ABSTRACT

Title of Document: INTEGRATION OF INTRA-AUDITORY
                                                 MODALITIES FOR THE ENHANCEMENT
                                                  OF MOTOR PERFORMANCE AND
                                                 COORDINATION IN A CONSTANT FORCE
                                                 PRODUCTION TASK

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One of most fundamental problems in the field of neuromechanics is to understand

how the central nervous system (CNS) integrates multiple sources of sensory

information and coordinates multiple effectors in human movement. Much attention

has been directed to the integration of multiple modalities between sensory organs

(e.g., visual and auditory, visual and tactile, or visual and proprioceptor), while little

is known about the integration of multiple modalities within one sensory (i.e., intra-

sensory integration), especially regarding the auditory sensory. This dissertation

investigated the mechanisms of intra-auditory integration for the control of multiple

fingers during constant force production tasks, specifically regarding how the CNS

utilizes multiple sources in auditory feedback, how the CNS deals with uncertainty in

auditory feedback, and how the CNS adapts or learns a motor task using auditory

feedback. The specific aims of this dissertation included: 1) development of analytical

tools for the quantification of motor performance and coordination in a hierarchical

structure of motor variability; 2) investigation into the effect of intra-auditory integration on motor performance and coordination (Experiment I); 3) investigation of the role of uncertainty in auditory information on the effectiveness of intra-auditory integration in motor performance and coordination (Experiment II); and 4) investigation of the auditory-motor learning in the context of motor performance and coordination (Experiment III). Results from Experiments I & II have indicated that the CNS can integrate frequency and intensity of auditory information to enhance motor performance and coordination among fingers. Intra-auditory integration was found to be most effective when uncertainty in auditory feedback was moderate between two extreme levels of uncertainty (low and high uncertainty). Results from Experiment III indicate that practice leads to the enhancement of performance by reducing individual finger variability without changes in inter-finger coordination. Further, the enhancement of performance and coordination after practice was specific to the intra-auditory modality that was available during practice. This dissertation discusses the mechanisms responsible for the changes in motor performance and coordination with auditory feedback and directions for future research are suggested.

INTEGRATION OF INTRA-AUDITORY MODALITIES FOR ENHANCEMENT
OF MOTOR PERFORMANCE AND COORDINATION IN A CONSTANT
FORCE PRODUCTION TASK

By

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auditory modality not provided (F group; $p=0.011$ and I group; $p=0.041$) when F condition was compared to I condition. *OMSE* with bimodal (FI condition) was significantly lower as compared to the auditory modality not provided through practice (F group; $p=0.037$ and I group; $p=0.003$), but not significantly different as compared to the auditory modality provided (F group; $p=0.764$ and I group; $p=0.523$) (upper left panel). In FI group, FI condition was significantly lower than either F only ($p=0.004$) or I only condition ($p=0.039$). There were no significant differences between F and I conditions ($p=0.742$). Using the HVD model, the changes in *OMSE* as a function of auditory modalities was mainly caused by the changes in VE_{OFF}. Post-hoc tests revealed that VE_{OFF} in both F and I groups were significantly lower with the auditory modality provided through practice as compared to the auditory modality not provided (F group; $p=0.008$ and I group; $p=0.048$). VE_{OFF} with bimodal (FI condition) was significantly lower as compared to the auditory modality not provided through practice (F group; $p=0.008$ and I group; $p=0.003$), but not significantly different as compared to the auditory modality provided (F group; $p=0.862$ and I group; $p=0.677$) (lower right panel). VE_{OFF} in FI group was significantly lower with the auditory modality provided through practice as compared to the auditory modality not provided (F vs FI condition; $p<0.001$ and I vs FI condition; $p=0.007$). There was no significant difference between F and I condition ($p=0.227$). The asterisk indicates the significant level (* $p<0.05$ and ** $p<0.01$). Error bars represent s.e.m. across subjects. 104

Chapter 1: Introduction

1.1 Motivation for the study

Visual impairment is a substantially limiting disability, affecting tens of millions of individuals in daily activities (e.g., limitations in performing tasks that need a level of detail, challenges in mobility, and difficulties in recognizing people and objects) [1]. There has been a considerable interest in visual rehabilitation using sensory substitution which is a technique to enable the blind to see using other senses [2-4]. For example, the blind and visually impaired individuals can perceive and interact with their environment using auditory information to convey visual information by systematically converting properties of vision (e.g., luminance, vertical and horizontal position of an object) into auditory properties (e.g., frequency and intensity). However, the mechanism of how the brain perceives & combines these auditory properties and how it learns to utilize them in relation to movement production has remained unanswered.

1.2 Problem Statement

During activities of daily life, the central nervous system (CNS) receives multiple source of information gathered by within one sense organ (e.g., color and shape of an object, frequency and intensity of sound, etc.) or between sense organs (e.g., visual, auditory, tactile, etc.) and sends appropriate motor commands to multiple effectors (e.g., muscles, joints, limbs, etc.) to generate the desired motor outcomes. In

this process, the CNS faces at least two challenges. First, the CNS must be able to incorporate the multiple inputs from the sensory organs for the understanding of the states of the external world and internal body. Our senses, however, provide imperfect information corrupted by intrinsic noise, leading to uncertainty in the estimate of the state. Thus, the CNS must be able to construct an accurate representation of the external world from noisy sensory signals [5]. Second, the CNS has to coordinate multiple effectors involved in achieving the motor outcomes. The musculoskeletal system usually has more effectors than what is required to perform a given motor action. In other words, any action or movement can be executed in infinite number of ways using different combination of effectors, which is commonly known as motor redundancy problem in motor control [6]. Thus, the CNS must select a particular solution among infinite number of solutions to achieve a motor task.

In the field of motor control, one of the fundamental questions the field is endeavored to investigate is how the CNS integrates signals from the multiple sensory modalities and how the CNS coordinates multiple motor effectors. Previous studies have investigated how the CNS integrates multiple sensory inputs and coordinates multiple motor outputs in the notions of multi-sensory integration [7-15] and motor synergies [16-19], respectively. Multi-sensory integration studies suggested that two independent sources of sensory information could be integrated (i.e., bimodal sensory integration) in statistically optimal fashion by minimizing uncertainty of individual sensory information, leading to the enhancement of motor performance. Previous studies on motor synergy have also provided considerable evidence that the CNS exploits the redundant degrees of freedom found in the motor system in order to

produce robust motor performance. However, our current knowledge is limited regarding how multiple sensory modalities especially multiple modalities in auditory system are integrated by the CNS and how the integration process influences motor performance[1], coordination[2] of multiple effectors, and learning of a motor task. The purpose of this dissertation is to investigate the effects of integration of intensity and frequency of auditory signals on motor performance of constant finger force production, coordination of multiple effectors, and adaptation through the motor learning process

1.2 Specific Aims, and Hypotheses

Specific Aim 1: To develop analytical techniques for quantification of motor performance and coordination in a hierarchical structure of motor variability.

The variability of motor outputs is often used to quantify motor performance for the accuracy and precision by means of systematic error and variable error [20] quantification. For a motor task involving a redundant motor system, uncontrolled manifold analysis has been used to measure synergistic interactions between motor effectors. The analysis of the motor synergy provides a means to investigate how the CNS resolves the redundancy problem in the motor system. The motor synergy is typically calculated as the ratio of variability in task-relevant space and in task-

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[1] In this dissertation, motor performance is defined in terms of accuracy and precision in motor outcomes in a goal-directed task. For example, in a multi-finger constant force production task, motor performance is measured by the deviation of a virtual finger force (VF force; sum of individual finger (IF) forces) from a target force, which is decomposed into accuracy and precision components.

[2] Motor coordination is defined as the patterns of multiple effectors in order to improve motor performance. In a constant force production, motor coordination can be measured by variation of IF forces and co-variation among IF forces.

irrelevant space [21, 22]. Many previous studies analyzed the motor synergy across multiple trials [16-19] while other studies investigated the motor synergy over time or within a trial [23, 24]. However, to my knowledge, an analytical tool that can allow trial-to-trial variability quantification, within-trial variability quantification, and motor synergy through a systematic decomposition of the variability in the motor outputs is missing. Specific Aim 1 therefore develops a novel analytical framework for the quantification of motor performance in both online (within trial) and offline (between trial) controls, in terms of accuracy and precision, along with the motor coordination of a multi-effector in a redundant motor system.

Specific Aim 2: To investigate the effect of intra-auditory integration on motor performance and coordination during a constant force production.

Humans integrate multiple sources of sensory information to estimate the state of the body and environment. Several empirical studies have shown that sensory information is integrated in a statistically optimal (i.e., minimum-variance) fashion following the Bayesian model [10, 25]. Much attention has been directed to the integration of multiple source of information between sensory organs (e.g., visual and auditory, visual and tactile, or visual and proprioceptor), or the movement at the task goal (e.g., the position of finger-tip for reaching movement). Little is known about how the CNS utilizes multiple sources within one sensory, especially auditory system (i.e., intra-auditory integration) to coordinate multiple effectors (i.e., coordination) for successful completion of a motor task (i.e., performance). Specific Aim 2 therefore

investigates the effect of intra-auditory integration on motor performance and coordination.

Hypothesis 1: Intra-auditory integration would enhance motor performance during a constant force production.

The Bayesian approach [10, 11, 25-27] to sensory integration is one of successful modeling in how humans integrate multiple sensory modalities. The Bayesian model suggests that the CNS integrates multiple modalities to enhance motor performance. According to the Bayesian model, motor performance of a constant force production task would be enhanced with the combined auditory feedback of two modalities (i.e., frequency and intensity) as compared to frequency only or intensity only feedback.

Hypothesis 2: Intra-auditory integration would enhance motor coordination during a constant force production.

Multi-finger coordination has been quantified as two aspects of motor variability: one in the task-relevant space which affects motor performance and one in the task-irrelevant space which does not [21, 22]. The ratio of these two variabilities has been used as index of multi-finger synergy. Previous studies [22, 24] have showed that the removal of one sensory feedback from combined visual and tactile feedbacks was associated with deterioration in multi-finger synergy. In other words, when combined visual and tactile information was provided, the index of motor synergy increases. Based on the findings in the previous study, multi-finger synergy will increase with the combined auditory feedback of two modalities (i.e., frequency and intensity) as compared to frequency only or intensity only feedback.

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Specific Aim 3: To investigate the role of uncertainty in auditory feedbacks on the effectiveness of intra-auditory integration.

The central nervous system (CNS) receives defective afferent signals from the sensory system and sends imperfect efferent signals to the motor system. Both signals are corrupted by intrinsic and extrinsic noises, leading to uncertainty in sensorimotor control [28]. Much attention has been directed to the mechanisms of how the CNS deals with uncertainty in sensorimotor control in tasks such as the reaching for and grasping of an object [29, 30]. However, little is known about the role of uncertainty in auditory-motor control on the integration of multiple modalities (i.e., intra-auditory integration). Specific Aim 3 therefore investigates the integration the role of uncertainty in auditor information on the effectiveness of intra-auditory integration in motor performance and coordination.

Hypothesis: intra-auditory integration would enhance motor performance for all levels of uncertainty in auditory feedback, following the Bayesian model.

In chapter 3, we found that the intra-auditory integration led to the enhancement of motor performance quantified as accuracy and precision. The enhancement of performance was found in the improvement of the precision while the accuracy of performance remains unchanged, following the Bayesian model. According to the Bayesian model, the precision of performance with a bimodal feedback would be predicted as the linear summation of the precisions with unimodal feedback. Therefore, intra-auditory integration would enhance motor performance for all levels of uncertainty in auditory feedback, following the Bayesian model.

Specific Aim 4: To investigate the auditory-motor learning in the context of performance and coordination during a constant force production.

Sensorimotor learning is one of fundamental capabilities in human movements, referred as to enhancement of motor performance through practice in sensory-guided motor task. Despite of the fact that auditory information is one of dominant sensory playing a critical role on sensorimotor learning, little is known about how multiple modalities in auditory information influence motor performance and coordination through practice. Specific aim 4 therefore investigates the effect of intra-auditory learning in the context of performance and coordination.

Hypothesis1: the enhancement of performance and coordination after practice would be specific to the intra-auditory modality that was available during practice.

It has been proposed that the sensorimotor learning is achieved through sensory-modality-specific practice which has been known as the specificity of learning hypothesis [31]. For example, in an early study of Adams et. al., (1972) [31, 32], the performance of a reaching task was enhanced with sensory information available through practice, whereas changing the sensory information for the transfer test caused deterioration in motor performance. Even in the recent study by Ronsse et. al., (2010) [33], it was found that neural activities increased in sensory-specific areas during practice using functional magnetic resonance imaging, supporting as the specificity of learning hypothesis. Based on the specificity of learning hypothesis, the enhancement of performance and coordination after practice would be specific to the intra-auditory modality that was available during practice.

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Hypothesis 2: practice leads to the enhancement of performance by reducing individual finger variability without changes in inter-finger coordination.

Another view of the sensorimotor learning is from Bernstein who postulated the redundancy problem which states that there are multiple ways to perform a particular task in order to achieve the goal-equivalent motor outcomes in human movement [6]. He suggested that in early stages of learning, the CNS tends to freeze or eliminate the redundant degrees of freedom (DOFs) in order to simplify the redundancy problem and find a unique solution, known as freezing hypothesis of motor learning [34]. Previous studies showed that variability of joint angles in a reaching task [35-37] and multi-finger forces in a pressing task [38] deceased, supporting the freezing hypothesis. According to the freezing-freeing hypothesis, practice leads to the enhancement of performance by reducing individual finger variability without changes in inter-finger coordination.

1.3 Dissertation organization

This dissertation is organized into seven chapters. The first two chapters elaborate the problem statement and literature review to justify the current research. This is followed by the four experiments, each corresponding to a specific aim, presented in Chapter 3 to 6. The experimental setup for all the studies is designed so that the biomechanical factors involved during the pressing task remain unaltered while auditory feedback was manipulated. Thus, any changes in the dependent

variables could be attributed to the changes in the motor commands emanating from the central nervous system due to the changes in auditory feedbacks.

Chapter 1 serves as an introduction to the research problems. The significance of the research is demonstrated. Four specific aims are proposed from the perspective of novel analytic technique, intra-auditory integration, the role of uncertainty in auditory feedbacks and auditory-motor learning, respectively. Chapter 2 elaborates mainly the sensory and the motor systems. In the sensory system, biological mechanisms behind multiple sensory information and theoretical frameworks to describe how the brain combines the multiple sensory information. Also, it briefly describes auditory system and some independent properties of auditory system. In the motor system, the control mechanisms of multiple effectors in redundant neuromuscular system are presented, along with the some analytic models to explain the control mechanisms. Chapter 3 reports development of an analytical technique for decomposition of motor variability into motor performance and coordination components in a hierarchical structure. Chapter 4 investigates the effect of intra-auditory integration on motor performance and coordination. Chapter 5 investigates the role of uncertainty in auditory feedbacks on the effectiveness of intra-auditory integration in the context of motor performance and coordination. Chapter 6 investigates the auditory-motor learning in the context of performance and coordination. Chapter 7 contains general discussion and future studies for the continuations of this dissertation.

Chapter 2: Literature review

2.1 Multi-input and multi- output (MIMO) system of human

While interacting with the natural world, we, humans, obtain different sensory information from the world in order to guide us through it. In other words, the central nervous system (CNS) simultaneously receives multiple sources of sensory information from various receptors via afferent neurons, and sends appropriate motor commands to multiple effectors (e.g., muscles, joints, or limbs) via efferent neurons. This type of motor control system is multi-input and multi-output (MIMO) system in closed-loop (Figure 2.1). Much research has been conducted to understand how the CNS integrates multiple sensory modalities and coordinates multiple motor effectors in the notion of sensory integration and motor synergy, respectively. In this chapter, I will mainly review the research about integration of multiple sensory modalities and coordination of multiple effectors to achieve a desired movement.
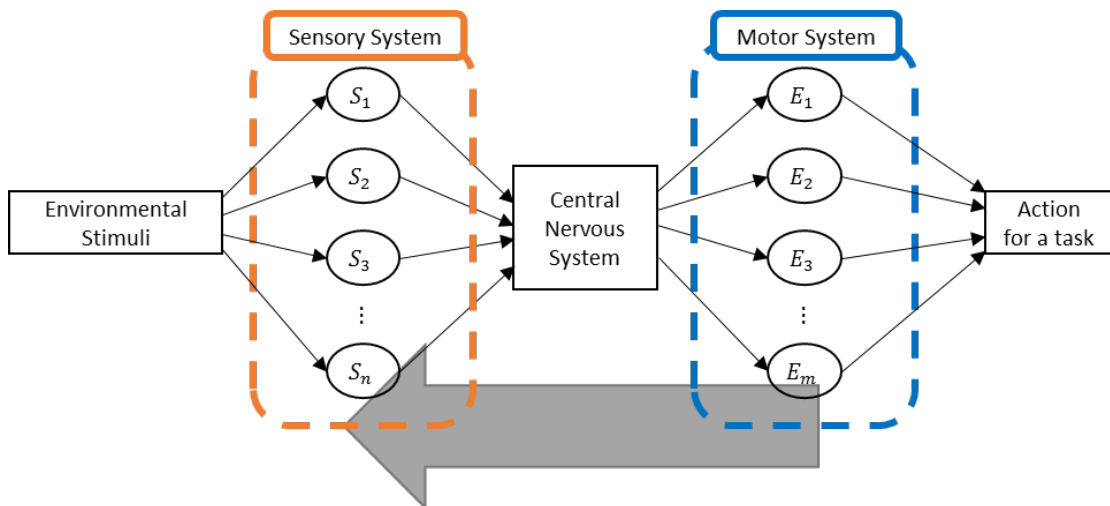
Figure 2.1. Schematic diagram of MIMO system of human. The central nervous system receives multiple modalities in the sensory system, S and sends appropriate motor commands to multiple effectors, E. An action executed by multiple effectors interacts with the environment, which is perceived by the sensory system.

