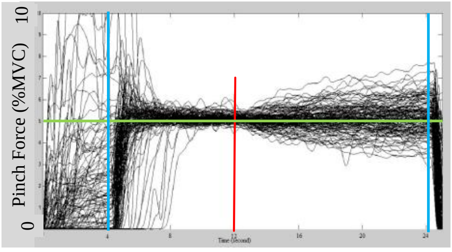
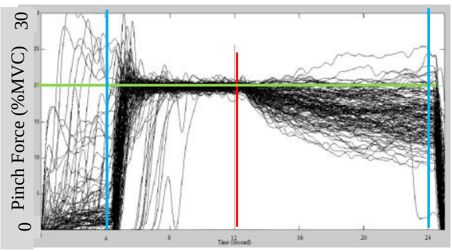
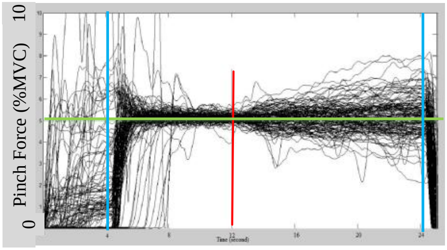
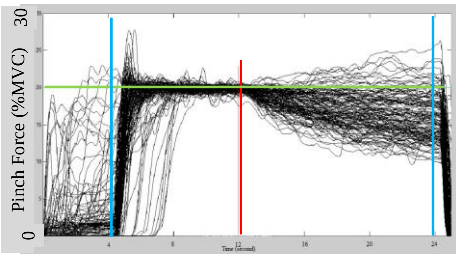
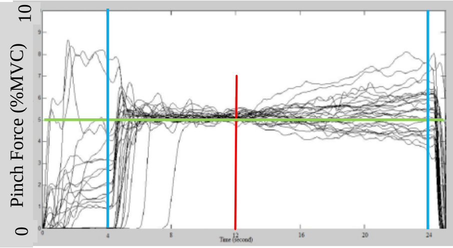
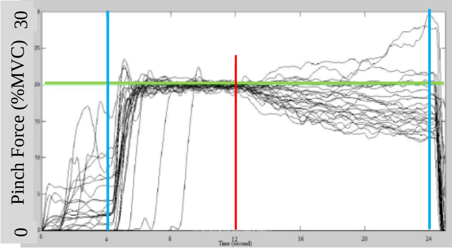
Noise intensity	Target force	
	5% maximum pinch force	20% maximum pinch force
Normal pinch		
60% sensory threshold		
80% sensory threshold		
120% sensory threshold		
Bandaged finger		

Figure 5: Force traces for each pinch force maintenance condition. Subjects started pinching at the first vertical blue line and ended pinching after the second vertical blue line. The vertical red line shows when the visual feedback was removed. The green line is the target force level.

As overall summary results, Figure 6 shows the mean pinch force error for each sensory manipulation condition and target force level. The first ANOVA showed that pinch force error changed with sensory manipulation differently depending on the target force level (ANOVA, $p<0.05$ for sensory manipulation × target force; Figure 6). Therefore, two separate ANOVAs were performed for each target force level as described in the next paragraph. Pinch force error was significantly greater when the target force level was 20% of the maximum pinch force compared to 5% of the maximum pinch force (ANOVA, $p<0.05$). Pinch force error did not significantly change with remote vibrotactile noise location (ANOVA, $p>0.05$).

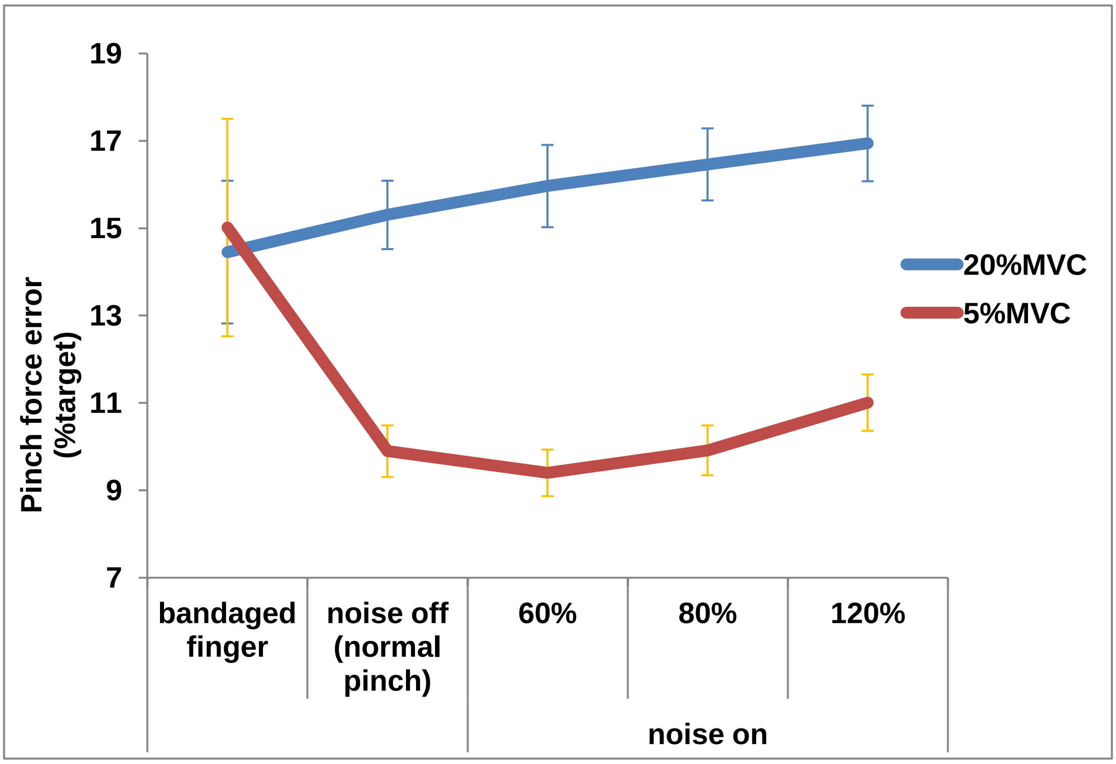


Figure 6: Mean ± standard error (SE) pinch force error during pinching at 20% and 5% maximum pinch force (pooled for noise locations and subjects). The pinch force error changed with sensory manipulation differently depending on the target force level (ANOVA, $p<0.05$ for sensory manipulation × target force). Pinch force error was significantly greater for target force level 20% target force level compared to 5% target force level for all conditions (ANOVA, $p<0.05$) except the bandaged finger (Tukey post-hoc, $p>0.05$). Pinch force error normalized by the target force was used for analysis.

Repeated measures ANOVA performed for only the 5% target force level showed that pinch force error significantly changed with sensory manipulation (bandaged finger condition, no noise, 60% noise, 80% noise, and 120% noise) (ANOVA, $p<0.05$; Figure 7). The other comparisons were not found to be significant (Tukey post hoc, $p>0.05$). On average, pinch force error was 5% greater for the bandaged finger condition compared to normal pinching condition. Noise at 60% sensory threshold resulted in 1% lower error compared to normal pinch, while noise at 80% and 120% sensory threshold did not help reducing error compared to normal pinch. Pinch force error did not change with remote vibrotactile noise location (ANOVA, *p*>0.05; Figure 8).

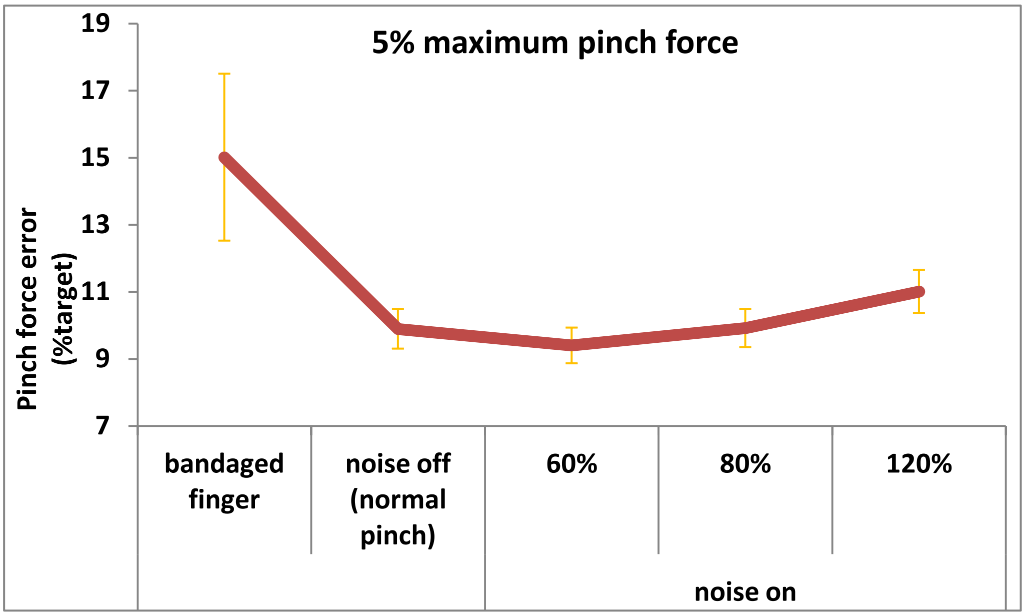


Figure 7: Mean ± standard error (SE) pinch force error (pooled for noise locations and subjects) during pinching at 5% maximum pinch force. The pinch force error was significantly changed with sensory manipulation (ANOVA, p<0.05). Pinch force error was normalized by the target force. Non-transformed data is shown in figure.

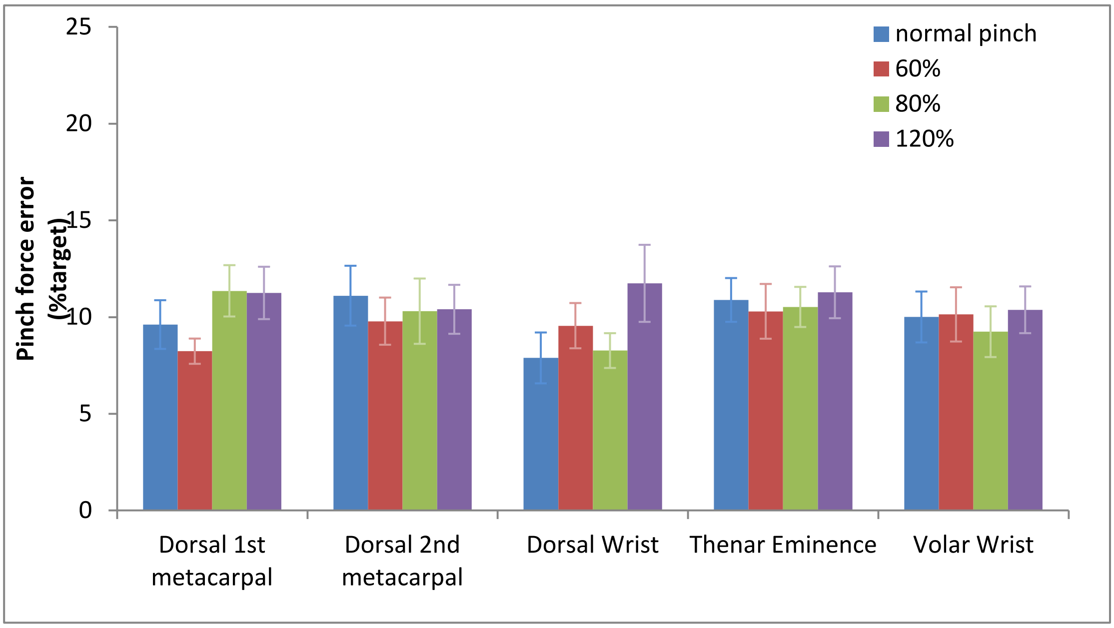


Figure 8: Mean ± standard error (SE) pinch force error (pooled for subjects) is shown for each noise location and noise intensity during pinching at 5% maximum pinch force. Pinch force error did not change with different locations of the remote vibrotactile noise (ANOVA, p>0.05) (target force = 5% of the maximum pinch force). Pinch force error was normalized by the target force.

Repeated measures ANOVA performed for only the 20% target force level showed that pinch force error did not change with sensory manipulation (ANOVA, *p*>0.05; Figure 0). Pinch force error did not change with noise location, either (ANOVA, *p*>0.05; Figure 10).

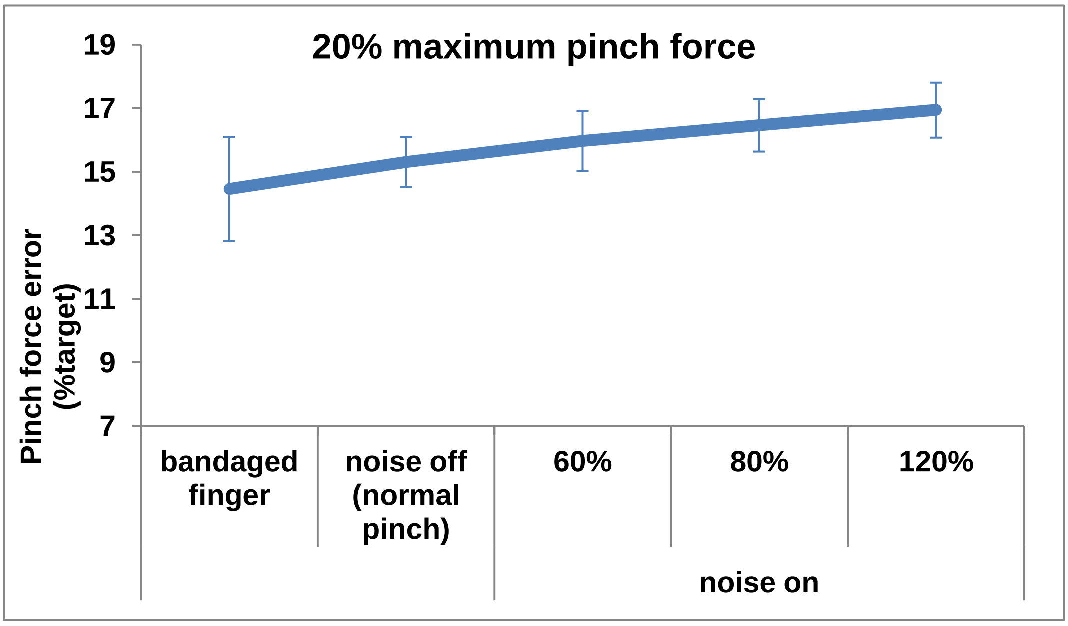


Figure 9: Mean ± standard error (SE) pinch force error (pooled for noise locations and subjects) during pinching at 20% maximum pinch force. The pinch force error did not change with sensory manipulation (ANOVA, $p>0.05$). Pinch force error was normalized by the target force.