2.2 Perception mechanism for multiple inputs in the sensory system

2.2.1 Inter-sensory integration

Inter-sensory integration is the integration of multiple sources of sensory information gathered by different modalities such as visual, auditory, tactile, or proprioceptors. Most of the early demonstrations of inter-sensory integration were described as perceptual illusions and the McGurk effect can certainly be regarded as belonging to the most impressive ones. McGurk and MacDonald (1976) [39] asked children and adult observers to repeat what an audiovisually presented speaker said. Unbeknownst to the participants, visual (lip movement) and auditory information were discrepant. Interestingly, nearly all adults (98%) and 80% of the children reported hearing /da-da/ when viewing the utterance /ga-ga/ while hearing /ba-ba/. Thus, visual and auditory information were merged into a combined percept, leading to inter-sensory integration. This effect was found to be very robust and also occurred with different pairings of visual and auditory information [40]. A second inter-sensory phenomenon that has received a considerable amount of attention is the Ventriloquism effect, which refers to the perception of speech sounds as coming from a direction other than their true direction due to the influence of visual stimuli from an apparent speaker. When you watch a movie in the theater, you perceive that the actor's voice comes from his/her mouse on the screen even though the speaker located at the side of the screen generates the sound of voice. Howard and Templeton (1966) [41] found that this phenomenon in which auditory location perception is shifted toward a visual information. Last inter-sensory phenomenon is redundant signal effect [42]. This effect characterizes an acceleration of response times to a

signal that is presented simultaneously in two modalities as compared to each single modality. Originally, it was tried to explain this phenomenon by the so-called race model. This model assumes that several modalities produce independent activations, with the faster activation triggering the motor response [43]. However, several studies clearly demonstrated that multimodal responses were faster than predicted by the race model [44, 45]. Thus, several modalities seem to be processed interactively rather than independently.

2.2.2 Intra-sensory integration

Sensory integration does not only occur between modalities. Such processes are also highly relevant for combining information within one modality. With respect to such intra-sensory integration, the largest amount of research was conducted on visual depth perception. Humans are extraordinarily capable of estimating distances and dimensions of objects in their proximal space to allow for an efficient interaction with them. This capability is particularly surprising because it relies on a two-dimensional projection of the viewed scene on the retinas of both eyes. Consequently, a vivid depth perception can even be produced by flat pictures [46]. Thus, the question arises how a three-dimensional perception is generated from two dimensional retinal images [47].

A vivid depth perception of an object can be obtained by various visual information such as size, texture, or slant of the object [48]. Much research has been investigated to explain this construction of depth perception by using those information so-called B integration. These cues can be roughly partitioned into (1) pictorial depth cues, such as perspective, texture gradient and shading, (2)

stereoscopic (i.e., disparity) and ocular depth cues, and (3) motion-induced depth cues that either result from an observer movement (i.e., motion parallax) or an animation of the viewed scene. In the previous studies, the subject judged the depth of an object without noticing the individual cue information. The subject perceived a unitary depth perception and not a fractionated pattern of multiple depth estimates. Thus, our sensory system apparently integrates several cues that encode spatial depth [49]. The advantages of such integration are very similar to the inter-sensory integration case. The combined estimate utilizes all information that is present in a given scene to disambiguate single cues as well as to enhance the reliability of the combined percept [50].

2.3 Theoretical model for sensory integration: the Bayesian sensory integration

The Bayesian probability model is one of the successful models to interpret the phenomenon of sensory integration described above. The Bayesian probability model provides a normative framework for modeling how individuals combine multiple sensory modalities to enhance motor performance [10, 25, 27, 51]. To illustrate this Bayesian integration scheme, individuals produce a constant pressing force of 10 N using four fingers in one hand while the desired force and the produced force as auditory information such as frequency (F) and intensity (I). Motor performance quantified as the deviation of the force being produced from the target during the motor task depends on an ability to estimate the target force. Using the

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Bayesian model, the posterior distribution, $p(T|F, I)$, which is estimation of the target

force, T using combined auditory information, can be calculated by

$$p(T|F, I) = \frac{p(F, I|T)p(T)}{p(F, I)}$$

where $p(F, I|T)$ and $p(T)$ represents the likelihood function and the prior probability

function, respectively. The denominator $p(F, I)$ is independent from the target force,

thus, it is constant and equation can be rewritten as

$$p(T|F, I) \propto p(F, I|T) \cdot p(T)$$

With some assumptions, the posterior probability function $p(T|F, I)$ can be expressed

in the simplified equation. With the first assumption of a uniform prior probability

function $p(T)$, the posterior probability function can be expressed by

$$p(T|F, I) \propto p(F, I|T) = p(F|T) \cdot p(I|T)$$

With the second assumption that the noise of individual estimates is independent and

Gaussian, the posterior equals the Maximum Likelihood Estimate (MLE). That is, the

posterior probability function can be calculated by Gaussian function with the

variance

$$V_{FI} = \frac{V_F + V_I}{V_F \cdot V_I}$$

and the mean

$$\mu_{FI} = \frac{V_I}{V_F \cdot V_I}\mu_F + \frac{V_F}{V_F \cdot V_I}\mu_I$$

where V_F and V_I are the variances, μ_F and μ_I are the means of likelihood functions,

$p(T|F)$ and $p(T|I)$ as shown in Figure 2.2.

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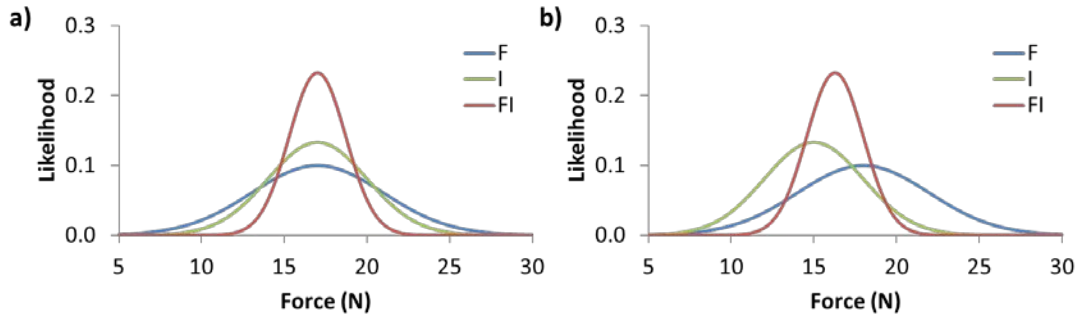
Figure 2.2. Two examples in which frequency, F, and intensity, I, of auditory information provide congruent (a) and incongruent (b) information about the target force T of 18 N. The estimation of the target force with frequency $p(T|F)$ and intensity $p(T|I)$ of auditory information has some variation due to the noise in the sensory system. To integrate frequency and intensity information, multimodal information must take into account the uncertainty associated with each modality. (a) When the frequency and intensity of auditory information provide the same target force (i.e., congruent), the multimodal estimation $p(T|F,I)$ is more precise and the mean of the estimation stays the same as the means of unimodal estimations. (b) When the frequency and the intensity information are incongruent (e.g., frequency and intensity provide the target force of 15N and 18N, respectively), the variance of the multimodal estimation is still more precise but the mean of the estimation is determined by a weighted sum of the estimation (μ) given the frequency (F) and intensity (I) modalities individually: $\mu = w_V \mu_V + w_A \mu_A$. The weights (w) are inversely proportional to the variances of the likelihood functions.

2.4 Auditory system as a candidate for sensory integration

2.4.1 Multiple inputs in auditory system: Frequency and Intensity

Audition is one of the sensory systems playing a crucial role in informing us about the state of our environment. Sound we hear is a pressure wave transmitted through the air, composed of frequencies and intensities within range of hearing from 20 Hz to 10000 Hz. The sound travels through the external canal and middle ear, and creates movement of the fluids inside the cochlear as shown in Figure 2.3. The movement of the fluids causes basilar membrane to vibrate, which leads to firing of hair cells by inflowing potassium. This is the process of conversion of sound waves

into neural impulse called action potential. When we perceive the sound through this process, the independent physical quantities of frequency and intensity of sound as shown in Figure 2.4, are hypothetically though to be transformed into the different neural signals and perceived as the independent physiological quantities of pitch and loudness, respectively.
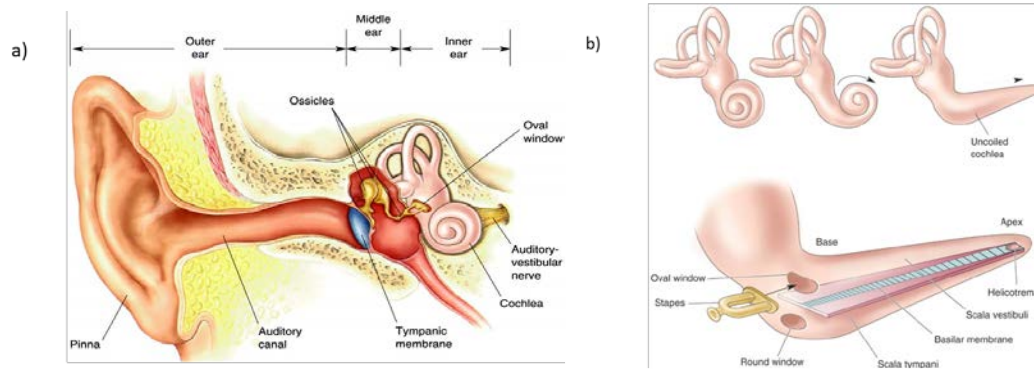
Figure 2.3. The structure of the auditory system (a) and cochlea (b). When a sound in the air travels to our inner ear, it causes the vibration of stapes in oval window. As a result, fluids in the cochlear starts to vibrate, creating the neural impulses in basilar membrane which are transmitted to the brain.
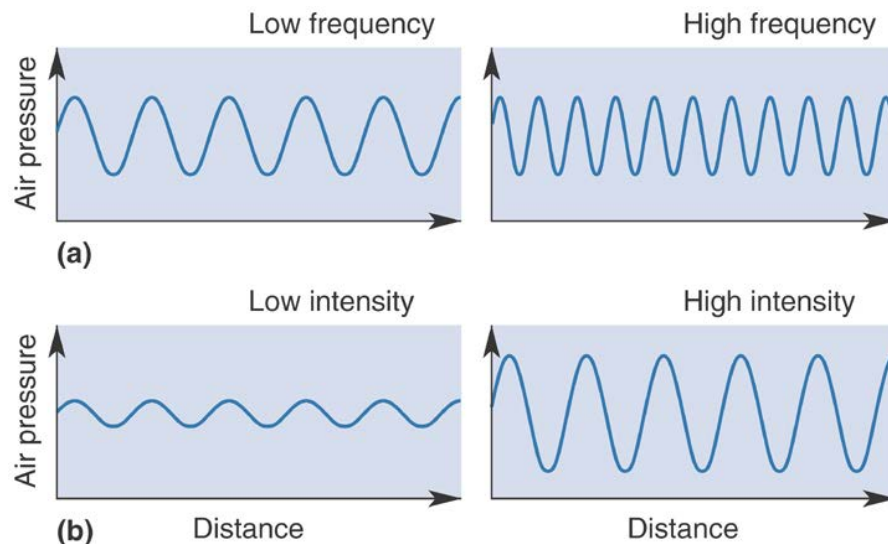
Figure 2.4. Physical properties of sound. A sound signal consists of two independent properties: frequency and intensity.

2.4.2 Perception mechanism of frequency and intensity

There are two theories proposed to explain how we distinguish the frequency of sound (i.e., pitch perception). Hermann Helmholtz [52] proposed place theory which is a theory of pitch perception which states that our perception of the frequency of sound depends on where each component frequency produces vibrations along the basilar membrane. Sensation of a low frequency derives exclusively from the motion of a particular group of hair cells, while the sensation of a high frequency derives from the motion of a different group of hair cells. Each sensation is perfectly identified with the action of an anatomical location along the basilar membrane (Figure 2.5).

Another theory for pitch perception is the temporal theory [53] which states that the frequency of sound is coded by the firing rates in the auditory nerve. In the theory, a low frequency tone causes slow waves of motion in the basilar membrane and that may give rise to low firing rates in the auditory nerve. A high frequency tone causes fast waves of motion in the basilar membrane and that may give rise to high firing rates.
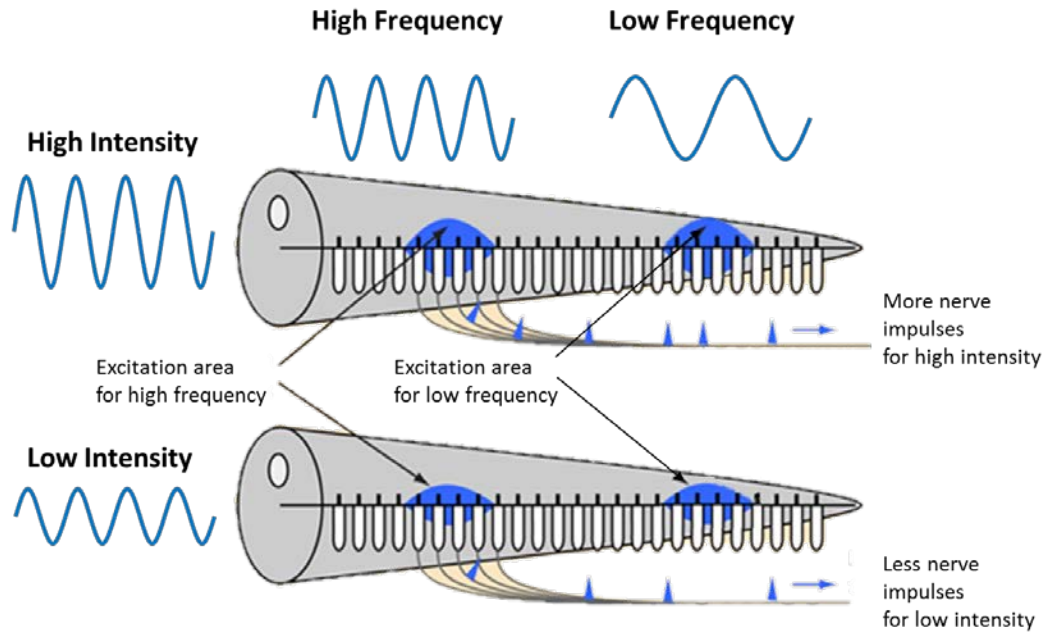
Figure 2.5. Theoretical scheme of the frequency and intensity perception in basilar membrane. The neural response to different frequencies occurs at different location of basilar membrane. A high frequency is responded by afferent neural signals from auditory nerve close to base of basilar membrane while a low frequency is by afferent neural signals from auditory nerve close to apex. The neural response to different intensities determines a number of neural impulses. High intensity creates more nerve impulses while low intensity creates less nerve impulse transmitted to the brain.

Similar to the mechanisms for pitch perception, there are two theories of perception of the intensity similar to the frequency perception. One of theories for the intensity perception is the firing-rate theory which states the rate of firing in the auditory nerve determines the intensity of sound. For low intensity sound, the basilar membrane is displaced little, hair cells are not pushed very far, and there are few spikes in the auditory nerve fibers. Another theory for the intensity perception is "number of neurons" theory. It states more neurons fire to a louder sound. As a traveling wave passes down the basilar membrane, each point of the membrane oscillates at the corresponding frequency of sound. When the sound is weak (low

intensity), displacements are generally quite small and only a small region of the basilar membrane moves sufficiently to evoke spikes. For strong sound intensity, the membrane is displaced by a larger amount, causing evoking spikes even in neighboring nerve fibers.