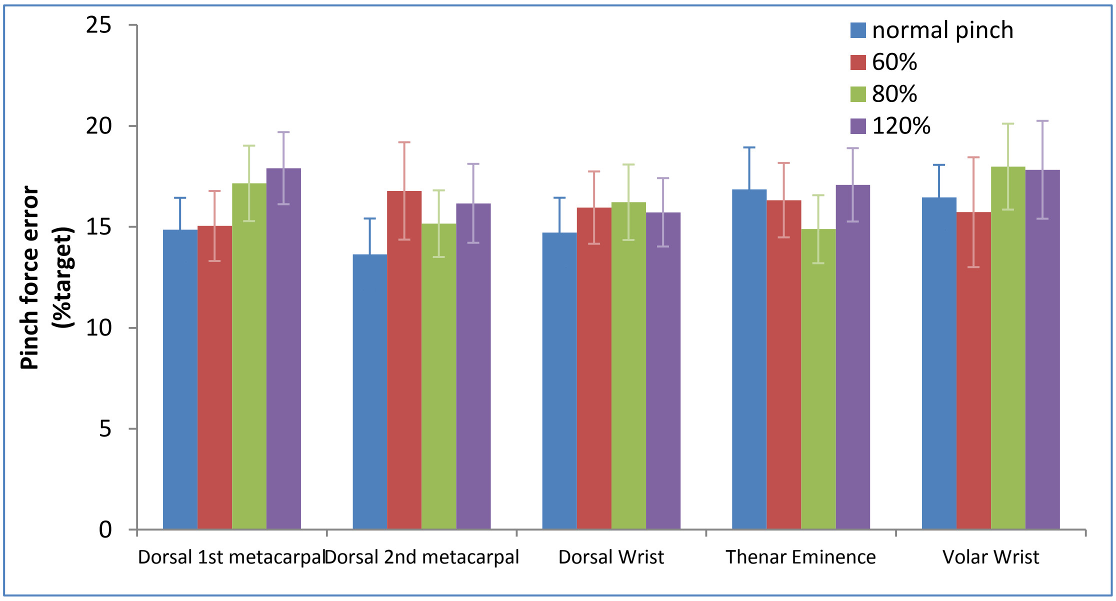


Figure 10: Mean ± standard error (SE) pinch force error (pooled for subjects) is shown for each noise location and noise intensity during pinching at 20% maximum pinch force. The pinch force error did not change with different locations of the remote vibrotactile noise (ANOVA, $p>0.05$) (target force = 20% of the maximum pinch force). Pinch force error was normalized by the target force.

1.4 Discussion

1.4.1 Tactile sensory feedback is important only for the low-force level

The fingers covered with the bandages had an impact on pinch force error (representing force accuracy) only when the target pinch force was 5% of the maximum pinch ($p<0.05$), but not 20% ($p>0.05$). Since the purpose of using the bandaged finger was to simulate light touch deficit, this finding is similar with the previous study that showed pinch force accuracy was affected by aging-related tactile sensation loss only at a low pinch force level (5% of the maximum pinch force), but not at high force levels (20% or 40% of the maximum pinch force) (De Serres & Fang, 2004). It is possible that during high pinch force exertions, mechanoreceptors may have been overloaded and may not have been able to detect small changes in pinch force, forcing people to rely on other sensory modalities for force maintenance such as proprioception (Gentilucci et al., 1994). This could also explain why pinch force error for the 5% target force level with the bandages was similar with that for the 20% target force level. The bandages were supposed to simulate a condition where tactile sensation does not provide proper information. Therefore, tactile sensation may not have been useful for all conditions for the 20% target force level and the bandaged condition for the 5% target force level for this force maintenance task.

1.4.2 The effect of remote vibrotactile noise on pinch force error

Remote vibrotactile noise did not significantly decrease pinch force error compared to normal pinching even at the 5% target force level. During pinching at 5% of the maximum pinch force, vibrotactile noise at 60% of the sensory threshold was observed to marginally reduce error, compared to normal pinching (Figure 7). It is possible that the tactile sensation from pinch grip may have been very strong, even during pinching at 5% of the maximum pinch force, thus minimizing the effect of noise. Collins et al. (1997) showed that while noise helped the detection of a weak signal that is just below the sensory threshold, noise deteriorated the detection accuracy when the signal was strong and well above the sensory threshold. Thus, the pinch force maintenance may have been a task that does not benefit from added noise or stochastic resonance in young health adults. Another potential reason for the seemingly lack of the noise effect may be that healthy young adults are already performing the pinch force maintenance task optimally with the good tactile sensation and motor control, leaving little room for improvement.

While remote noise at 60% of the sensory threshold minimally decreased the pinch force error compared to normal pinching, remote noise at 80% of the sensory threshold did not change the pinch force error compared to normal pinching (Figure 7). Remote noise at 120% of the sensory threshold rather increased the pinch force error

1% compared to normal pinching. Such results of the *remote* noise are consistent with the previous literature regarding *direct* noise that showed that foot tactile sensation improved with direct tactile noise with the intensities at either 33%, 50%, or 67% of the sensory threshold, compared to noise intensities at 0% (no noise), 83% or 100% of the sensory threshold (with the "∩" shape curve describing the relationship between the foot tactile sensation and noise intensity from 0% to 100%) in healthy adults (Wells et al., 2005).

The noise location did not influence the pinch force error. Thus, no conclusion could be made regarding potential mechanisms (e.g., nerve sharing or nerve integration in the central nervous system as described in Introduction).

1.4.3 Limitations/Future direction

As discussed earlier, the lack of the effect of remote noise in young, healthy adults may have been related to the motor task of the choice in this study. A force level that is lower than 5% of the maximum pinch force may have required mote tactile sensitivity, if for maintaining 5% pinch force were too strong to have the stochastic resonance effect shown. Alternatively, a different motor task could have been used such as safety margin, since *direct* noise has been shown to impact healthy adults' safety margin regulation (Kurita et al., 2011). In addition, the effect of the remote noise applied to the hand and wrist on the fingertip tactile sensation could have been recorded, because although previous studies showed the effect of remote noise on healthy young adults' baroreflex function (Hidaka et al., 2000) and stroke survivors' fingertip sensation (Enders et al., 2012), there was no previous study demonstrating the effect of the remote noise on healthy young adults' fingertip sensation. If the lack of the effect of remote noise was because healthy young adults were already performing the pinch force maintenance task optimally, we could potentially test the remote noise in affecting old adults' performance, especially for the elders with reduced tactile sensation (Gescheider et al., 1994) or deteriorated grip force control (Cole & Beck, 1994).

1.5 Conclusions

Remote vibrotactile noise did not significantly change pinch force drift when visual feedback was removed. The reason for the lack of the noise effect could be that the pinch force maintenance task involved strong tactile signals whose detection could not be helped with noise, or that healthy young adults were already performing the pinch force maintenance task optimally with good tactile sensation and motor control.

Tactile sensation appeared to be important for maintaining pinch force at the low force level (5% of the maximum pinch force), but not at the high force level (20% of the maximum pinch force) as indicated by the significantly higher drift in the bandage condition. It may be that during pinch at the high force level, mechanoreceptors may have been overloaded and people relied more on proprioception to maintain the pinch force instead of tactile sensation. The results of this study are inconclusive as to whether subthreshold remote noise could help with young adults' motor task at low force levels.

AIM 2:

EFFECT OF REMOTE VIBROTACTILE NOISE ON THE SOMATOSENSORY CORTEX ACTIVITY

2.1 Introduction

The objective of this pilot project was to demonstrate the feasibility for quantifying the effect of remote vibrotactile noise on electroencephalography (EEG) activity in response to monofilament stimulation of the index fingertip. EEG is a non-invasive technique to record people's brain activity. EEG can be used to examine the cortical responses to vibrotactile stimulation to the hand/wrist. One of the methods to analyze EEG data to understand the meaning of the brain activity is event-related potential (ERP). ERP can show the direct results for people's brain activity in response to a specific sensory, cognitive, or motor event (Luck, 2005). For instance, the peak-to-peak ERP amplitude and the ERP latency were shown to change when healthy young adults touched a rough texture surface than a smooth texture surface (Ballesteros et al., 2009).

Another method to analyze EEG data to understand the meaning of the brain activity is analysis of power spectral density in certain frequency bands. Increased activity in the α band (8-12 Hz) in the hand somatosensory area was shown to be related to cortical idling, whereas reduced activity in the α band in the hand somatosensory area was related to the touch stimuli to the index fingertip pad and index finger movement (Pfurtscheller, 1992). In addition, during reading or foot movement that did not involve any stimuli to the hand or hand movement, the α band activity of the hand sensorimotor cortex increased (Pfurtscheller & Klimesch, 1992; Pfurtscheller et al., 1994). Based on the available evidence, Pfurtscheller et al. (1994) suggested that decreased α band activities in the somatosensory cortex may is related to sensory information processing.

Increased β band (15-30 Hz) activity was shown to be related to sensory feedback (Baker, 2007; Riddle & Baker, 2005). Riddle and Baker (2005) had subjects pinch and hold two compliant levers. The two levers were initially wide open. Then the subjects pinched the levers to a target distance between the two levers. Riddle and Baker (2005) described that as the target distance between the two levers becomes small, there is a greater discrepancy between the efferent copy (expected motor output) and the actual motor output (sensed using sensory feedback), requiring a greater extent of sensory feedback. They found that with decreasing target distances, the β band activity increased and the β band coherence between the sensorimotor cortex EEG activity and the finger flexor muscle EMG increased. Thus, the authors concluded that increased β band activity at the sensorimotor cortex is related to sensory feedback.

Increased θ band (4-8 Hz) activity was shown to be related to enhanced sensorimotor integration in humans (Cruikshank et al., 2012). Cruikshank et al. (2012) asked subjects to reach a target on a touch screen with a finger when an auditory cue was given. They found that θ band activity in the hand sensorimotor cortex increased at the initiation of the movement and during the movement. The authors suggested that the increased θ band activity may reflect strengthened sensorimotor integration.

EEG provides a method to investigate the signal and noise integration in the central nervous system of humans. The level of signal and noise integration for stochastic resonance has been investigated by recording somatosensory cortex and spinal cord activity in cats using invasive techniques involving needles inserted using a glass micropipette and surgery (Manjarrez et al., 2003). Such invasive techniques cannot be used in humans.

EEG was used to investigate the effect of *direct* noise on brain activity (Manjarrez et al., 2002). Specifically, Manjarrez et al. (2002) recorded EEG signals of the somatosensory cortex (C4 electrode) in response to vibrotactile stimulation of the fingertip that was added with varying levels of noise in healthy young adults. They computed a signal-to-noise ratio where the denominator was the power of the EEG signals when only noise was applied to the fingertip (without the main stimulation signal), and the numerator was the power of the EEG signal when the main stimulation signal was applied with a varying level of noise. Manjarrez et al. (2002) showed that the signal-to-noise ratio in the EEG signals of the somatosensory cortex (C4 electrode) in response to vibrotactile stimulation of the fingertip increased when the level of noise increased from no noise to a certain level and then decreased when the noise level increased further from the optimal level in healthy young adults.

However, such representation of stochastic resonance in EEG signals has not been shown with *remote* noise. Previous studies on remote noise have only described behavioral changes, not neural representations (Enders et al., 2012; Hidaka et al., 2000). Specifically, Enders et al. (2012) showed that remote subthreshold vibrotactile noise in the hand and wrist enhanced tactile sensation in stroke survivors, and the authors also suggested that the signal and noise integration in the central nervous system, although direct evidence did not exist. In other words, the integration of signal and noise in the central nervous system has not been demonstrated in humans (while demonstrated in cats (Manjarrez et al., 2003)).

Therefore, a long-term goal of the laboratory is to investigate the effect of remote vibrotactile noise on the EEG activity in the somatosensory cortex in response to fingertip stimulation. In other words, even though the noise and signal are applied in different body parts, if the signal and noise integration occurs in the central nervous system, the EEG activity in response to the signal may be different with vs. without remote noise. The immediate goal of this study was to demonstrate the feasibility for quantifying the effect of remote vibrotactile noise on EEG activity in response to monofilament stimulation of the index fingertip. Specifically, the event-related potential and power spectral density for the α, β, and θ bands known to be related to sensation or sensory processing were compared with remote noise with varying levels of intensities from a single subject in this proof-of-concept pilot study.

2.2. Methods

2.2.1 Subject

As a pilot study, one healthy young (27 years old) with no history of sensory disorders participated in this study. Subject signed a consent form and followed a protocol approved by the Institutional Review Board at the University of Wisconsin-Milwaukee.

2.2.2 Procedure

The subject was seated in a chair with his left index fingertip strapped to a customized fixture (Figure 11a). Monofilament touched the subject's index fingertip pad (Figure 11a) while remote vibrotactile noise was applied to the dorsal hand skin over the 2nd metacarpal bone (Fig. 11b). This noise location was chosen out of the five locations tested in Aim 1, because pinch force error decreased with noises in multiple intensities the most in this noise location, compared to no noise condition (although none were significantly different than another; Figure 8). As in Aim 1, three remote vibrotactile noise intensities (60%, 80% and 120% of the sensory threshold) were compared against no vibrotactile noise (0% of the sensory threshold). As in Aim 1, the vibrotactile noise was a white noise with frequencies between 0 to 500 Hz, which covered the sensitive frequencies for all 4 cutaneous mechanoreceptors, including Ruffini's end organ, Meissner's corpuscle, Pacinian corpuscle and Merkel's disc (Johansson & Flanagan, 2009). The vibrotactile noise was generated by C-3 Tactor (Engineering Acoustics Inc., Casselberry, FL, USA).

The 64-channel EEG data were collected continuously during the test at 1kHz with a Synamps^2 amplifier system (Advanced Medical Equipment Ltd., Horsham, West Sussex, UK) using the international 10-20 system for the EEG electrode placement (Brain Products GmbH, Gilching, Germany) (Figure 13). To minimize auditory and visual stimuli to subject (such as the sound from the monofilament stimulation device and the motion of the monofilament), the subject wore ear plugs and headphones with white noise, and was instructed to look at a fixation dot throughout the experiment. The subject's hand, the monofilament stimulation device, and the vibrotactile noise device were behind a screen so that subject could not see the vibrotactile noise device and the motion of the monofilament stimulation (Figure 11c).

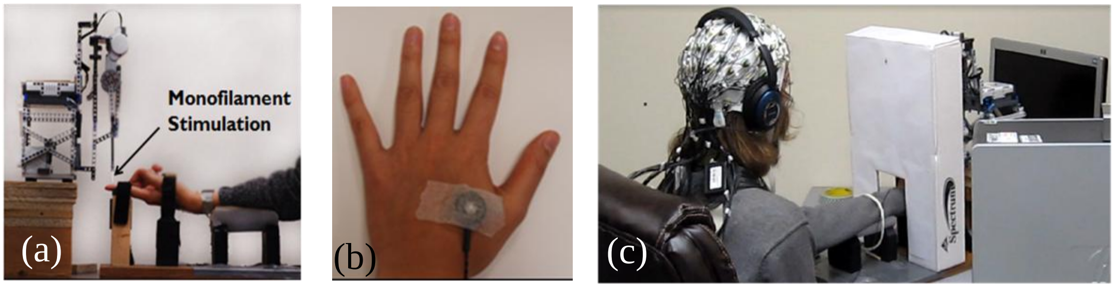


Figure 11: (a) Monofilament stimulation and hand fixture. (b) Vibrotactile noise was applied at the dorsal hand skin over the 2nd metacarpal bone. (c) Experimental setup.