2.5 Control mechanism for multiple outputs in the motor system

2.5.1 Motor redundancy

The problem of motor redundancy occurs where the number of degree of freedom (DOF) is greater than minimally required DOF for the completion of a certain movement. For example, when you touch your noise with the tip of your right index finger, you may have infinite number of joint-angle configurations without losing the contact between the fingertip and the nose. How does the CNS select a particular joint combination out of infinite feasible solutions?

In the field of motor control, the understanding of how the CNS controls or solves the problem of motor redundancy is one of fundamental problems. In the 1920s, Nikolai Bernstein [6] tried to understand the problem by studying the kinematics of the hitting movements professional blacksmiths used to strike the chisel with the hammer. After training by performing the same movement hundreds of times, he noticed that the variability of the trajectory of the hammer tip across a series of strikes was smaller than the variability of the trajectories of individual joints in the subject's arm. He concluded that the joints did not act independently but corrected each other's errors. This study suggested that the CNS did not try to find a unique

solution for the problem of motor redundancy but rather used the apparently redundant set of joints to ensure more accurate performance of the task. Later, this phenomenon has been studied in the notion of motor synergy and referred to as principle of motor abundance.

2.5.2 Motor synergy

The word "synergy" has originated in Greek and means "work together". The synergy has commonly used in the field of motor control to explain how the CNS solves the problem of motor redundancy. The definition of synergy is that the redundant set of effectors work together to achieve a common goal or a set of given tasks. The synergy consists of three components that can qualitatively be quantified as the term of sharing, error compensation, and task-dependence (Figure 2.6) [54]. First, in terms of sharing, effectors should at least contribute to a particular task to deserve being called a synergy. For example, when you hold an object with hand, your individual fingers must generate a certain amount of force to the object in order to create synergic action between effectors or work together. This sharing typically used as the term *sharing pattern* can be quantified as the percentage of the required grip force produced by individual digits. Second, effectors should compensate each other errors to perform a task properly. In the example of holding the object, imagine that one finger produces more or less than its expected force. Other fingers should compensate it by changing their contributions in order to prevent failure of the task. This error compensation has been widely studied in the notion of kinetic synergy [55-57]. It was found that when subjects performed the multi-finger pressing task over multiple trials, the individual finger forces were co-varied negatively across trials in

order for the task force (i.e., sum of individual finger forces) to be produced constantly. Lastly, task-dependence is the ability of motor synergy to change its functioning in a task-specific way. In other words, the same set of effectors is formed into different synergy when the task is changed. For example, humans can perform variety of task with hands such as typing a text message, writing with a pen or playing a musical instrument. The completion of such different tasks requires the ability of a synergy to change the functional configuration of effectors involved in a task.
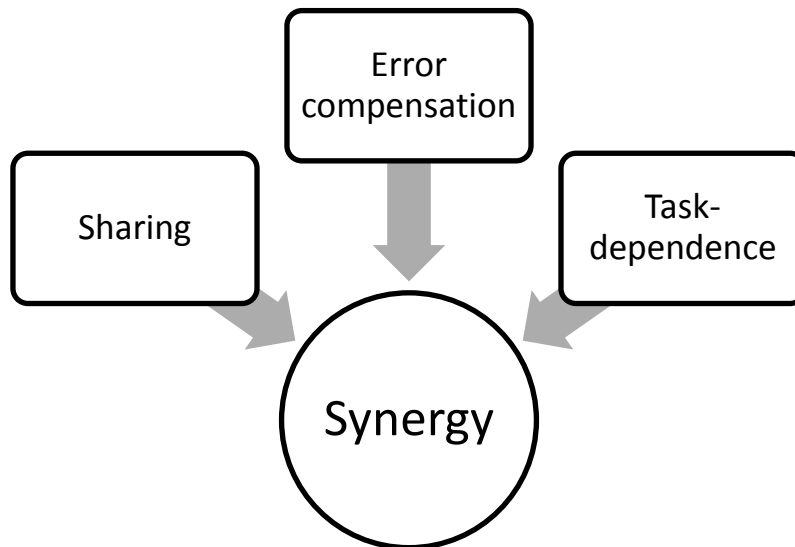
Figure 2.6. The definition of synergy in terms of three components. To deserve being called a synergy, effectors should contribute to a particular task (i.e., sharing), effectors should compensate each other's errors (i.e., error compensation), and the system has ability to change its functioning in a task-specific way (i.e., task-dependence).

2.6 Analytic models for motor synergy

Numerous computational modeling have been suggested to explain neuromuscular mechanisms underlying multi-digit synergy, on the basis of a variety of behavioral and neurophysiological evidence [58-60]. The modeling can be

primarily divided into two approaches. First approach is optimization which states that a movement is executed in a way to optimize implicit biomechanical or physiological goals [61]. The criteria include minimal jerk (the rate of change of acceleration) [62], minimal energy consumption (e.g., squared sum of force, mode, or kinematic variables) [63], minimal entropy function [64] and minimal torque change [65]. Dissimilar to optimization, second approach is to investigate the different aspects of variability in movement. The variability had been considered to errors in motor performance until this approach was proposed. This computational approach to analysis of variability is known as the uncontrolled manifold (UCM) hypothesis and principle component analysis (PCA), which can theoretically quantify one of the synergy components, the error compensation. Two central phenomena of control mechanism in movements have been revealed via these approaches. First, biological systems control their important functions using hierarchically organized multi-level structures. Second, when the CNS faces a problem of redundancy, it does not select a unique solution, but rather facilitate families of solutions that are equally capable of solving the problem without increasing performance error. I will elaborate UCM and PCA in next section.

Although UCM and PCA provide a means to investigate how the CNS resolves the redundancy problems in the motor system, these computational methods are limited in capturing accuracy of motor performance, and also limited in examining the contribution of total amount of errors and motor synergy to motor performance. Thus, combining the computational methods with limited factors

mentioned above would be beneficial to better understand the CNS control mechanisms.

2.6.1 Uncontrolled Manifold Analysis

Scholz and Schöner (1999) developed a quantitative method to analyze variability in movement called uncontrolled manifold (UCM) [21]. UCM provides a new way to quantify the motor variability by decomposing the total variability into the variability which affects performance error and the variability which does not. For example, when you perform 10N production task with index and middle fingers, the finger forces should satisfy a task equation:

$$[1 \quad 1]\begin{bmatrix} f_1 \\ f_2 \end{bmatrix} = 10N$$

Given that both the sensory and the motor systems have intrinsic noise, it is nearly impossible to produce exact 10N. Thus, the demeaned force you produce with two finger tips will have error as follows:

$$[1 \quad 1]\begin{bmatrix} f_1 \\ f_2 \end{bmatrix} = \varepsilon$$

By decomposing individual finger forces into two components satisfying as follows:

$$[1 \quad 1]\begin{bmatrix} f_1 \\ f_2 \end{bmatrix}_{10} = 0, \text{ and } [1 \quad 1]\begin{bmatrix} f_1 \\ f_2 \end{bmatrix}_{\varepsilon} = \varepsilon$$

where

$$\begin{bmatrix} f_1 \\ f_2 \end{bmatrix} = \begin{bmatrix} f_1 \\ f_2 \end{bmatrix}_{10} + \begin{bmatrix} f_1 \\ f_2 \end{bmatrix}_{\varepsilon},$$

we can quantify the force which affects the performance error, $\begin{bmatrix} f_1 \\ f_2 \end{bmatrix}_\varepsilon$, and the force

which does not, $\begin{bmatrix} f_1 \\ f_2 \end{bmatrix}_{10}$. That is, with the changes in the force, $\begin{bmatrix} f_1 \\ f_2 \end{bmatrix}_{10}$, the performance

error, ε, remains the same while the changes in the force, $\begin{bmatrix} f_1 \\ f_2 \end{bmatrix}_{10}$, are directly related

to the performance error, ε. Assume that individual finger forces are distributed as

black dots shown in Figure 2.7. By projecting the force data onto UCM coordinates

(note that UCM coordinates are defined by the subspace parallel to the task equation

so-called UCM space and the subspace orthogonal to UCM space), two force

variabilities mentioned above can be calculated.
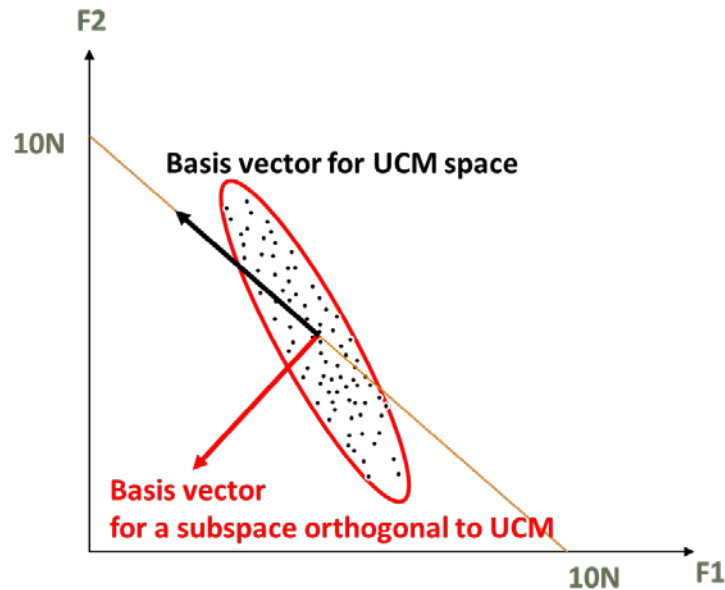
Figure 2.7. Illustration for uncontrolled manifold (UCM) hypothesis. UCM is the linear transformation methods by transforming individual finger forces as black dots in force spaces onto UCM space (black arrow) and a subspace orthogonal to UCM (red arrow).

Let the projection of finger force f in the orthogonal space $f_\perp$ and in the UCM (null)

space $f_\parallel$ be defined as:

$$f_\perp = \sum_{i=1}^{n_1} (f_i\, e_i)\, e_i$$

$$f_\parallel = \sum_{i=1}^{n_2} (f_i\, o_i)\, o_i$$

$\{e_i\}, \{o_i\}$ and n_1, n_2 are the bases and dimensions of the orthogonal space and the UCM space, respectively. Note that sum of n_1 and n_2 is the number of total degree of freedom. To quantify the synergy, delta variance (ΔV) which is defined as the difference of variance per degree of freedom in the UCM space and in the orthogonal space, normalized by total variance per degree of freedom has been proposed.

$$\Delta V = \frac{V_{UCM}/n_1 - V_{ORTH}/n_2}{(V_{UCM} + V_{ORTH})/(n_1 + n_2)}$$

where V_{UCM} and V_{ORTH} are the variance of $f_\parallel$ and $f_\perp$, respectively. If ΔV is greater than zero, a synergy is said to exist to stabilize the performance variable; if ΔV is less than zero, the synergy does not exist.

2.6.2 Principle component analysis

Principle component analysis (PCA) has been used to quantify the synergy in field of motor control. PCA is a similar method to UCM since both methods are based on the linear transformation. In other words, both methods are computational approach to analysis of motor variability into new coordinate system each method defines. Main difference between two is the way of determining new coordinate system. The coordinate system of UCM is based on the task equation, but the

coordinate system of PCA is based on the distribution of observed data as shown in Figure 2.8.
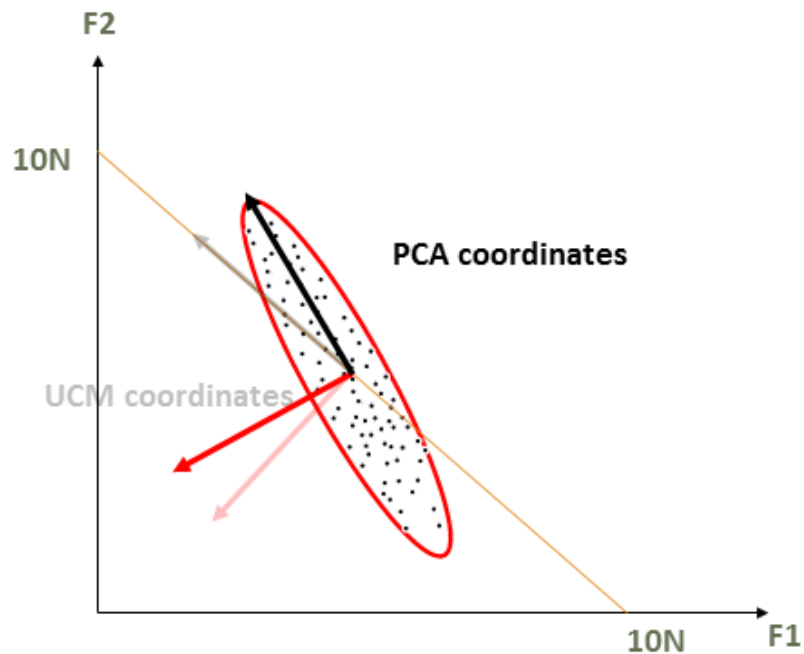
Figure 2.8. Difference between PCA and UCM coordinates. PCA defines the coordinates based on data distribution while UCM defines it based on the task equation.

2.7 Human hands as an example to study on the motor synergy

The human hand is an excellent candidate to study the mechanism of how the CNS controls multiple effectors because of several reasons. First of all, the human hand is one of most redundant parts including many different bones, muscles, and ligaments, allowing for a large amount of fine motor skills and dexterities [66]. Anatomical structure of human hand as shown in Figure 2.9 consists of 27 bones primarily categorized in phalanges, metacarpals and carpals. Phalanges are the 14 bones that are found in the fingers of each hand. According to anatomical locations, phalanges are categorized into three parts: the distal, middle, and proximal for index,

middle, ring, and little fingers and two parts for the thumb. Metacarpal bones consist of 5bones located in the middle part of the hand. Carpal bones are 8 bones connected to two bones of the arm, the ulnar bone and the radius bone.
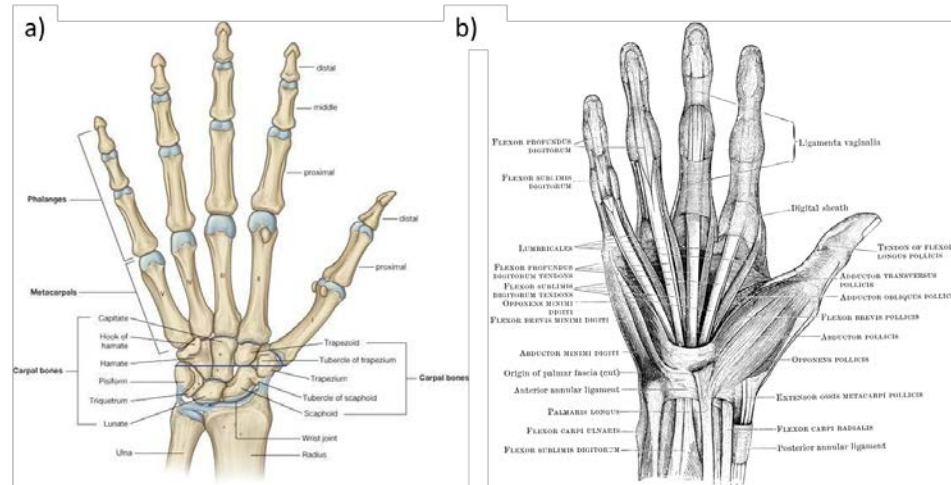
Figure 2.9. Musculoskeletal structure of the hand. The skeleton of the hand consisting of 27 bones (a). The muscular structure of the hand including the muscles and tendons (b).

The movements of the human hand are accomplished by two sets of muscle groups: the extrinsic and intrinsic muscles. The extrinsic muscles are the long flexors and extensors. They are called extrinsic because the muscle belly is located on the forearm. The intrinsic muscle groups are the thenar and hypothenar muscles (thenar referring to the thumb, hypothenar to the small finger), the interosseus muscles (between the metacarpal bones, four dorsally and three volarly) and the lumbrical muscles. These muscles arise from the deep flexor (and are special because they have no bony origin) and insert on the dorsal extensor hood mechanism. In all, 27 bones in the human hand are controlled by 39 muscles. There are many degrees of freedom available for hand motion, yet joint movements are not independent.