There were four testing conditions within each noise intensity condition: (1) monofilament stimulation at the index fingertip without remote vibrotactile noise; (2) monofilament stimulation at the index finger tip with remote vibrotactile noise; (3) rest with remote vibrotactile noise (without monofilament stimulation); and (4) rest without remote vibrotactile noise (without monofilament stimulation). The monofilament had a diameter of 0.23 mm (similar to the 3.61 monofilament of the monofilament clinical kit (Winstein, 1991)). These four conditions were tested in a single experimental session comprised of eight consecutive blocks (Fig. 11). The conditions for monofilament stimulation with and without remote vibrotactile were recorded in three blocks each (gray blocks in Figure 12). The order of monofilament stimulation with and without noise was randomized (Figure 12). In each of those blocks, monofilament touched the index fingertip pad 50 times, with random intervals ranging from 1 to 2 seconds. A total of 150 monofilament touches were made for monofilament stimulation with and without noise conditions, each. EEG data for resting with and without vibrotactile noise were recorded in a 60 second-long block, each (black blocks in Figure 12). The whole sequence was repeated for each of the three noise intensity conditions (60%, 80%, and 120%). The testing of the three noise conditions was randomized.

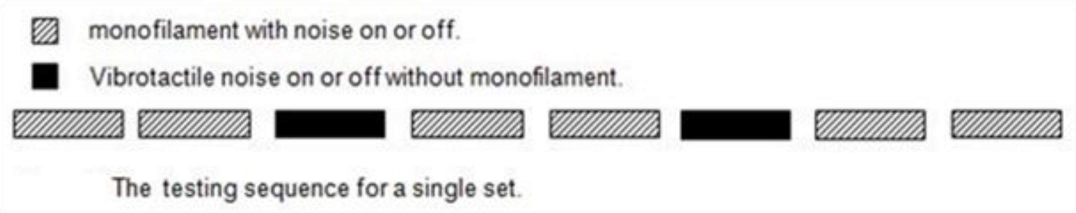


Figure 12: The testing sequence. The monofilament stimulation touched subjects' index fingertips 50 times with and without remote vibrotactile in three blocks each (gray blocks). Resting with and without vibrotactile noise were recorded in a 60 second-long block, each (black blocks). The order of monofilament stimulation with and without noise was randomized.

2.2.3 EEG data pre-processing

All data processing and analysis were performed using MATLAB (v8.0; The MathWorks, Natick, MA) and the EEGLAB toolbox (Delorme & Makeig, 2004). EEG data were filtered with a high pass filter with a cutoff frequency of 0.5 Hz to remove drifts. Then, EEG data were filtered with a low pass filter with a cutoff frequency of 50 Hz to remove line noise. Then, the EEG data were visually inspected and segments containing gross artifacts due to head movements or bad electrode impedance were excluded. Independent component analysis (ICA) linearly decomposes the original EEG channel data into an array of maximally independent components (Bell & Sejnowski, 1995). ICA was used for further identification of artifacts. Specifically, time courses, spectra, and topographic distributions of all independent components were inspected to identify independent components that reflected eye movements, scalp muscle artifacts and movement artifacts. To identify those specific independent components for artifacts, the algorithm called ADJUST (artifact detector based on the joint use of spatial and temporal features) was used following the literature (Mognon et al., 2010). These independent components that were identified as artifacts were removed from the data. For further analysis, EEG activity for two electrodes was examined among 64 electrodes of the International 10-20 system. The two electrodes were C4 and CP4 (Figure 13a). They were chosen due to their proximity to the contralateral hand somatosensory area (Fig. 13b). In addition, we were able to identify an independent component that showed somatosensory activity by visually inspecting the somatosensory topography of the component map (Figure 13c). The map shows that C4 and CP4 electrodes were located in the center of the activity of this somatosensory independent component and could reflect the somatosensory activity.

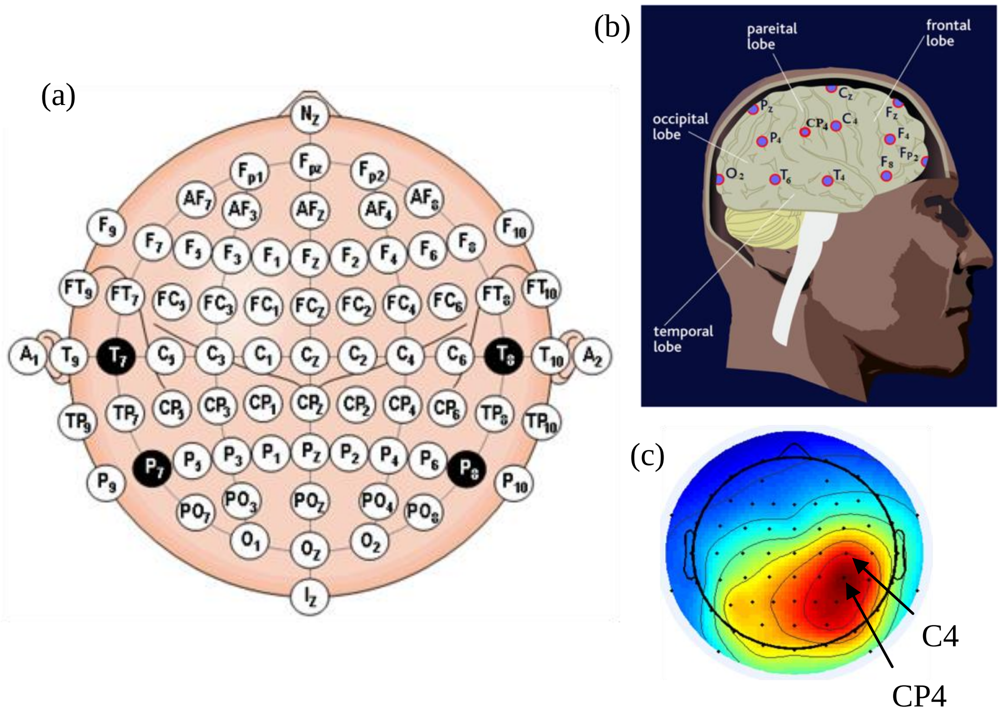


Figure 13: The international 10-20 system. (a) The international 10-20 system as standardized by the American Electroencephalographic Society (Sharbrough et al., 1991). (b) The electrodes C4 and CP4 are proximity to the contralateral hand somatosensory area. (c) Somatosensory cortex activity in response to the contralateral fingertip tactile stimulation is shown.

For the monofilament stimulation trials with and without noise, event-related potentials (ERP) and power spectral densities (PSD) were determined. ERP was determined in the following way. For each monofilament stimulation condition (either with or without noise at a certain intensity), there were 150 repetitions. Each epoch (each trial of the monofilament touching the index fingertip pad) was identified in the time period between 350 ms before and 650 ms after the monofilament touch. The time period before the monofilament touch served as the baseline brain activity. In other words, the EEG activity from 0 ms to 650 ms after the monofilament touch was subtracted by the average baseline EEG activity (350 ms prior until the monofilament touch). The epoch window was limited to 1 second, because the time interval between two monofilament touches ranged between 1 and 2 seconds. After the baseline adjustment, the 150 epochs were averaged. The averaged epoch for each condition is shown in Figure 14. Then, the peak-to-peak ERP amplitude after the monofilament touch was determined for each condition.

PSDs were determined for each condition in the following way. The same 150 epochs were used. The data were transformed using fast Fourier transform algorithm to get PSD. Hamming window (n=256) was applied to the data to minimize the artifacts due to finite lengths of the data. Also, the data were overlapped with 50% overlapping to minimize data leakage (i.e., misrepresentation of frequency component due to nonperiodicity of the data). In summary, PSD was determined after applications of the Fourier transform algorithm, windowing, and overlapping.

For the rest conditions without monofilament stimulation, the entire 60 second period was used to generate PSD for each condition. The same procedure described in the above paragraph was used. All analysis was performed in MATLAB.