Chapter 3: The new analytical technique for motor performance in redundant system: The role of tactile sensation in online and offline hierarchical control of multi-finger force synergy

3.1 Abstract

The hand, one of the most versatile but mechanically redundant parts of the human body, must overcome imperfect motor commands and inherent noise in both the sensory and motor systems in order to produce desired motor actions. For example, it is nearly impossible to produce a perfectly consistent note during a single violin stroke or to produce the exact same note over multiple strokes, which we denote online and offline control, respectively. To overcome these challenges, the central nervous system synergistically integrates multiple sensory modalities and coordinates multiple motor effectors. Among these sensory modalities, tactile sensation plays an important role in manual motor tasks by providing hand-object contact information. The purpose of this study was to investigate the role of tactile feedback in individual finger actions and multi-finger interactions during constant force production tasks. We developed analytical techniques for the linear decomposition of the overall variance in the motor system in both online and offline control. We removed tactile feedback from the fingers and demonstrated that tactile sensors played a critical role in the online control of synergistic interactions between fingers. In contrast, the same sensors did not contribute to offline control. We also demonstrated that when tactile feedback was removed from the fingers, the combined motor output of individual fingers did not change while individual finger behaviors did. This finding supports the idea of hierarchical control where individual fingers at the lower level work together to stabilize the performance of combined motor output at the higher level.

Signals from multiple sensory modalities are independently detected through individual sensory organs, but synergistically integrated by the central nervous system (CNS) to enhance our perception of the state of the body [10, 67]. Using this sensory feedback, the motor system fine-tunes the control of motor effectors, such as multiple fingers, to produce the desired movement outcomes [18, 21, 68, 69]. For example, to produce a constant sound, a violinist's digits holding the bow must work synergistically to impart the desired force on the bow and the necessary vibrations of the strings. This fine tuning of motor effector control can be used to generate consistent task performance during a single violin stroke (moment-to-moment control which we denote online control), or to produce the same performance, the exact same note, over multiple strokes (trial-to-trial control which we denote offline control) [70].

During a motor task, when discrepancies between the expected and actual motor outputs, detected through sensory systems, the CNS would try to correct the errors by making changes in the motor outputs. For example, when a violinist tries to play a constant sound, but detects a deviation between the sound produced and the sound desired, the violinist will make changes in muscle activation such as adjusting the finger position on the string and/or change the forces being produced on the bow. In a laboratory setting, if a research participant is asked to produce a constant pressing force of 10 N using four fingers in one hand while watching the desired force and the produced force on a computer screen [71], the participant will try to

minimize the deviation of the force being produced from the target force during the motor task.

Human motor tasks typically involve the degrees of freedom (DOFs) in the motor system that outnumbers the number of DOFs minimally required for the execution of the motor task [68, 72, 73]. During the four-finger pressing task mentioned above, the participant needs only one finger to produce 10 N in order to successfully perform the motor task. Nonetheless, there exist three extra DOFs in the motor system [68, 72, 73], which offers an infinite number of finger force combinations to successfully perform the task of producing 10 N force using all four fingers. A large body of literature suggests that the CNS synergistically controls the motor effectors (e.g. fingers, muscles, joints, etc.) when there are redundant DOFs [16, 17, 23, 24]. One of the central features of motor synergy is error compensation between motor effectors [71, 74, 75]. For example, if one finger produces more force than necessary, which causes movement errors during the four-finger pressing task, one or multiple other fingers would reduce forces in order to compensate for the error of the first finger. This phenomenon of error compensation between fingers has been shown to be influenced by visual feedback conditions [24, 76]; however, the role of tactile feedback such as the mechanoreceptors in the finger-tip pads on the phenomenon of error compensation during multi-finger pressing tasks is not well known.

In manipulation tasks with the hand and fingers, tactile afferents provide the CNS with information regarding physical interactions between the hand and the object it is manipulating. The tactile signals generated through these physical

interactions may be used to plan and execute the manipulation task [77]. Recently, our group demonstrated that the maximum finger forces could be reduced by 25% on average when fingertip tactile feedback was eliminated using ring block anesthesia [78]. This study provided evidence that manipulation of tactile feedback affects descending motor commands, reducing maximal muscle contraction even when the physiological properties of the system (e.g. finger muscle mass) are unchanged.

In the current study, we developed analytical techniques for the decomposition of the variance in the motor outputs into online (moment-to-moment) and offline (trial-to-trial) components and investigated the role of tactile feedback in sub-maximal constant finger force production using these techniques. During the experiment, subjects experienced or did not experience the tactile feedback of finger force at the individual finger-tips while the visual feedback of all-finger force sum (virtual finger force) was shown on a computer screen for both tactile conditions (Figure 1). We hypothesized that the removal of tactile feedback would be associated with behavioral changes at the individual finger level, not at the virtual finger level, supporting a hierarchical organization of multi-finger control.
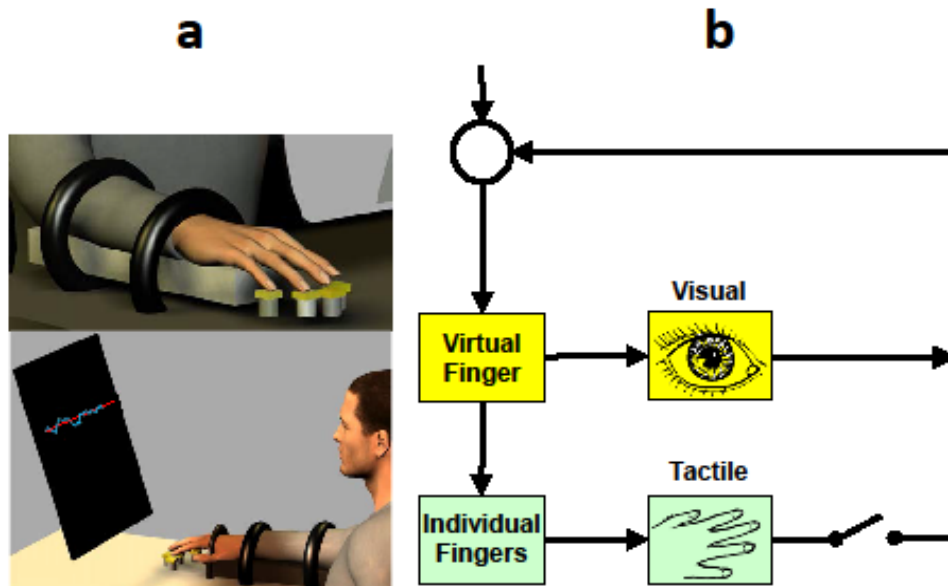
Figure 3.10. The experimental setup (a) and a schematic of the sensory-motor task (b). Subjects were asked to use the 2nd-5th individual fingers (IF) of the right hand, and statically press the force sensors at fingertips while matching the four-finger force sum (i.e., virtual finger (VF) force [79, 80]) to 20N over ten seconds for each of 12 trial. In each trial, the subjects watched a computer screen displaying the target force as a fixed red horizontal line and the VF force as a blue trace flowing from left to right in time. Each subject (n=20) repeated the task for twelve trials for each tactile condition. The motor task therefore required constant time-course (or online) outputs of 20N force in single trials as well as repetitive (or offline) outputs of the same force over multiple trials. The experiment was designed so that the visual feedback could be provided at the VF level and the tactile feedback at the IF level. Other sensory systems are not shown in the schematic.

3.3 Methods

3.3.1 Participants

Eighteen healthy volunteers (sex: males, age: 23.95±1.00 years, body mass: 68.00±5.21 kg, height: 174.67±5.59 cm) with no history of neurological disorders participated in the experiments. All the participants were right handed according to the Edinburgh handedness test criteria. The hand length measured from the middle

finger tip to the lunate of the wrist was 17.2±1.0 cm, and the hand width measured across the metacarpophalangeal (MCP) joints of the index and little fingers was 9.5±0.6 cm. All the participants gave informed consent based on the procedures approved by Korea University of Institutional Review Board.

3.3.2 Experimental Procedures

Subjects were asked to rest the distal phalanges of each of the four fingers of the right hand on force sensors (Models 208 M182 and 484B, Piezotronics, Inc., Depew, NY) (Figure 1), such that all joints were slightly flexed and the hand formed a dome shape. To minimize tactile feedback from the cutaneous receptors in the palm, neither the palmar surface nor the fingers were physically restrained. Additional details of the experimental set up is described elsewhere [78].

Each subject performed two conditions of 12 trials per tactile condition. In each trial, the subject was asked to produce a constant force of 20 N using all four fingers of the right hand (index, middle, ring and little fingers) over 12 seconds. Subjects were shown the sum of finger forces along with the target force in the form of a horizontal bar on a computer screen (Figure 1a). In the "no tactile" condition, a topical anesthetic (Dermacain Cream 5%, Hana Pharm Co., Ltd., Seoul, Korea) was applied to middle phalanges of each finger. Five minutes later, a local anesthetic (Lidocaine HCI 1%, DaiHan Pharm. Co., Ltd., Seoul, Korea) was injected at four sites around the middle phalanges of each finger (3.5 cc. for index, middle and ring fingers; 2.5 cc. for little finger). Injection was followed by a stroking massage in the direction of distal phalanges. Von Frey tactile hair stimulation was used to assess the threshold of tactile sensation in the normal and anesthesia conditions [81]. Cutaneous

anesthesia was defined as the inability of the subjects to detect the application of a Von Frey filament exerting a pressing force on the distal pad of the digits. In the "tactile" condition, all subjects were able to detect the filament size of (2,44) and corresponding force magnitude of 0.4 mN, while in the "no tactile" condition, no subject was able to detect the filament with the maximum diameter (size 6,65; corresponding force of 3 N). This study used a repeated design and the same subjects were tested for two different experimental conditions. Two conditions were administered on two different days: a half of the subjects experienced "tactile" condition on the first day and "no tactile" on the second day of experiment, while the other half had the opposite order of the conditions.

3.3.3 Data Analysis

In the current study, we developed new analytical techniques for the decomposition of the variance in the motor outputs into online and offline control and investigated the role of tactile feedback in sub-maximal constant finger force production using these techniques (Figure 2). In the beginning of each trial, subjects were required to increase the finger forces from 0 N to 20 N, and all subjects were able to reach the variability of one standard deviation within 5 seconds. Since the goal of this study was to investigate the constant force production by multiple fingers, the following six-second window of "stable" force data between 5 s and 11 s were extracted for further analysis.. The "virtual finger force" (VFF) was calculated as the sum of four time-varying finger forces. In order to partition the error in VFF relative to the target 20-N force, the VFF for trial i, $y_i(t)$, was modeled as the sum of three components:

$$y_i(t) = X_i(t) + E_i + m \tag{1}$$

where $X_i(t)$ is demeaned VFF for trial i, m is the mean VFF after averaging over all timesteps of all 12 trials, and E_i is the difference between the mean VFF for trial i and m.
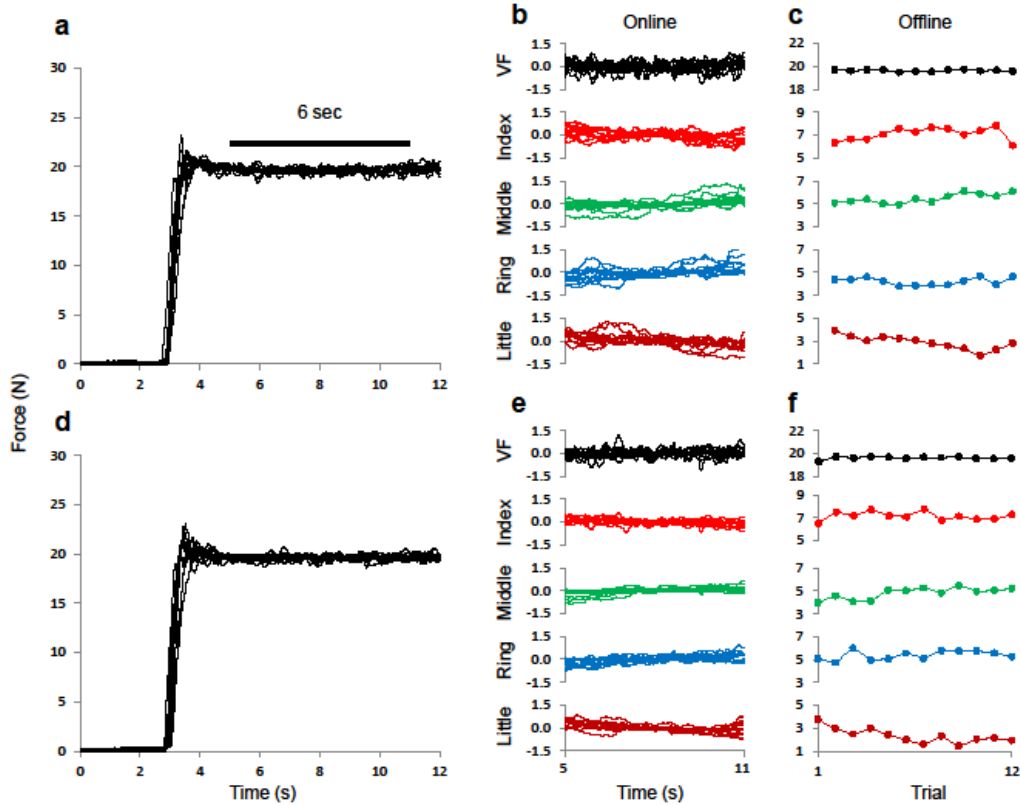
Figure 3.11. Sample experimental data under tactile (**a**, **b**, and **c**) and no tactile conditions (**d**, **e**, and **f**). Time courses of the VF force in black are shown in time-force dimensions (**a**, with tactile, and **d**, without tactile). Demeaned time-force (i.e., online) signals for VF and IF forces are shown in time-force dimensional views (**b**, with tactile, and **e**, without tactile). Trial-force (i.e., offline) signals for VF and IF forces are shown in trial-force dimensional views (**c**, with tactile, and **f**, without tactile).

Task performance was quantified as the overall mean-squared error (*OMSE*), the averaged squared deviation of the VFF from the target 20-N force:

$$OMSE = \frac{1}{N}\sum_{i=1}^{N}\left\{\frac{1}{\tau}\int[f_T - y_i(t)]^2 dt\right\}$$

where τ is the duration of $y_i(t)$ (6 s here), f_T is a target force (20 N here), and N is the number of trials.