2.2.4 Analysis

For this pilot data from one subject, the peak-to-peak ERP amplitude and PSD at three different frequency bands were visually compared among different conditions. Specifically, the peak-to-peak ERP amplitude in response to the monofilament stimulation was compared among no noise, 60% noise, 80% noise, and 120% noise. Similarly, PSD for the epochs with the monofilament stimulation was compared among no noise, 60% noise, 80% noise, and 120% noise. Also, PSD during rest without the monofilament stimulation was compared among no noise, 60% noise, 80% noise, and 120% noise. For PSD comparisons, the three different band activities were examined (Baker, 2007; Cruikshank et al., 2012; Pfurtscheller et al., 1996).

2.3. Results

2.3.1 Peak-to-peak ERP amplitude in response to the monofilament stimulation of the index fingertip while remote noise at different noise intensities was applied

The peak-to-peak ERP amplitude in response to the monofilament stimulation of the index fingertip pad is shown for each noise condition in Figure 14. Remote vibrotactile noise at the intensity of 60% sensory threshold increased the peak-to-peak ERP amplitude compared to no noise (Figure 14a). The peak-to-peak ERP amplitude decreased with 80% noise compared to no noise (Figure 14b). The peak-to-peak ERP amplitude also decreased with 120% noise (Figure 14b). When all three noise intensity conditions were compared (with the peak-to-peak ERP amplitudes for no noise averaged), it can be seen that the trend of peak-to-peak ERP amplitude increased with 60% noise, but not with 80% or 120% noise (Figure 15).

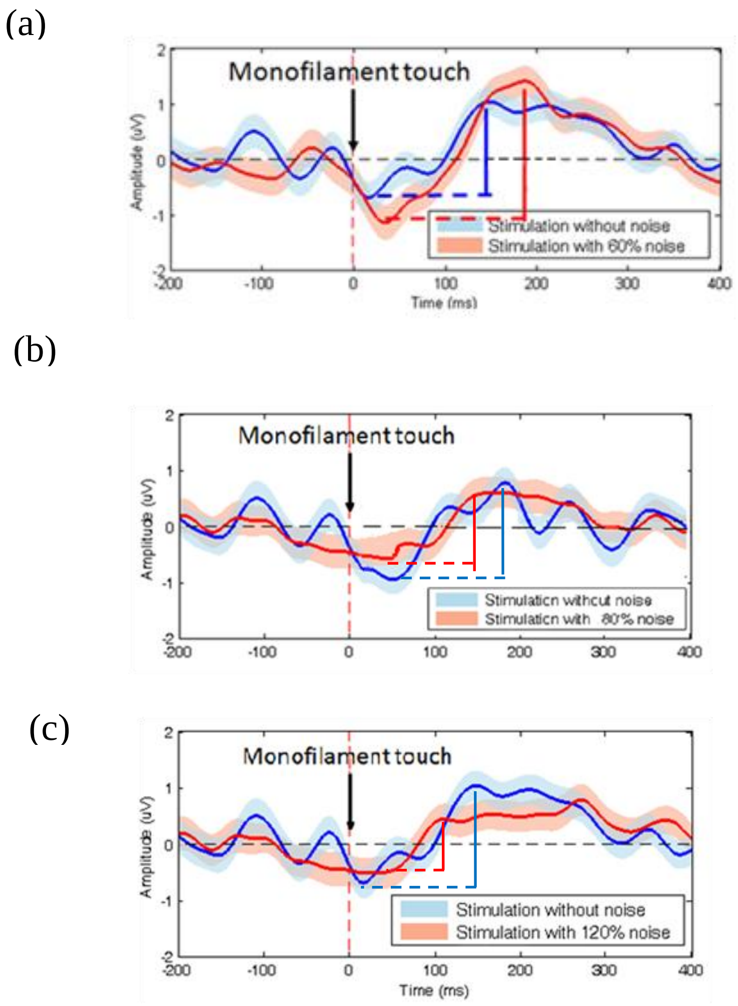


Figure 14: The event-related potential waveform in response to the monofilament touch (average of 150 epochs) with (a) 60%, (b) 80%, and (c) 120% vibrotactile noise, compared to no noise.

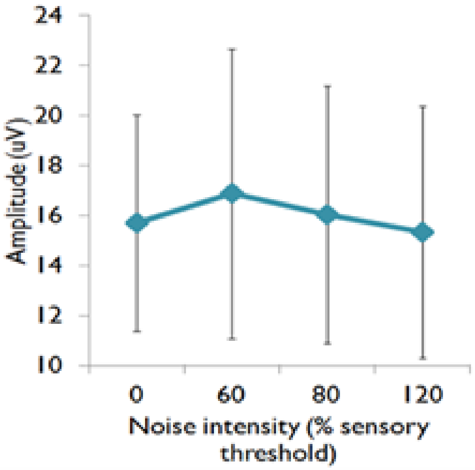


Figure 15: The mean ± standard deviation peak-to-peak ERP amplitude in response to the monofilament stimulation.

The peak-to-peak ERP amplitude in response to monofilament stimulation increased with 60% noise, but not with 80% or 120% noise in this subject.

2.3.2 PSD for monofilament stimulation with remote vibrotactile noise

The θ band activity (4 to 8 Hz) increased with 60% noise compared to no noise, while it did not change much with 80% noise and decreased with 120% noise compared to no noise (Figure 16). The α band activity (8 to 12 Hz) decreased with 60% noise compared to no noise, while it increased with 80% noise and did not change much with 120% noise compared to no noise (Figure 16). The β band activity (15 to 30 Hz) increased with 60% noise and 80% noise compared to no noise. 120% noise decreased β band activity (Figure 16).

When all three noise intensity conditions were compared (with the PSD amplitudes for no noise averaged), the PSD amplitude changes with remote noise intensity for each of the three bands can be compared as shown in Figure 17. The PSD amplitudes at 5 Hz, 10 Hz, and 23 Hz were used for comparisons within each frequency band, since the changes of these frequencies within each frequency band were related to tactile sensation (Baker, 2007; Cruikshank et al., 2012; Pfurtscheller et al., 1996). It can be seen that the PSD amplitude for the θ band (5 Hz) increased with 60% noise, but not with 80% noise. The PSD amplitude rather decreased with 120% noise (Figure 16). For the α band (10 Hz), the PSD amplitude decreased with 60% noise, increased with 80% noise, and did not change much with 120% noise. For the β band (23 Hz), the PSD amplitude increased with 60% noise, but not with 80% and 120% noise.