OMSE was partitioned into three error components:

1. The "online variance" $\overline{Var(X)}$, defined as the variance within a trial, averaged over all trials,

2. The "offline variance" $Var(E)$, defined as the variance between trials, and

3. The "systematic error", defined as $(f_T - m)^2$.

The online and offline variances quantify the consistency of the motor task (i.e., precision), and the systematic error is overall deviation of VFF from the target force (i.e., accuracy). The online and offline variances can be defined in terms of the individual finger forces (IFF):

$$OMSE = \overline{Var(X)} + Var(E) + (f_T - m)^2$$

$$= \overline{Var\left(\sum_{j=1}^{n} x_j\right)} + Var\left(\sum_{j=1}^{n}\varepsilon_j\right) + (f_T - m)^2$$

where x_j is demeaned IFF of jth finger and ε_j is the IFF differences of jth finger between the mean across time for each trial and the mean across all time steps and all trials, *n*=4 is the number of task fingers. The overhead bars indicate means over trials. Using the hierarchical structure of variability (Figure 2), the online and offline variances at the virtual finger level can be further decomposed as the sum of IFF variances plus between-finger covariances at the individual finger level:

$$\overline{Var\left(\sum_{J=1}^{n} x_J\right)} = \overline{\sum_{J=1}^{n} Var(x_J)} + \overline{\sum_{j \neq k} Cov(x_J, x_k)}$$

$$Var\left(\sum_{j=1}^{n} \varepsilon_j\right) = \sum_{j=1}^{n} Var(\varepsilon_j) + \sum_{j \neq k} Cov(\varepsilon_j, \varepsilon_k)$$

The sum of IFF variances is the total variance in the motor task, while the between-finger covariance reflects synergistic interactions of the finger forces. Motor synergy has been considered as task specific interactions between motor effectors employed by CNS for enhancement of motor performance and utilization of redundant degrees of freedom in the motor system. To quantify motor synergy (*Syn*) between effectors in neuromechanically redundant systems, previous studies [17-19, 24, 54] have assessed differences in effector variance in the task-irrelevant space ($\overline{Var(x_\parallel)}$, $Var(\varepsilon_\parallel)$) that signifies the CNS' utilization of redundant degrees of freedom, and the task-relevant space ($\overline{Var(x_\perp)}$, $Var(\varepsilon_\perp)$) that indicates the motor task error. The task-irrelevant variance is also known as variance in Uncontrolled Manifold (UCM) space or redundant subspace, while the task-relevant variance is the variance in the sub-space orthogonal to the UCM space [82]. In this scheme, the former does not affect the motor task performance, indicating the system's "flexibility" while the latter represents motor task error [54]. We provide the proof below that the calculation of motor synergies employed in previous studies is a simple negation of covariation between effector motor outputs. Thus, we used negative covariance values as an index of motor synergy between fingers.

$$Syn(X) = \overline{Var(x_\parallel)} - (n-1)\overline{Var(x_\perp)} = -\sum_{j \neq k} Cov(x_J, x_k)$$

$$Syn(E) = Var(\varepsilon_{\parallel}) - (n-1)Var(\varepsilon_{\perp}) = -\sum_{j \neq k} Cov(\varepsilon_j, \varepsilon_k)$$

since

$$\overline{Var(x_{\perp})} = \frac{1}{n}\overline{Var\left(\sum_{j=1}^{n} x_j\right)}, \qquad Var(\varepsilon_{\perp}) = \frac{1}{n}Var\left(\sum_{j=1}^{n} \varepsilon_j\right)$$

$$\overline{\sum_{j=1}^{n} Var(x_j)} = \overline{Var(x_{\perp})} + \overline{Var(x_{\parallel})}, \qquad \sum_{j=1}^{n} Var(\varepsilon_j) = Var(\varepsilon_{\perp}) + Var(\varepsilon_{\parallel})$$

Error compensation between IFFs occurs when there exists negative covariances between IFFs during constant VFF production using IFFs [73]. Thus, negative covariance values ($-Cov(\cdot,\cdot)$) between IFFs correspond to synergistic actions between fingers for the multi-finger pressing task employed in our experiments. A large magnitude of $Syn(X)$ and $Syn(E)$ indicates that there exist a small motor task errors, along with a wid motor repertoire is used in the task-irrelevant space (i.e., more motor variability is used to complete the task without impacting task performance). $Syn(X)$ and $Syn(E)$ are the indices of intra-trial synergy and inter-trial synergy between finger forces, which we denote online synergy and offline synergy, respectively. In other words, a large magnitude of Syn (X) indicates a large degree of dynamic error compensations between finger forces over 6 s, while a large magnitude of Syn (E) denotes a large degree of error compensations between finger forces over all 12 trials.
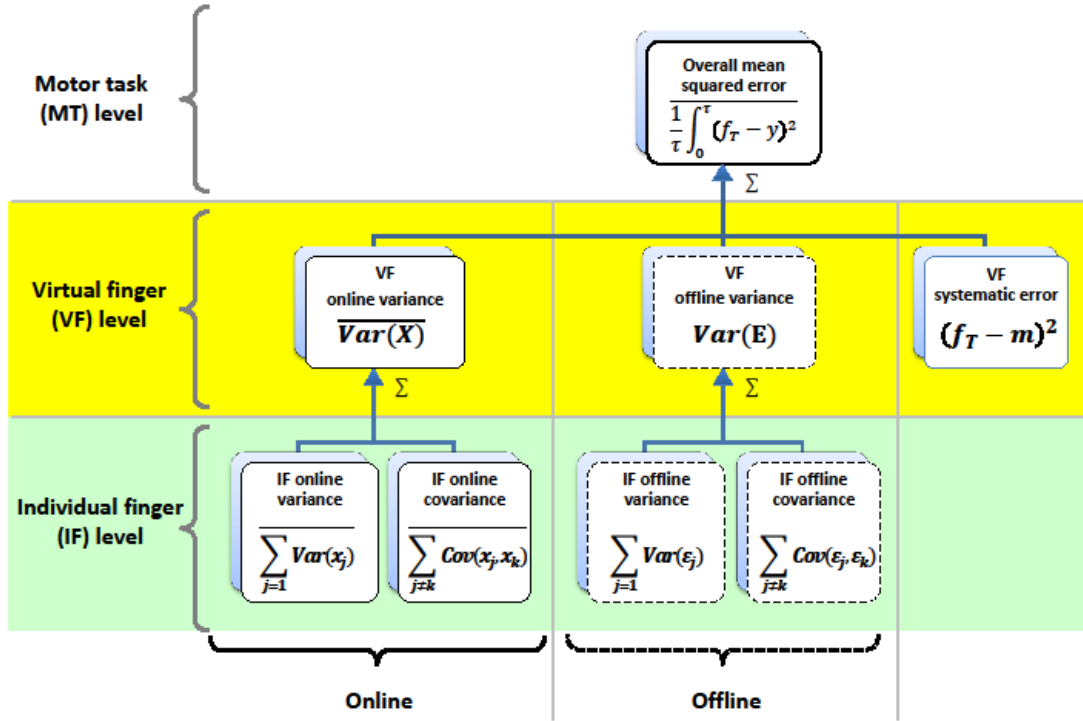
Figure 3.12. Hierarchical organization of multi-finger force variability in a redundant hand system. The overall mean squared error is composed of or the linear sum of the intra-trial moment-to-moment (online) variance ($\overline{Var(X)}$), the trial-to-trial time-averaged (offline) variance ($Var(E)$), and the systematic error ($(f_T - m)^2$) at the virtual finger (VF) level where the task is performed with the sum of all finger forces (VF force). The online and offline variances at the VF level are composed of or the linear sum of individual finger (IF) force variances ($\overline{Var(\sum_{j=1}^{4} x_j)}$ and $Var(\sum_{j=1}^{4} \varepsilon_j)$) and between-finger force covariances ($\overline{\sum_{j \neq k} Cov(x_j, x_k)}$ and $\sum_{j \neq k} Cov(\varepsilon_j, \varepsilon_k)$) at the IF level.

3.3.3 Statistics

One-way repeated measures ANOVAs were used to compare two feedback conditions. The level of statistical significance was set at $p=0.05$.

3.4 Results

Figure 3.3 shows that VFF and IFF measured from a representative subject during submaximal constant force production task under tactile and no tactile conditions. All subjects produced VFF slightly below the 20-N target force, resulted in a small negative systematic error $(f_T - m) = -0.32 \pm 0.03$ N (mean ± s.e.m. across all subjects and both conditions). *OMSE* remained unchanged between tactile conditions (tactile: 0.24 ± 0.03 N^2 vs. no-tactile: 0.23 ± 0.03 N^2 ($F_{1,17}$=0.26, *p*=.615)). The online variance, offline variance, and systematic errors were also unchanged between tactile conditions ($F_{1,17}$=1.70, *p*=0.21 for online, $F_{1,17}$=1.34, *p*=0.26 for offline, and $F_{1,17}$=0.35, *p*=0.56 for systematic error). Thus, subjects performed the task similarly at the virtual finger level regardless of the finger tactile conditions.

At the individual finger level, removal of tactile feedback decreased IFF synergy ($F_{1,17}$=5.44, *p*=0.032) (Figure 3.4a,b) and IFF variance in online control ($F_{1,17}$=6.72, *p*=0.019) (Figure 3.4e,f). However, in offline (trial-to-trial) control, tactile feedback did not affect IFF variance ($F_{1,17}$=0.74, *p*=0.40) nor synergy ($F_{1,17}$=0.71, *p*=0.41) (Figure 3.4c,d,g,h). Follow-up analysis showed that when tactile feedback was removed, the task-irrelevant variance decreased ($F_{1,17}$=6.47, *p*=0.021) (Figure 3.4i) while the task-relevant variance remained unchanged (Figure 3.4j). Thus, the changes in the task-irrelevant variance were the main cause of the decreases in IFF synergies (Figure 3.4b) and IFF variances (Figure 3.4f).
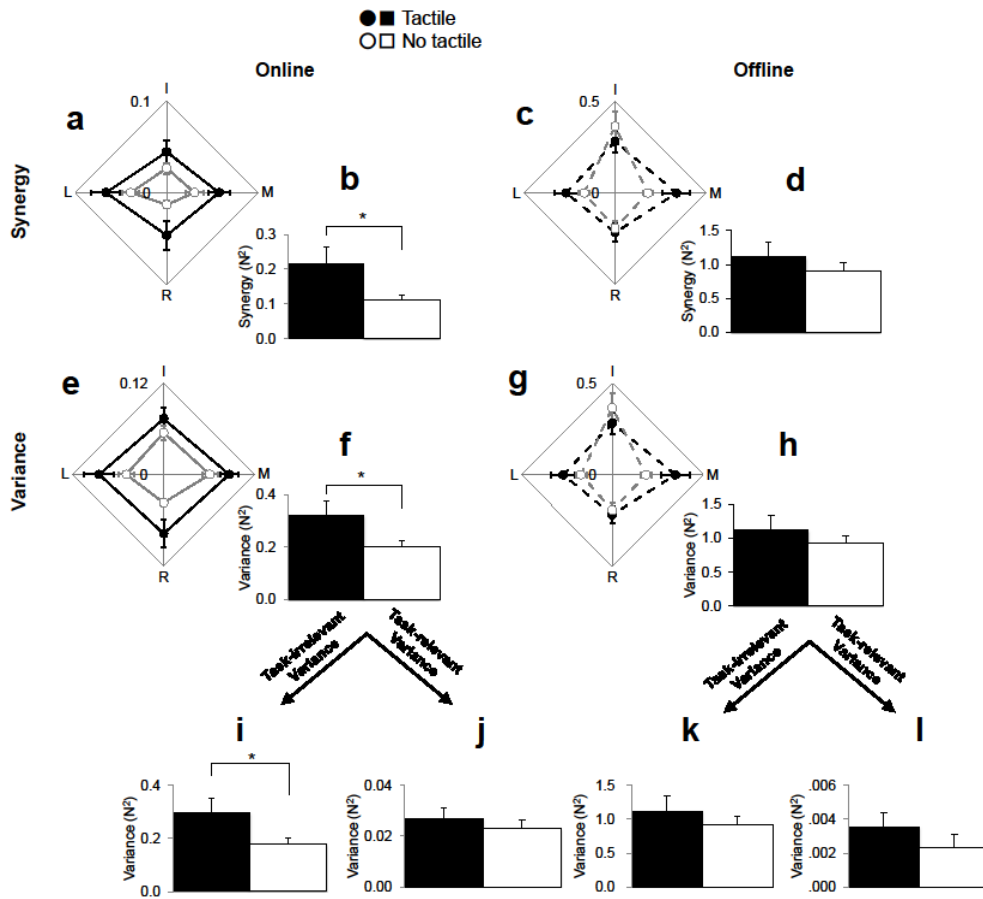
Figure 3.13. Multi-finger synergy and individual finger force variance for online and offline controls under tactile and no tactile conditions at the individual finger (IF) level. The individual fingers' contributions to the overall synergy and variance values are shown in the 4-dimensional diamond graphs (a, e, c, and g). Error bars represent s.e.m. across subjects. The accompanying bar graphs show the overall synergy and variance values (b, d, f, and h). A repeated-measures analysis of variance was performed on the overall variance and synergy values to test if these values are different between tactile and no tactile conditions. The synergy and variance, only in online control, showed statistically significant differences (asterisk, $p < 0.05$ for both variance and synergy) between tactile and no tactile conditions, but not in offline part. For the further analysis, the sum of individual finger force variances were divided into task-irrelevant variance and task-relevant variance for online and offline (i, j, k, and l). The only statistically significant difference ($p < 0.05$) was found in the task-irrelevant variance in online.

3.5 Discussion

New analytical development for decomposition of motor variability into online and offline components in a hierarchical structure

Many previous studies analyzed multi-finger force variability between trials [16-19] while other studies investigated variability over time within a trial [23, 24]. Note that we refer to these quantities as "offline" and "online" variabilites, respectively. Although a previous study used both online and offline analyses [24], the study mainly used correlations between individual finger forces for both between- and within-trial analysis of multi-finger synergies. The current study offers a new analytical framework for the linear decomposition of the variance in the motor system in both online and offline control, along with the quantification of variable and systematic errors in outcomes of a multi-effector motor system. The decomposition at virtual finger and individual finger levels also offers hierarchical analysis of multi-effector system behaviors. The new technique is not limited to finger force assessment, but may be used to study other multi-effector motor systems such as multiple muscles, multiple joints, etc.

Critical role of tactile feedback in online motor control and hierarchical organization

Our study showed that the removal of tactile feedback was associated with the decreased IFF variability ($\overline{Var(x_J)}$) and decreased index of synergy ($Syn(X)$) in online control. This result suggests that tactile sensation plays an important role in the online control of VFF via IFF synergy in goal-directed multi-finger force production. However, the tactile sensors do not contribute significantly to offline control. Our

previous simulation study on central back coupling hypothesis demonstrated that it was theoretically possible for a simple feedforward neural system to show actions apparently synergistic between finger forces without a sensory feedback [83]. However, our current study shows that it is likely that the finger tactile sensors play an active role in online control in multi-finger motor task.

In day-to-day motor tasks such as holding a glass of water with all five digits [79, 80] and holding a tray with two hands [84], the motion of the objects in manipulation is visually perceived at the virtual finger level as the consequence of the resultant force and resultant torque of all digits and hands and tactile feedback is processed at the individual finger level, similarly to our experimental design. The "virtual finger" model of multi-finger tasks [16, 85, 86] leads naturally to analysis of IFF as effectors in a VFF-oriented task [16]. The current study showed that VFF variability did not change, while IFF variability and index of synergy did change, in the absence of tactile sensory feedback. This finding supports the idea that multi-finger actions are organized in a hierarchical manner and the different sensory modalities, visual and tactile as shown in Figure 1, may be processed at different levels of the hierarchy.

The principle of non-individualized control suggested by [87] states that elements of a complex system are united as task-specific structural units, commonly addressed as 'synergies' in contemporary literature. They also introduced a principle of minimal interaction in two hierarchical levels: at a local level, the inputs to individual elements are minimized, and at a global level, the functional output of the system is minimized by relative contributions of the elements. The unchanged

variability at the virtual finger level regardless of the tactile conditions and the decreased variability at the individual level in online control without tactile feedback suggest that the CNS responded to the deprivation of the tactile feedback by minimizing or reducing the IFF variability without changing the overall behavior at the task level.

In addition to the visual feedback, the subjects naturally received feedback of pressing force from other sensory modalities such as tactile and proprioception. Assuming that the integration of multiple sensory feedbacks follows Bayesian rules [10, 11, 88], the removal of one or more sensory modalities from all sensory modalities used in a closed-loop motor task would be accompanied by an evident decrease in the motor performance, in our study, a potential increase of overall mean square error. On the contrary, we found no changes in the performance at the motor task level after removing the tactile feedback. It is rather surprising that motor performance at the virtual finger level was not affected by removal of tactile feedback. Previous studies have suggested that tactile feedback is critical for manual manipulation of objects [77]. However, the unchanged virtual finger behaviors found in this study may be due to the dominant role of visual feedback in motor tasks while working with tactile feedback and/or the differences of the visual and tactile feedbacks existing at different levels in the hierarchy. It has been suggested that visual feedback plays a dominant role in motor tasks even in the presence of other feedback modalities [89]. The dominant role of the visual feedback might have taken over the overall feedback control at the task level [90, 91]. Also, in our experiment, visual feedback of VFF was shown to subjects on a computer screen and the tactile

feedback was naturally perceived or not perceived at the individual fingers. During the multi-finger pressing task employed in our experiment, the tactile information might have been processed at the individual-finger level while minimally affecting the process of the visual feedback at the virtual finger level, thus, resulting in changes at motor outputs only at the individual finger level but no changes at the virtual finger level when the tactile feedback was deprived.

Task-relevant variability and task-irrelevant variability

The decreased variability in task-irrelevant space found after the removal of tactile feedback in our study may reflect decreased utilization of the motor system's redundant degrees of freedom. Note that the CNS responded to the loss of hand tactile feedback by reducing the "work space" of finger forces only in the task-irrelevant space while maintaining the same task performance as in the normal tactile condition. Mathematically, the decrease in the variability in the task-irrelevant space with a constant variability in the task-relevant space is directly associated with decreases in the magnitudes of covariances or correlations between finger forces (i.e., covariances or correlation coefficients becoming close to zero), reflecting more independent actions or less dependent actions between finger forces. Thus the variability decreases in the task-irrelevant space found under no tactile condition in our study may be interpreted as decreased dependency or increased independence between individual fingers without tactile feedback, although the underlying mechanism responsible for this phenomenon requires further investigation.

Limitations

During multi-finger actions, individual fingers show phenomena of mutual dependence due to the anatomical design of the hand and fingers and the neural organization of finger control [92-94]. In this analysis, the hypothetical CNS commands to individual fingers, called finger force modes, are calculated from experimentally observed individual finger forces and virtual finger forces, estimation of couplings between individual finger forces, called finger enslaving [95], and estimation of finger number dependent force changes, called force deficits [96]. The analysis of our experimental data in the finger mode space may have provided an additional insight into the actions fingers and interactions between them. However, the mode analysis demands a new method for accurate quantification of the finger force modes though careful experiments and modeling because the enslaving may be subject to changes during the dynamic process of finger force production [97]. Due to the analytical challenges caused by the potentially non-constant enslaving, the analysis of our study was limited in the finger force space. However, if the enslaving is assumed to be constant, the main findings of our study should still stay hold, specifically those differences observed in our study between two tactile conditions."

In a recent study, Tessitore and colleagues used a tree-structured organization and suggested that the hand actions can be formed by hierarchically structured synergies where kinematic characteristics of multiple types of hand actions could be reconstructed as a simple linear combination of the same set of synergies , [98]. Although the model suggested by Tessitore was limited to hand kinematics and the interpretation of synergies are not the same as ours (i.e., error compensations between

effectors), their general approach provides a way to investigate a hierarchical organization in multi-finger actions without a bias in combining an arbitrary set of fingers for investigation. Our study assumed that four individual fingers constitute a virtual finger because their role were similar in that they produced pressing forces in the same direction for the successful motor task required by our experiment. However, many day-to-day manipulation tasks may require different roles of individual fingers or subsets of fingers and these fictional groups may be easily detected by a tree-structured organization.

Summary

We developed new analytical techniques for the linear decomposition of the overall variability in a redundant motor system in both online and offline control, along with the quantification of precision and accuracy in outcomes of a multi-effector motor system. Our experiments show that tactile feedback plays a critical role in the online control, but not in offline control, during isometric multi-finger force production. We also demonstrate that combined motor output of fingers does not change while individual finger behaviors do change when tactile feedback is removed from the fingers. This finding supports the idea that multi-finger actions are organized and controlled in a hierarchical manner.

Chapter 4: Optimal integration of intra auditory modalities in motor performance and coordination during constant finger force production

4.1 Abstract

Humans are capable of combining multiple modalities of sensory information for the enhancement of motor performance. Most of previous studies have examined the integration of multiple modalities between sensory (i.e., inter-sensory integration). However, little is known about integration of multiple modalities within one sensory especially the auditory system (i.e., intra-auditory integration) and its effect on motor performance and coordination. Here, we investigated the effect of intra-auditory integration (i.e., integration of the frequency and intensity of auditory information) on motor performance and coordination during a multi-finger force production task. It was hypothesized that intra-auditory integration would enhance motor performance and coordination based on the findings in previous studies. For the experiment, the subjects were instructed to match the reference force of 18 N with the virtual finger force (VF force: the sum of all finger forces) where the reference force and VF forces were presented as auditory feedbacks to different ears. The feedback signal for the reference force was a sinusoid signal with a constant frequency and intensity while the feedback signal for VF force was a sinusoid signal that changed with the VF force. Three conditions were used in the experiment: frequency condition (F; the frequency changed with VF force), intensity condition (I; the intensity changed with VF force), and both frequency and intensity condition (FI; both changed with VF force). Motor performance and motor coordination was quantified using a previously developed variance decomposition analysis. Motor performance was enhanced for FI condition as compared to F or I conditions through reduced variable error in the VF force. Motor coordination was improved in FI condition through reduced error

amplification among the IF forces. Our results provide evidence that the central nervous system can integrate the frequency and intensity of auditory signals for the improved motor performance and coordination, supporting the idea of the Bayesian model.

4.2 Introduction

From a simple action such as drinking a glass of water to a more complex movement such as driving a car, we constantly receives stream of information from various sensory systems and generate motor commands to create actions through multiple motor effectors (e.g., muscles, joints, or fingers). In this process, the CNS faces at least two challenges. First, the CNS must be able to construct an accurate representation of the internal body and external world's state with sensory information gathered from various receptors [5]. Second, the CNS must be able to coordinate the redundant effectors in the motor system.

Previous studies on sensory integration have revealed mechanisms of integration between different sensory systems (e.g., visual and auditory, visual and tactile, or visual and proprioceptor), which is referred to as "inter-sensory" integration [10-15]. In these studies, it has been suggested that the CNS combines multiple sensory modalities in a statistically optimal fashion (i.e., minimum-variance) in order to improve the estimates or to reduce the uncertainty in sensory information, referred to as the Bayesian model or maximum likelihood estimation (MLE). However, our knowledge on integration of different modalities within a same sensory system (i.e. "intra-sensory" integration) is limited. Moreover, most of the previous studies on intra-sensory integration were on the vision (e.g., integration of color, motion, depth and shape) [7-9]. Despite the fact that we are constantly exposed to sounds in daily activities, very little is known about how the CNS processes and integrates multiple modalities in auditory system.

The sound we hear is caused by vibrations of air. The sound waves consist of physical properties such as the frequency and intensity. The frequency and intensity are the most salient features to contribute to the perception of sound such as pitch and loudness, respectively. It has been suggested that these two quantities are perceived independently [52, 99]. Here, we tested whether the frequency and intensity in auditory information can be integrated to enhance motor performance, following the Bayesian model.

Many previous studies investigated the CNS's mechanisms for coordinating multiple motor effectors. These studies investigated underlying mechanisms of the CNS for simultaneously controlling multiple fingers [16, 73, 75, 100-102], multiple muscles [103, 104], multiple joints [105-107], multiple body segments [108], etc. The notion of motor synergy has been developed to describe the simultaneous control of multiple motor effectors for the stabilization of a given motor task [73]. The motor synergy between motor effectors typically involved two different forms of synergy, within-trial synergy and between-trial synergy, which are thought to reflect the CNS's different control strategies [24]. The within-trial synergy refers to synergistic actions in fluctuations of multiple motor effectors over time with purpose to minimize a particular motor task error on moment-to-moment basis (i.e., online control). In contrast, a between-trial synergy refers to synergistic actions in variations of multiple motor effectors during repetitions of a particular motor task in order to achieve equivalent motor outcomes to on trial-to-trial basis (i.e., offline control). Despite the fact that the influence of sensory feedback is an important factor in the formation of

motor synergies [24, 109], it remains unknown how the integration of multiple sensory modalities influence on the changes of the motor synergies.

Previous studies [22, 24] have showed that the removal of one sensory feedback from combined visual and tactile feedbacks was associated with deterioration in multi-finger synergy. Ranganathan et. al., (2008) found that multi-finger synergy decreased when the visual feedback was removed. On the other hands, in recent work, we found that multi-finger synergy also decreased when the tactile feedback was removed. However, the mechanisms of how the integration of multiple modalities influences the formation of multi-finger synergy are not clear.

Recently, we have developed analytical techniques for the decomposition of the variance in the motor outputs in the context of motor performance and coordination [22]. In this model, motor performance is quantified as mean-squared error of a particular motor task outcome, which is mathematically decomposed into two aspects as accuracy and precision of the motor task. Motor coordination is quantified as variations and co-variations of multiple effectors, which are contributed to the precision of performance. The benefit from the model is to allow to investigate the integration of multiple sensory modalities using the Bayesian model as well as to quantitatively examine the several aspects of the CNS's control ability for a given motor task in the context of motor performance and coordination.

In the current study, we investigated the effect of intra-auditory integration on motor performance and coordination during a constant force production task. To accomplish these aims, we developed a novel technique to generate an aquatic signal with each of the property; the frequency and intensity can be independently

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manipulated by finger force in real-time. We hypothesized that 1) intra-auditory integration would reduce variability of virtual finger force (VF force: sum of individual finger (IF) forces combined) followed by the Bayesian model and 2) intra-auditory integration would increase multi-finger synergy in both online and offline controls.

4.3 Methods

4.3.1 Participants

Ten right-handed volunteers (10 males; mean age 24.2 years + 1 year SD) participated in the study. Participants were also free of neurological disorders, psychiatric disorders, speech-language disorders, and motor impairments. No participant had more than one year of musical training. Participants provided written informed consent. All procedures were approved by the University of Maryland College Park Institutional Review Board.

4.3.2 Experimental setup

Force data were collected using a 6 degree of freedom load cell (ATI Nano 17) at a sampling frequency of 1,000 Hz with data acquisition hardware (National Instruments DAQ- card-6024E) using a custom program written with Labview (National Instruments Labview 8.2). This program manipulated the frequency and intensity of an auditory signal played to the subjects via a headphone (Bose AE2) using a dual channel function generator (Agilient 33522A). To ensure that frequency response characteristics [110] of the headphone were minimized, we calibrated the

auditory signal to produce a constant intensity across all frequencies. Calibration was performed in a soundproof room by manipulating frequency from 20 to 10,000 Hz in 1 Hz increments and normalizing intensity at each increment.

4.3.3 Procedures

Participants sat, wearing headphones, with their head in a chin rest. Their right hands were placed on the load cells (Figure 4.1). Participants were asked to produce 18N with four fingers by pressing down the sensors, and completed fifteen 20-s trials in each of three conditions, with 30 s rest between trials. The reference force was selected to be 18 N based on our earlier experience that showed no fatigue during force production with such characteristics, while the range allowed sufficient resolution of force measurement. During the task, the reference force was provided as an auditory signal, a sinusoid signal with frequency 1000 Hz and intensity 70 dB (i.e. reference tone), played to the subject's left ear. The frequency and intensity of the reference tone was selected as 1000 Hz and 70 dB in order to minimize the influence of binaural beats [111, 112]. The force generated by the subject was also provided as a sinusoid signal (i.e. tracking tone) to their right ear. The tracking tone had three feedback conditions:

1)   Frequency condition (F): the frequency of the tracking tone changed depending on the deviation of the subject's sum of finger forces from 18 N, with a constant intensity of 70 dB.

2)   Intensity condition (I): the intensity of the tracking tone changed depending on the deviation of the subject's total finger force from 18 N, with a constant frequency of 1000 Hz.

3)   Frequency & Intensity condition (FI): both the frequency and intensity of the tracking tone changed depending on the sum of finger forces.

The feedback gains of frequency and intensity per Newton were set as 7Hz/N and 0.7dB/N, respectively, according to minimum detectable differences previously reported [4, 5]. The feedback conditions were presented to participants in a random order. Participants completed 15 trials of 20 s with 30 s rest between each trial. Prior to the experiment, participants were given 5 familiarization trials. If the VF force was quickly dropped (in 5ms or less) to below 5 N, we considered this trial as failed one. Failed trials were 31 out of 450 trials; maximum 12 out of 150 trials per condition.
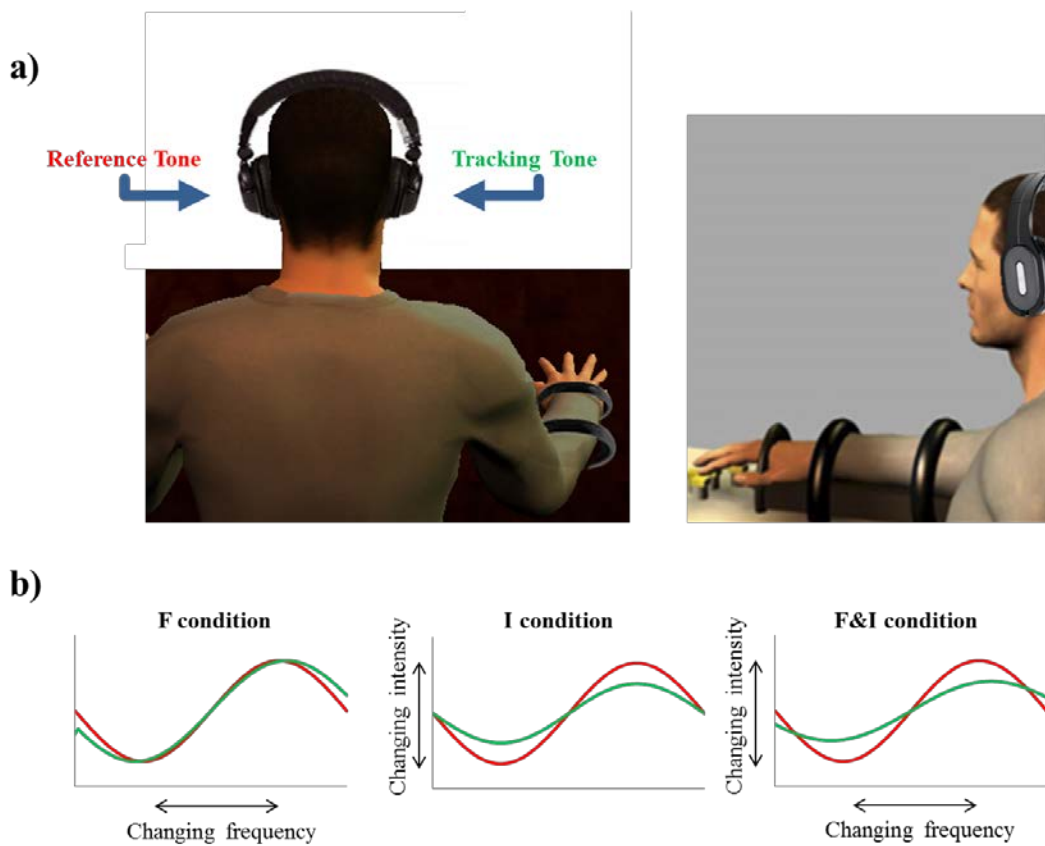
Figure 4.1. Experimental setup. The subjects sit and place their right hand finger tips on the sensors, wearing the headphones (a). The subject is asked to produce 20N with four fingers while the reference and the tracking force the subject produce are provided as an auditory feedback. Reference tone (i.e., auditory feedback for

reference force) (b in red) is a sinusoid signal with a constant frequency of 1000 Hz and intensity of 70 dB to left ear while tracking tone (i.e., auditory feedback for the tracking force) (b in green) is a sinusoid signal determined by three feedback conditions; Frequency condition (F): the frequency of the tracking tone changed depending on the deviation of the subject's sum of finger forces from 18 N, with a constant intensity of 70 dB, 2) Intensity condition (I): the intensity of the tracking tone changed depending on the deviation of the subject's total finger force from 18 N, with a constant frequency of 1000 Hz, and 3) Frequency & Intensity condition (FI): both the frequency and intensity of the tracking tone changed depending on the sum of finger forces.

The changing in frequency and intensity per Newton were set as 7Hz/N and 0.7dB/N according to previous Just Noticeable Difference studies [113, 114]. The feedback conditions were presented to participants in a random order. Participants completed 15 trials of 20 s with 30 s rest between each trial. Prior to the experiment, participants were given 5 familiarization trials. If the VF force was quickly dropped to below 5 N, we considered this trial as failed one. Failed trials were 31 out of 450 trials; maximum 12 out of 150 trials per condition.

4.3.4 Data analysis

Bayesian model
Using the framework of the Bayesian or maximum likelihood estimates (MLE), the bimodal estimate, $\hat{S}_{FI}$, of a finger force from both the frequency and intensity modalities can be expressed as a weighted sum of the frequency, $\hat{S}_F$, and intensity estimates ,$\hat{S}_I$;

$$\hat{S}_{FI} = w_F\hat{S}_F + w_I\hat{S}_I$$

If the estimates are considered a Gaussian random variable with mean μ and variance σ^2, the optimal estimate is more precise (lower variance) than the uni-modal estimates as follows:

$$\sigma_{FI}^2 = \frac{\sigma_F^2 \sigma_I^2}{\sigma_F^2 + \sigma_I^2}$$

The variance of combined estimate, σ_{FI}^2, is lower than the variances of the frequency, σ_F^2, and intensity estimates, σ_I^2. The combined bias b_{FI} $(= (f_T - \mu_{FI})$ where f_T is a reference force (18N here)) is expressed by a weighted average of the frequency bias, b_F, and the intensity bias, b_I with the weights, $w_F = \frac{\sigma_I^2}{\sigma_F^2 + \sigma_I^2}$ and $w_I = \frac{\sigma_F^2}{\sigma_F^2 + \sigma_I^2}$ [115, 116];

$$b_{FI} = w_F b_F + w_I b_I$$

To test whether auditory modalities are optimally integrated, first we quantified motor performance as the overall mean-squared error (*OMSE*), the averaged squared deviation of the VFF from the reference force:

$$OMSE = \frac{1}{N} \sum_{i=1}^{N} \left\{ \frac{1}{\tau} \int [f_T - y_i(t)]^2 dt \right\}$$

where $y_i(t)$ is VF force at trial i, and τ is the duration of $y_i(t)$. Note that eleven-second window of "stable" force data (between 6-17s) was used for analysis.