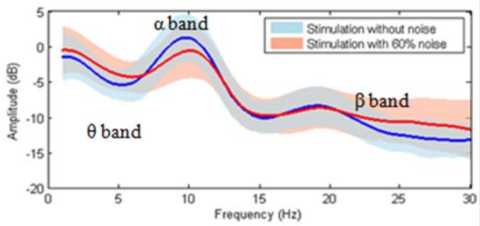
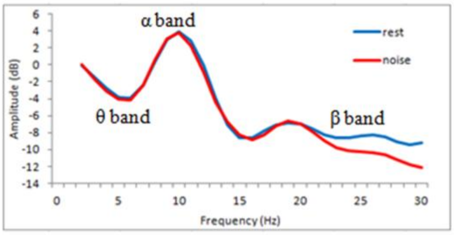
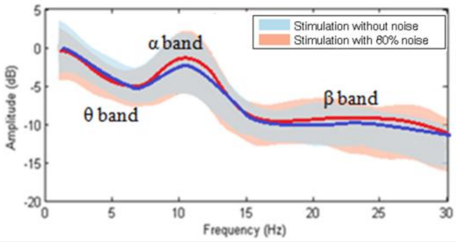
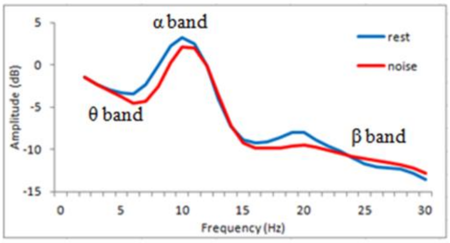
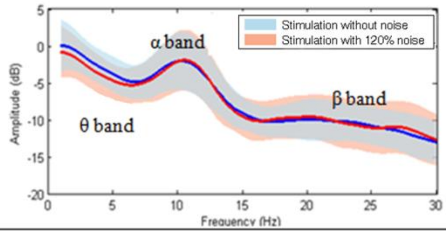
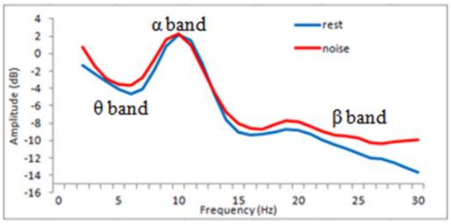
Noise intensity	Monofilament stimulation with and without noise	Rest with and without noise
60% of sensory threshold (a)		
80% of sensory threshold (b)		
120% of sensory threshold (c)		

Figure 16: The PSD during the monofilament stimulation (left column) and during rest (right column) with or without noise at different intensities (a) 60% of the sensory threshold, (b) 80% of the sensory threshold, and (c) 120% of the sensory threshold.

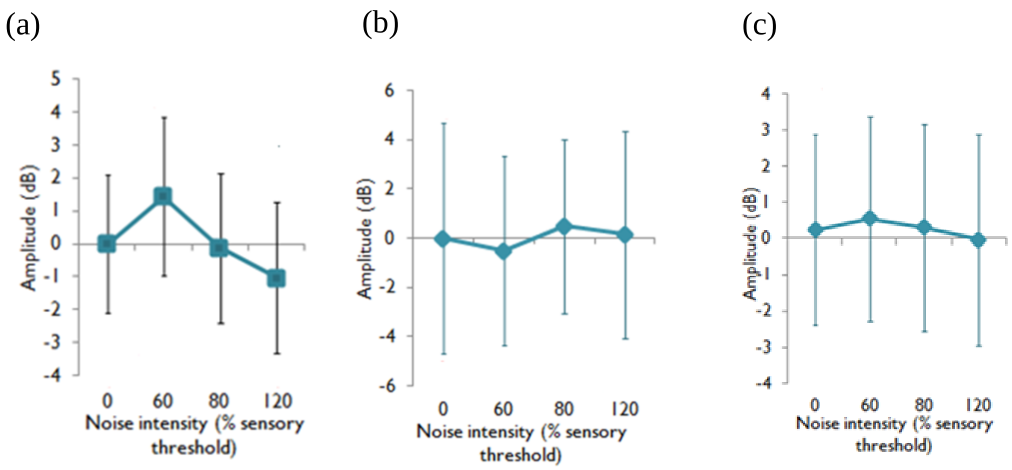


Figure 17: PSD amplitudes at (a) 5 Hz, (b) 10 Hz, and (c) 23 Hz with remote vibrotactile noise at different intensities.

2.3.3 PSD during rest with and without remote vibrotactile noise

PSDs during rest with vs. without remote noise at the three intensities are shown in Figure 16. It can be seen that the changes in PSD amplitudes at different frequency bands with remote noise are not consistent between when the monofilament stimulation was applied (Figure 16 left column) and when it was not (Figure 16 right column). Specifically, during rest with 60% remote noise, the PSD amplitude for the θ (4 to 8 Hz) and *α* (8 to 12 Hz) bands did not change much, while the *β* band (around 23 Hz) activity decreased (Fig. 16a). During rest with 80% noise, the θ and *α* band activity decreased, while the *β* band activity did not change consistently (Fig. 16b). During rest with 120% noise, the θ and *β* band activity increased, while the α band activity did not change much (Fig. 16c). These trends during rest are different from the trends during monofilament stimulation.

2.4. Discussion

2.4.1 Feasibility for quantifying the effect of remote vibrotactile noise on EEG activity in response to monofilament stimulation of the index fingertip.

This study demonstrated the feasibility for quantifying the effect of remote vibrotactile noise on EEG activity in response to monofilament stimulation of the index fingertip. Specifically, the peak-to-peak ERP amplitude in response to the monofilament stimulation and PSD at different frequency bands in response to the monofilament stimulation and during rest with and without vibrotactile noise were quantified. These variables showed changes with remote noise in the single subject examined in this study.

Specifically, for this one subject, the peak-to-peak ERP amplitude in response to the monofilament stimulation of the index fingertip pad seemed to be increased with 60% noise. In addition, θ and β band activities increased while α band activity decreased. If these trends were found in a greater sample, they could be interpreted to indicate increased brain activity in response to the monofilament stimulation of the index finger with noise, as well as strengthened sensory feedback (Pfurtscheller et al., 1996) and sensorimotor information processing (Baker, 2007) and integration (Cruikshank et al., 2012) (based on the β, α, and θ band activity, respectively).

When the remote noise had an intensity of 80% of the sensory threshold, conflicting results were obtained. Specifically, with 80% noise, the peak-to-peak ERP amplitude tended to decrease compared to no noise, indicating reduced brain activity. Negative changes in the α band activity was observed in terms of sensorimotor information processing (Baker, 2007), while no apparent change was observed in the θ band and positive change was observed in the β band activity, in terms of sensorimotor information integration (Cruikshank et al., 2012) and sensory feedback (Pfurtscheller et al., 1996), respectively. Thus, more subjects need to be assessed to determine the effect of remote vibrotactile noise at 80% of the sensory threshold.

Remote noise at 120% of the sensory threshold had overall negative changes in the brain activity. With 120% noise, the peak-to-peak ERP amplitude decreased compared to no noise, indicating reduced brain activity in this on participant. In addition, changes in all three band activities indicated weakened sensorimotor information integration (Cruikshank et al., 2012) and processing (Baker, 2007), and sensory feedback (Pfurtscheller et al., 1996) (based on the θ, α, and β band activity, respectively).

Such a trend of the benefit with 60% noise and the adverse effect of 120% noise in this one subject is similar with Aim 1 and other previous studies (Wells et al., 2005), although these results need to be interpreted with caution. Subthreshold 60% noise may be more effective in influencing the brain activity than 80% noise, and suprathreshold 120% noise may have negative impact on the brain activity in response to tactile stimulation as explained by the masking effect in the previous study (Collins et al., 1997). Future study will be required to test the hypothesis that brain activity positively changes with remote subthreshold noise, while suprathreshold remote vibrotactile noise has a negative effect on the sensorimotor cortex activity in response to tactile stimulation of the fingertip.

2.4.2 Effect of remote noise for sensing fingertip stimuli vs. effect of noise itself

Changes in the PSD with the remote noise were inconsistent between when the fingertip was stimulated by the monofilament and when the fingertip was at rest (not touched by the monofilament) (Figure 16). Consistency across multiple subjects through more data collection needs to be demonstrated to confirm such a trend. If the trend is observed consistently across multiple subjects, it may imply that the changes in the brain activity with the remote noise were related to sensing fingertip tactile stimuli, not the noise itself.