Then, we compared the experimentally obtained *OMSE* to the *OMSE* predicted by the MLE   as   follows:

$$OMSE_{FI} = \sigma_{FI}^2 + b_{FI}^2$$

$$= \frac{\sigma_F^2 \sigma_I^2}{\sigma_F^2 + \sigma_I^2} + (w_F b_F + w_I b_I)^2$$

Hierarchical variability decomposition

The VF force for trial i, $y_i(t)$, was modeled as the sum of three components:

$$y_i(t) = X_i(t) + E_i + m$$

where $X_i(t)$ is the demeaned VF force for trial i, m is the mean VF force after averaging over all timesteps of all 15 trials, and E_i is the difference between the mean VF force for trial i and m.

In the hierarchical variability decomposition (HVD) model [22], *OMSE* was partitioned into three error components as performance variables: the "online variable error" $\overline{\sigma_X^2}$, defined as the variance within a trial, averaged over trials, the "offline variable error" σ_E^2, defined as the variance between trials, and the "systematic error", b^2, defined as squared deviation between target and m. Note: sum of online and offline variable error is the variable error of VF force $(\overline{\sigma_X^2} + \sigma_E^2 = \sigma^2)$ and the systematic error is the squared bias of VF force $((20 - m)^2 = b_{FI}^2)$.

The online and offline variance can be defined in terms of the IF forces:

$$OMSE = \overline{\sigma_X^2} + \sigma_E^2 + b^2$$

$$= \overline{\sum \sigma_{x_\iota}^2} + \overline{\sum \sigma_{x_\iota}\sigma_{x_J}} + \sum \sigma_{e_i}^2 + \sum \sigma_{e_i}\sigma_{e_j} + b^2$$

where x_j is demeaned IF force of jth finger and ε_j is the IF force differences of jth finger between the means across time and mean across all time steps of 15 trials, n is the number of task fingers (n = 4) and the overhead bars indicate means over trials.
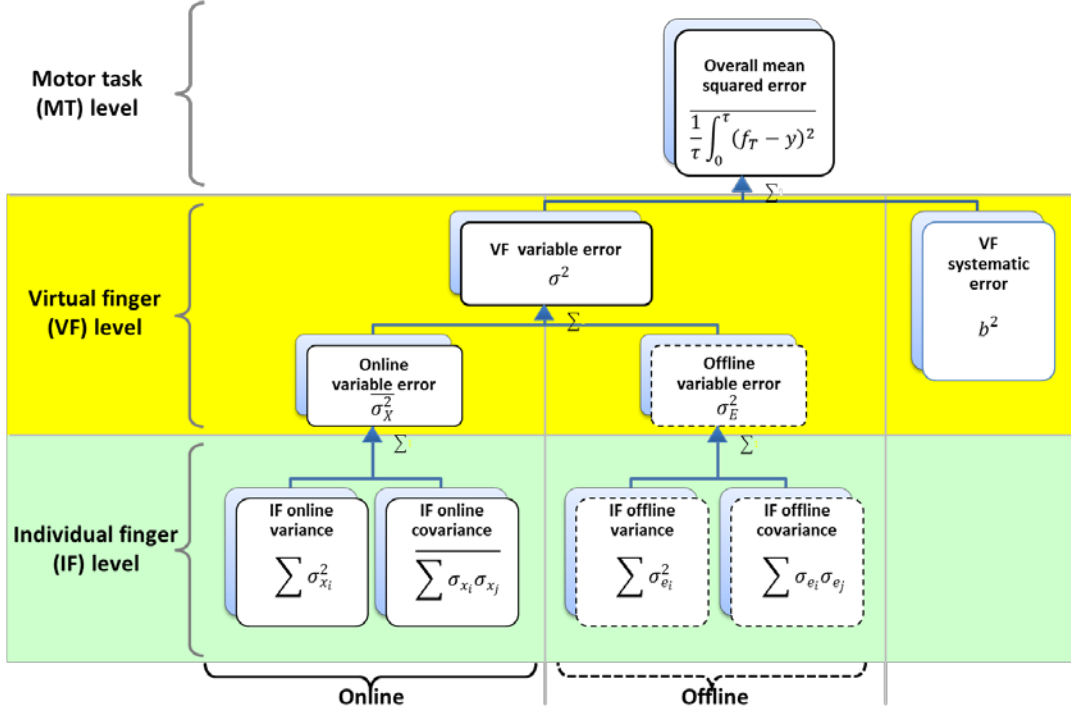
Figure 4.2. Hierarchical organization of multi-finger force variability in a redundant hand system. The overall mean squared error is composed of or the linear sum of the intra-trial moment-to-moment (online) variable error ($\overline{\sigma_X^2}$), the trial-to-trial time-averaged (offline) variable error (σ_E^2), and the systematic error (b^2) at the virtual finger (VF) level where the task is performed with the sum of all finger forces (VF force). The online and offline variances at the VF level are composed of or the linear sum of individual finger (IF) force variances ($\overline{\sum \sigma_{x_i}^2}$ and $\sum \sigma_{e_i}^2$) and between-finger force covariances ($\overline{\sum \sigma_{x_i} \sigma_{x_j}}$ and $\sum \sigma_{e_i} \sigma_{e_j}$) at the IF level.

Using the hierarchical structure of variability (Figure 4.2), the online and offline errors can be further defined as the sum of IF force variances, plus between-finger covariances: (Note that IF force varainces and covariances are used as coordination variables) $\overline{\sigma_X^2} = \overline{\sum \sigma_{x_i}^2} + \overline{\sum \sigma_{x_i} \sigma_{x_j}}$ and $\sigma_E^2 = \sum \sigma_{e_i}^2 + \sum \sigma_{e_i} \sigma_{e_j}$. Here, we use the covariances $\overline{\sum \sigma_{x_i} \sigma_{x_j}}$, and $\sum \sigma_{e_i} \sigma_{e_j}$ as index of online and offline error amplification (or error compensation), respectively. Note that negative covariance indicates that IF acts to compensate each other errors (i.e., error compensation) while

positive covariance is that IF acts to amplify the VF force (i.e., error amplification). A negation of covariance value is mathematically the same as the motor synergy quantified in previous studies [17-19, 24, 54] which is calculated by difference in effector variance in the task-irrelevant space that signifies the CNS' utilization of redundant degrees of freedom, and the task-relevant space that indicates the motor task error. Here, we use online and offline covariances as indices of online and offline synergies.
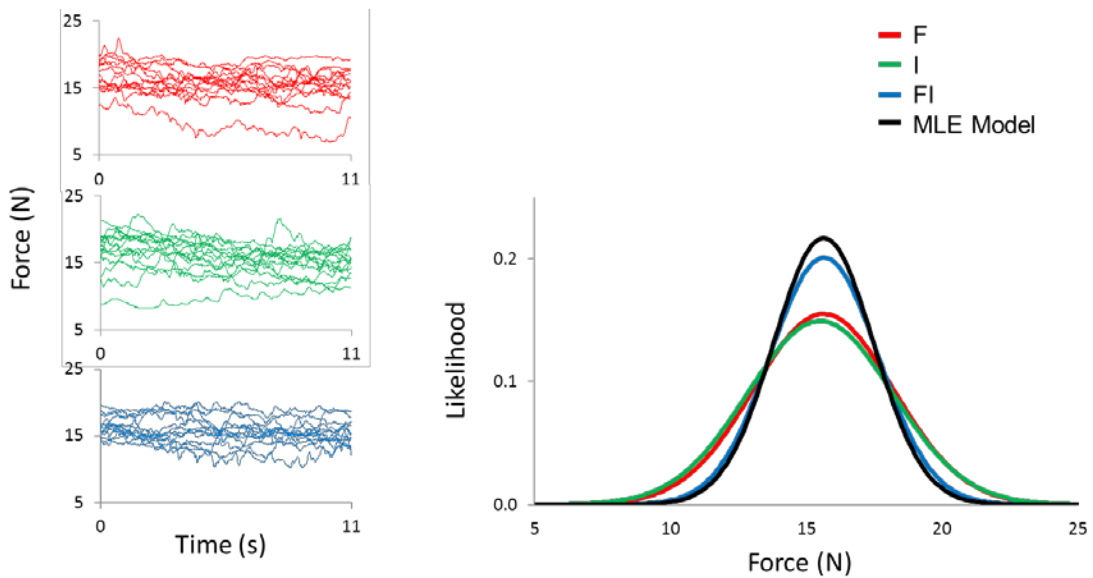
Figure 4.3. Sample experimental data from one representative subject. Force-time profile data for multiple repetitions under frequency (red), intensity (green) and frequency + intensity conditions (blue) are shown in left panel. Best-fitted Gaussian distributions for each condition and MLE model (black) were shown in right panel.

4.4 Results

4.4.1 Effects of intra-auditory integration on performance

In the comparison of MLE model, the *OMSE* from experimental data did not differ from the MLE (t(9)=0.896, p=0.393), along with no significant differences for

VF variable error (t(9)=0.614, p=0.554) and the systematic error (t(9)=2.10, p=0.065) (Figure 4.3). In the comparison of feedback conditions, repeated measures ANOVA revealed that *OMSE* was significantly lower with combined FI feedback than with F or I feedback alone ($F_{2,9}$=12.76, *p*=0.000; FI vs F; *p*=0.003, and FI vs I; *p*=0.004). At the VF level, both online ($F_{2,9}$=8.92, *p*=0.002; FI vs F; *p*=0.009, and FI vs I; *p*=0.002) and offline variances ($F_{2,9}$=10.07, *p*=0.001; FI vs F; *p*=0.003, and FI vs I; *p*=0.015) were lower with combined FI feedback than with F or I feedback alone while the systematic errors remained unchanged across the feedback conditions ($F_{2,9}$=2.088, *p*=0.153) (Figure 4.4). Thus, reductions of *OMSE* were mainly due to the reduction of both online and offline variances.
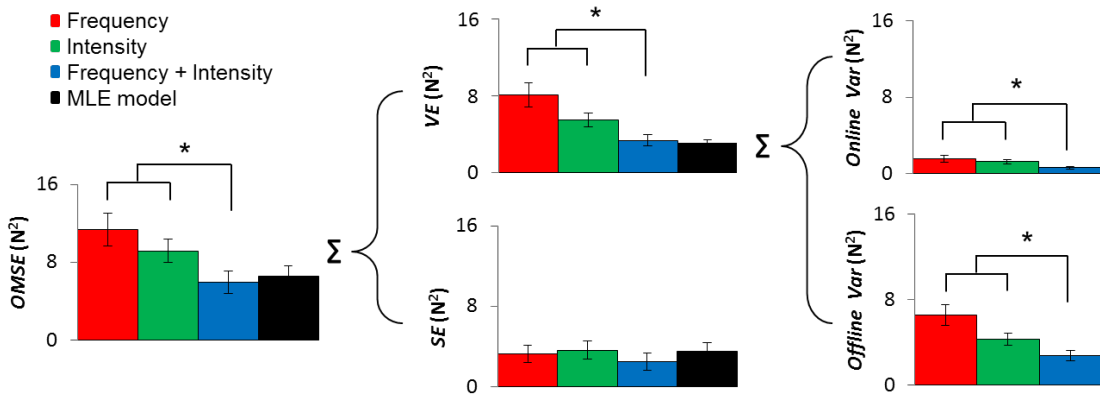
Figure 4.4. Multi-finger pressing performance under frequency (red), intensity (green), frequency + intensity conditions (blue), and MLE model (black). The overall mean squared error (OMSE) is composed of the variance and systematic error. The variance is further decomposed of online and offline variances. Error bars represent s.e.m. across subjects. A repeated-measures analysis of variance was performed on all values to test if these values are different among the feedback conditions. In the comparison of MLE model, the OMSE for bimodal condition (frequency + intensity) was well predicted by the model, along with the variance and systematic error. In the comparison among the feedback conditions, the OMSE for bimodal condition showed statistically significant lower (asterisk, *p*<0.05) than either of frequency and intensity conditions, along with the variance, online and offline variances.

4.4.2 Effects of intra-auditory integration on coordination

In the HDV model, each VF online and offline variances is mathematically equal to the sum of IF variance and covariance (Figure 4.2), allowing us to investigate the source of changes in VF variances. Online IF variance ($F_{2,9}=6.86$, $p=0.006$; FI vs F; $p=0.019$, and FI vs I; $p=0.016$) and covariance ($F_{2,9}=7.38$, $p=0.005$; FI vs F; $p=0.011$, and FI vs I; $p=0.003$) were significantly lower with combined FI feedback than with F or I feedback alone. In contrast, offline IF variance ($F_{2,9}=9.92$, $p=0.001$; FI vs F; $p=0.002$, and FI vs I; $p=0.064$) remained unchanged but offline IF covariance ($F_{1.276,9}=9.85$, $p=0.006$; FI vs F; $p=0.004$, and FI vs I; $p=0.019$) was decreased. In analyses of task-relevant and -irrelevant spaces, both online and offline IF variances in the task-relevant space decreased (note: online and offline IF variances in task-relevant space are mathematically equal to one fourth of online and offline VF variance, respectively) while both online and offline IF variances in task-irrelevant space remained unchanged throughout the conditions.
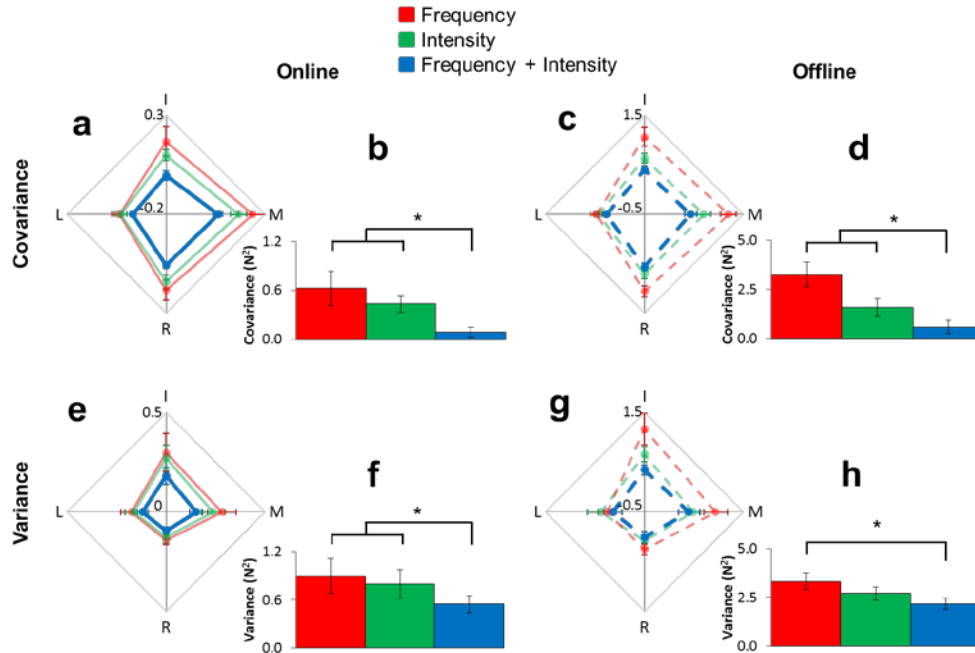
Figure 4.5. Multi-finger synergy and individual finger force variance for online and offline controls under frequency (red), intensity (green), and frequency + intensity conditions (blue) at the individual finger (IF) level. The individual fingers' contributions to the overall synergy and variance values are shown in the 4-dimensional diamond graphs (a, c, e, and g). Error bars represent s.e.m. across subjects. The accompanying bar graphs show the overall synergy and variance values (b, d, f, and h). A repeated-measures analysis of variance was performed on the overall variance and synergy values to test if these values are different among the feedback conditions. The synergy and variance, only in online control, showed statistically significant differences (asterisk, $p<0.05$ for both variance and synergy) among the feedback conditions.

4.5 Discussion

The purpose of the current study was to investigate effect of intra-auditory integration on sub-maximal multi-finger force production task. Using the hierarchical model, we found that intra-auditory integration enhances motor performance by improving the precision of the motor task (or producing the required force with less variation) in both online and offline controls while unchanging the systematic error.

In addition, intra-auditory integration enhanced motor coordination by reducing error amplification among IF in both online and offline controls.

Humans integrate multiple sensory modalities not only within the same sensory [10-15], but also between sensory [7-9] to obtain a common belief about the state of world. The Bayesian model has been proposed to interpret how the CNS integrates multiple modalities of sensory information. In integration of congruent multiple sensory modalities, this Bayesian model predicts that motor performance (e.g., goal-directed movement) is enhanced with combined sensory information. In current study, we tested whether the Bayesian model supported intra-auditory integration. The results showed that the Bayesian model well predicts intra-auditory integration during isometric multi-finger force production. Indeed, participants produced and sustained the required force level with less variable error (i.e., inverse of precision) without changes in systematic error (i.e., inverse of accuracy) when combined auditory feedbacks were presented, leading to enhancement of motor performance. These results are consistent with previous studies of inter- and intra-sensory integration [7-15, 26, 115, 116]. Thus, these results join a growing body of literature indicating that humans have the ability to optimally integrate intra-auditory modalities, enhancing motor performance.