2.4.3 Limitations/Future directions

Since this study demonstrated that EEG can be used to detect changes in the brain activity induced by application of remote noise, more subjects will need to be tested in the future to address the long-term goal of investigating the effect of remote vibrotactile noise on the EEG activity in the somatosensory cortex in response to fingertip stimulation. The present study used a random time interval of 1 to 2 seconds between consecutive monofilament touches. This time interval may increase to 2-3 seconds, because brain activity may be inhibited 1.5 to 2 seconds after tactile stimulation (Pfurtscheller et al., 2001). In the present study, the exact timing of the monofilament touch was estimated based on when the computer generated a signal to the motor of the monofilament stimulation device and the typical time it takes for the monofilament stimulation device to move and touch the fingertip pad. The present study's apparatus may be improved by implementing a device that specifically measures when the monofilament touches the fingertip pad, using different sensors.

Additional analyses such as latency of ERP (Ballesteros et al., 2009) may be performed in case remote noise facilitates early detection of tactile signals. The effect of remote noise on the brain activity in young healthy adults may need to be further investigated depending on the hand dominance, because the brain activity tends to be larger when tactile stimulation is applied to the right dominant hand than to the left non-dominant hand (Pfurtscheller et al., 2001).

2.5. Conclusion

This study demonstrated the feasibility for quantifying the effect of remote vibrotactile noise on EEG activity in response to monofilament stimulation of the index fingertip. In one subject, the 60% subthreshold, but not 120% suprathreshold, vibrotactile noise at the dorsum hand positively changed the activity of the somatosensory cortex hand area in response to fingertip stimulation, with increased peak-to-peak event-related potential, increased β and θ band activity, and decreased α band activity, which are associated with greater brain activity, strengthened sensation/sensory feedback and sensorimotor information integration and processing, respectively. Changes in the brain activity in response to the tactile stimulation of the fingertip pad with remote noise would indicate integration of the signal (stimulation) and remote noise occurred at or before the cortex. The positive changes in the brain activity seen with the remote subthreshold noise at 60% of the sensory threshold may encourage use of subthreshold remote noise in enhancing cortical activity related to sensing fingertip stimuli.

CONCLUSIONS

The objectives of this thesis were to elucidate the effect of remote vibrotactile noise on hand motor control (Aim 1) and to demonstrate feasibility for quantifying the effect of remote vibrotactile noise on EEG activity (Aim 2). This thesis demonstrated that the remote vibrotactile noise had little effect on young healthy people's ability to maintain a target pinch force without visual feedback. This thesis also showed that EEG could be used to detect changes in the somatosensory cortex activity with remote vibrotactile noise.

Specifically, for Aim 1, remote subthreshold vibrotactile noise at 60% of the sensory threshold was observed to only slightly improve the ability to maintain low pinch force, while the 80% noise did not change the low pinch force maintenance accuracy and the 120% suprathreshold noise was observed to degrade low pinch force maintenance accuracy (5% of maximum pinch force) in young healthy adults. A potential reason for the lack of the noise effect could be that the pinch force maintenance task involved strong tactile signals whose detection could not be helped with noise, or that healthy young adults were already performing the pinch force maintenance task optimally with good tactile sensation and motor control ability, with little room for further improvement with enhanced tactile sensation.

Interestingly, while tactile sensory manipulation such as adding bandages on the fingertips affected the pinch force maintenance accuracy at the low pinch force level (5% of the maximum pinch force), at the high pinch force level (20% of the maximum pinch force, tactile sensory manipulation, even the bandages did not affect the pinch force maintenance accuracy. Specifically, at the high pinch force level, pinch force error was similar for pinching with the bandaged fingers, pinching with remote vibrotactile noise at all intensities, and normal pinching. Furthermore, this invariant pinch force error with tactile sensory manipulation at the high pinch force level was similar with the pinch force error for the bandage condition at the low pinch force level. Since the bandages were supposed to simulate a condition where tactile sensation does not provide proper information, it can be said that tactile sensation may not have been useful during the high pinch force maintenance as well as the bandaged condition at the low pinch force maintenance. The potential reason that tactile sensation may not have been useful during the high pinch force maintenance may be that mechanoreceptors have been overloaded with high force on the fingertip pads and may not have been able to detect small changes in pinch force. People may have relied on other sensory modalities for force maintenance such as proprioception (Gentilucci et al., 1994).

For Aim 2, EEG could detect the changes in the somatosensory cortex activity in response to tactile stimulation at the fingertip pad with remote vibrotactile noise.

Specifically, the EEG analysis was able to determine the peak-to-peak ERP amplitude and β, θ, and α band activities in PSD for each remote noise condition. These four variables were the focus of in this EEG analysis because they are associated with the magnitude of brain activity, sensation/sensory feedback, sensorimotor information integration, and sensorimotor information processing (Baker, 2007; Cruikshank et al., 2012; Pfurtscheller et al., 1996).

In one subject, the 60% subthreshold, but not 80% and 120%, vibrotactile noise at the dorsum hand positively changed the activity of the somatosensory cortex hand area in response to fingertip stimulation, with an increased peak-to-peak event-related potential, increased β and θ band activity, and decreased α band activity, which are associated with greater brain activity, strengthened sensation/sensory feedback, sensorimotor information integration, and sensorimotor information processing, respectively (Baker, 2007; Cruikshank et al., 2012; Pfurtscheller et al., 1996). Changes in the brain activity in response to the tactile stimulation of the fingertip pad with remote noise in a larger sample of participants would indicate integration of the signal (fingertip stimulation) and remote noise in the central nervous system. The positive changes in the brain activity seen with the remote subthreshold noise at 60% of the sensory threshold may encourage continued data collection to confirm these results.

In both Aim 1 and Aim 2, 60% noise appeared to be better than 80% and 120% noise, and 120% noise appeared to make matters worse, although these trends were not significant. In Aim 1, 60% noise marginally improved the low pinch force maintenance accuracy, compared to pinching without noise, whereas 80% noise did not affect the accuracy and 120% worsened the accuracy compared to normal pinching without noise. In Aim 2, 60% noise positively changed the somatosensory cortex activity with an increased ERP, increased β and θ band activity, and decreased α band activity, while 80% noise did not have a consistent effect on the EEG activity and 120% noise negatively changed the EEG activity. Such a trend for the effect of the *remote* noise intensity is consistent with the previous findings in stochastic resonance with *direct* noise in which there is an optimal level of noise, while excessive noise was thought to overwhelm the signal. Therefore, future studies with remote noise may utilize remote vibrotactile noise at the wrist and dorsal hand with the intensity of 60% of the sensory threshold to influence brain activity for perceiving fingertip touch sensation or to influence hand motor performance in healthy young adults.

This thesis represents initial investigation on the effect of remote vibrotactile noise. The results of this thesis may guide future studies in investigating the use of remote noise for influencing motor performance involving low force levels and in investigating evidence for integration of signal and remote noise in humans using EEG.

The remote noise could be useful for rehabilitation applications in the future, for those with sensorimotor deficit such as the elderly (Cole & Beck, 1994; Gescheider et al., 1994) and stroke survivors (Carey & Matyas, 2011; Hermsdorfer et al., 2003). There is a device already developed to apply *direct* noise to the fingertip to enhance tactile sensation and motor performance in healthy adults (Kurita et al., 2011). However, noise generators attached around the finger can interfere with hand-object manipulation and hand function in daily life. A noise-generating device away from the fingertips that still improves sensation would be more practical than having the device right by the fingertips to not interfere with typical daily activities with the hands. However, in order for the remote noise to be adopted for rehabilitation applications, its impact in the elderly and patient populations needs to be further examined. This thesis provides examples for methods and some preliminary findings in healthy adults that could be exploited by future studies in investigating the effect of remote noise and developing a novel rehabilitation engineering technique. For instance, use of the EEG technique to improve understanding of the mechanism behind sensory enhancement with remote subthreshold noise may help guide its clinical application. If use of the EEG technique demonstrates the signal and noise integration in the central nervous system in healthy young adults, this knowledge can be applied to other subject populations of interest for specific assistive purposes for sensing and signal detection.

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