Our study showed that the intra-auditory integration was associated with decreased co-variations of IF forces in online and offline controls. This indicates that the intra-auditory integration leads to the enhancement of motor coordination in order to improve motor performance. Although the central back coupling hypothesis proposed in the previous study demonstrated the theoretical possibility of generating

synergistic actions without an active involvement of sensory feedback, the current study suggests that the intra-auditory integration plays an important role on the formation of multi-finger synergy in goal-directed multi-finger force production

It is quite surprising that our results showed IF forces are positively co-varied for both online and offline controls. Many of previous studies showed IF forces have been co-varied negatively in a constant force production task in order to stabilize the VF force [16-19]. As a result, the relatively high variability of the IF forces results in a much lower variability of the VF force. In other words, IF forces are coordinated to compensate for error caused by variability of IF forces. Why do the IF forces act to amplify the task error (i.e., VF force variability) during a constant force production in this study? During the task, the subject relied on the auditory feedback about the information of the reference and tracking forces the subject produced, which induced relatively high task uncertainty as compared to the visual feedback used in previous studies [16-19]. The task uncertainty may cause relatively high fluctuation in the VF force consequently. As a result, the IF forces are coupled (or positively co-varied) so as to quickly increase or decrease the VF force.

Todorov and Jordan (2002) [109] proposed a principle of minimal intervention where the CNS uses feedback to correct deviations that interfere with the task goal (or minimize the variability in task-relevant space), but allows the variability in task-irrelevant space. Our results show that intra-auditory integration only decreases the variability in task-relevant space while the variability in task-irrelevant space was remained unchanged for both online and offline control, supporting the principle of minimal intervention. Note that the reduction of variability

in task-relevant space was the main cause of reduction in IF covariance and VF variance in both online and offline controls, leading to the reduction on *OMSE*. This indicates that the CNS coordinates IF forces to minimize the variability in task-relevant space while allowing the variability in task irrelevant space.

Analysis of online and offline variability has been used to reveal different aspects of the control mechanism in the redundant system [24, 57]. In a constant force production task, analysis of online control can be used to investigate the CNS's ability to perform the task on a moment-to-moment basis (i.e., *consistency*). On the other hand, analysis of offline control can be used to quantify the *repeatability* of the CNS which is an ability to reproduce the same task goal on trial-to-trial basis. In the hierarchical variability decomposition model, both *consistency* (i.e., online variable error) and *repeatability* (i.e., offline variable error) can be achieved by total amount of error by IF forces (i.e., IF variance) and the amount of error compensation (or amplification) among IF forces (i.e., IF covariance) in the lower level (IF level). We found that in the intra-auditory integration decreased covariance among IF forces in both online and offline controls. This indicates that the CNS responded to the intra-auditory integration by decreasing error amplification among IF forces in order to enhance the *consistency* and *repeatability* of the system. In addition, online IF variance and covariance are much lower than offline IF variance and covariance, respectively. This may indicate that the CNS tends to maintain the individual finger force levels initially produced in online control as compared in offline control.

One of the limitations of the current study is an assumption that a uniform prior distribution, meaning that no prior knowledge, exists. Prior knowledge is task

specific knowledge that is achieved through experience with a particular task. According the Bayesian model, prior knowledge can be integrated with new sensory information obtained in order to achieve a more reliable estimate. Future research specifically on prior knowledge will enhance our understanding of the role of intra-auditory integration.

Another limitation of the current study includes our research only on the integration of congruent auditory feedbacks. Previous sensory integration studies have suggested humans integrate either congruent or incongruent multi-sensory modalities in order to enhance motor performance, following the Bayesian model; however, our experimental design did not include incongruent auditory feedback due to different target force levels required for incongruent auditory feedback. According to the previous studies, force magnitude is associated with force variability [117-119]. In other words, the force variability can affect motor performance and potentially coordination as well. Our experiment did not involve incongruent auditory feedback in order to prevent adding additional complexity in the study design. However, the systematic investigation of incongruent auditory feedback would enhance our understanding on intra-auditory integration mechanism.

In conclusion, we investigated that the effect of intra-auditory integration on motor performance and coordination during a constant force production. It was found that intra-auditory integration enhanced motor performance and coordination. These findings support the idea of the Bayesian sensory integration which states that the CNS integrates multiple sensory modalities to enhance motor performance. In

addition, our results provide evidence that the CNS integrates multiple auditory modalities to enhance motor coordination of multi-finger.

Chapter 5: The role of uncertainty in auditory feedback on the effectiveness of intra-auditory integration

5.1 Abstract

The central nervous system (CNS) receives defective afferent signals from the sensory system and sends imperfect efferent signals to the motor system. Both signals are corrupted by intrinsic and extrinsic noises, leading to uncertainty in sensorimotor control. Much attention has been directed to the mechanisms of how the CNS deals with uncertainty in sensorimotor control in various ranges of tasks. However, little is known about the role of uncertainty in auditory-motor control on the integration of multiple auditory modalities (i.e., intra-auditory integration). Here, we investigated the role of uncertainty in auditory-motor control on intra-auditory integration in the context of the performance and coordination. For the experiments, the subjects were instructed to match the reference force of 18 N with the virtual finger force (VF force: the sum of all finger forces) where the reference force and VF forces were presented as auditory feedbacks to different ears. The feedback signal for the reference force was a sinusoid signal with a constant frequency and intensity while the feedback signal for VF force was a sinusoid signal that changed with the VF force. Three conditions were used in the experiment: frequency condition (F; the frequency changed with VF force), intensity condition (I; the intensity changed with VF force), and both frequency and intensity condition (FI; both changed with VF force). Four levels of uncertainty (high, moderate high, moderate low, and low) were manipulated by changing the auditory feedback gain. We found that motor performance and coordination were enhanced when two auditory feedbacks (the frequency and intensity) are combined compared to unimodal feedback (either the frequency or intensity of auditory feedback alone) across all of the level of uncertainties, with

significance enhancement observed at the moderate-high uncertainty. Our results indicate that the CNS integrates multiple auditory modalities to enhance the performance and coordination. Furthermore, intra-auditory integration is most effective when uncertainty in auditory feedback is moderate between two extreme levels of uncertainty (low and high uncertainty).

5.2 Introduction

The central nervous system (CNS) receives defective afferent signals from the sensory system and sends imperfect efferent signals to the motor system [5]. Both signals are corrupted by intrinsic and extrinsic noises, leading to uncertainty in sensorimotor control. For example, when playing a constant note, a violinist controls the accurate action needed to produce a desired sound; however, it is nearly impossible to repeat the same action for that sound [6]. The violinist uses the sound generated from the action in order to estimate how the note is being played; however, auditory system provides imperfect information due to the inherent noise in the neural pathway [5].

In the motor domain, it has previously been shown that the CNS coordinates multiple effectors involved in a goal-directed task so as to robust motor performance [73]. This phenomenon, known as motor synergies, has been observed in various types of hand and arm movements such as reaching, grasping and pressing [16-19, 120]. In the sensory domain, it has been suggested that the CNS integrates multiple sensory modalities in order to minimize uncertainty in the sensory system. This sensory integration has been examined in the framework of the Bayesian model. The sensory integration has been observed not only in the integration of multiple modalities within the same sensory (i.e., intra-sensory integration) [10-15], but also between sensory (i.e., inter-sensory integration) [7-9].

In the previous work, we found that the CNS integrates multiple auditory modalities (i.e., intra-auditory integration): the frequency and intensity which are the most salient features to contribute to the perception of sound in terms of pitch and

loudness [52, 99]. The intra-auditory integration leads to robust motor performance during a multi-finger constant force production task followed by the Bayesian model. Additionally, the intra-auditory integration improves synergistic actions among fingers for the enhancement of motor performance. The improvement of multi-finger synergy occurred at two different forms of variability: within-in trial variability which reflects fluctuations of multiple effectors while producing and sustaining a desired action on moment-to-moment basis using online sensory feedback (i.e., online synergy), and between-trial variability which indicates variations of multiple motor effectors during repetitions of a particular motor task in order to achieve equivalent motor outcomes to on trial-to-trial basis (i.e., offline synergy). However, it still remains unclear how intra-auditory integration affects motor performance and coordination as uncertainty in auditory feedback increases.

Previous studies found that uncertainty in sensory feedback was highly associated with motor performance and coordination in multi-finger pressing task [22, 24]. A manipulation that has been used to alter the uncertainty in visual feedback is a gain of visual feedback [24]. For example, in a constant pressing force of 20N production using four fingers of one hand, visual feedbacks for the desired force and the produced force are provided as horizontal lines on the computer screen. The uncertainty was introduced by systematically manipulating physical properties of visual feedback such as the pixel/Newton. Similarly, uncertainty in the auditory feedback can be manipulated by the changing feedback gain of frequency and intensity (e.g., Hertz/Newton, and decibel/Newton).

In the present study, we investigated the role of uncertainty in auditory feedback on effectiveness of auditory integration in sub-maximal constant force production as level of uncertainty in the auditory feedback (UAF) increases. We expected that motor performance would be enhanced by reducing the variability of the force the subject produced when frequency and intensity of auditory feedbacks are presented for all levels of UAF, following the Bayesian model. We also expected that based on our previous finding, both online and offline synergy would increase with combined auditory feedback for all levels of UAF.

5.3 Methods

5.3.1 Participants

Ten right-handed volunteers (10 males; mean age 24.5 years + 1 year SD) participated in the study. Participants were also free of neurological disorders, psychiatric disorders, speech-language disorders, and motor impairments. No participant had more than one year of musical training. Participants provided written informed consent. All procedures were approved by the University of Maryland College Park Institutional Review Board.

5.3.2 Experimental setup

Force data were collected using a 6 degree of freedom load cell (ATI Nano 17) at a sampling frequency of 1,000 Hz with data acquisition hardware (National Instruments DAQ- card-6024E) using a custom program written with Labview (National Instruments Labview 8.2). This program manipulated the frequency and

intensity of an auditory signal played to the subjects via a headphone (Bose AE2) using a dual channel function generator (Agilient 33522A). To ensure that frequency response characteristics [110] of the headphone were minimized, we calibrated the auditory signal to produce a constant intensity across all frequencies. Calibration was performed in a soundproof room by manipulating frequency from 20 to 10,000 Hz in 1 Hz increments and normalizing intensity at each increment.

5.3.3 Procedures

Participants sat, wearing headphones, with their head in a chin rest. Their right hands were placed on the load cells (Figure 5.1). Participants were instructed to produce an isometric force of 18N (20% of a typical healthy participant's maximum voluntary force [100]) by pressing the sensors with 2nd to 5th digits, and to sustain the force consistently for 20 seconds. During the task, the reference force was provided as an auditory signal, a sinusoid signal with a constant frequency and intensity (i.e., reference tone), played to the subject's left ear via the headphones. The frequency and intensity of the reference tone were selected as 1000 Hz and 70 dB in order to minimize the influence of binaural beats [111]. A second auditory signal corresponding to the force generated by the participant was provided as a sinusoid signal (i.e., tracking tone) to their right ear. Tracking tone properties were defined by three feedback conditions:

1) Frequency condition (F): the frequency of the tracking tone changed depending on the deviation of the subject's sum of finger forces from 18 N, with a constant intensity of 70 dB.

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2)   Intensity condition (I): the intensity of the tracking tone changed depending on the deviation of the subject's total finger force from 18 N, with a constant frequency of 1000 Hz.

3)   Frequency & Intensity condition (FI): both the frequency and intensity of the tracking tone changed depending on the sum of finger forces.

Participants were instructed to match the tracking tone to the reference tone with background noise of 40 dB SPL

Figure 5.1. Experimental setup. The subjects sit and place their right hand finger tips on the sensors, wearing the headphones (a). The subject is asked to produce 20N with four fingers while the reference and the tracking force the subject produce are provided as an auditory feedback. Reference tone (i.e., auditory feedback for reference force) (b in red) is a sinusoid signal with a constant frequency of 1000 Hz and intensity of 70 dB to left ear while tracking tone (i.e., auditory feedback for the tracking force) (b in green) is a sinusoid signal determined by three feedback conditions; Frequency condition (F): the frequency of the tracking tone changed

depending on the deviation of the subject's sum of finger forces from 18 N, with a constant intensity of 70 dB, 2) Intensity condition (I): the intensity of the tracking tone changed depending on the deviation of the subject's total finger force from 18 N, with a constant frequency of 1000 Hz, and 3) Frequency & Intensity condition (FI): both the frequency and intensity of the tracking tone changed depending on the sum of finger forces.

In order to present the uncertainty in the auditory feedback, we manipulated the auditory feedback gain (AFG) in frequency and intensity per Newton. For baseline condition, the AFG for frequency and intensity conditions were set as 7Hz/N and 0.7dB/N according to previous Just Noticeable Difference studies [113, 114], respectively. There were four AFGs used per each feedback (7, 24, 86, and 300 Hz/N for the frequency, and 0.7, 1.2, 3, and 7.5 dB/N for the intensity) which were categorized as high, moderate high (Mod-High), moderate low (Mod-Low), and low uncertainties. AFGs were obtained by the same increments in log scale from baseline conditions to 300Hz/N for frequency condition and 7.5dB/N for intensity condition where the experimental data showed the maximum performance. The feedback conditions were presented to participants in a random order. Participants completed 5 trials of 20 s per each condition with 30 s rest between each trial. Prior to the experiment, participants were given 5 familiarization trials.

5.3.4 Data analysis

Bayesian model

Using the framework of the Bayesian or maximum likelihood estimates (MLE), the bimodal estimate, $\hat{S}_{FI}$, of a finger force from both the frequency and

intensity modalities can be expressed as a weighted sum of the frequency, $\hat{S}_F$, and intensity estimates, $\hat{S}_I$;

$$\hat{S}_{FI} = w_F \hat{S}_F + w_I \hat{S}_I$$

If the estimates are considered a Gaussian random variable with mean μ and variance σ^2, the optimal estimate is more precise (lower variance) than the uni-modal estimates   as   follows:

$$\sigma_{FI}^2 = \frac{\sigma_F^2 \sigma_I^2}{\sigma_F^2 + \sigma_I^2}$$

The variance of combined estimate, σ_{FI}^2, is lower than the variances of the frequency, σ_F^2, and intensity estimates, σ_I^2. The combined bias b_{FI} ($= (f_T - \mu_{FI})$ where f_T is a reference force (20N here)) is expressed by a weighted average of the frequency bias, b_F, and the intensity bias, b_I with the weights, $w_F = \frac{\sigma_I^2}{\sigma_F^2 + \sigma_I^2}$ and $w_I = \frac{\sigma_F^2}{\sigma_F^2 + \sigma_I^2}$ [115, 116];

$$b_{FI} = w_F b_F + w_I b_I$$

 To test whether auditory modalities are optimally integrated, first we quantified motor performance as the overall mean-squared error (*OMSE*), the averaged squared deviation of the virtual finger force (VFF) from the reference force:

$$OMSE = \frac{1}{N} \sum_{i=1}^{N} \left\{ \frac{1}{\tau} \int [f_T - y_i(t)]^2 dt \right\}$$

where $y_i(t)$ is VFF at trial i, and τ is the duration of $y_i(t)$.

Then, we compared the experimentally obtained *OMSE* to the *OMSE* predicted by the MLE which are divided into variable error, σ_{FI}^2, (i.e., inverse of precision) and systematic error, b_{FI}^2, (i.e., inverse of accuracy) as follows:

$$OMSE_{FI} = \sigma_{FI}^2 + b_{FI}^2$$

$$= \frac{\sigma_F^2 \sigma_I^2}{\sigma_F^2 + \sigma_I^2} + (w_F b_F + w_I b_I)^2$$

Hierarchical structure of motor variability

The VFF for trial i, $y_i(t)$, was modeled as the sum of three components:

$$y_i(t) = X_i(t) + E_i + m$$

where $X_i(t)$ is the demeaned VFF for trial i, m is the mean VFF after averaging over all timesteps of all 15 trials, and E_i is the difference between the mean VFF for trial i and m.

In this model [22], *OMSE* as index of motor performance was partitioned into three error components as performance variables:

1) The "online variable error (VE_{ON})" $\overline{\sigma_X^2}$, calculated as the averaged variance of $X_i(t)$

2) The "offline variable error (VE_{OFF})" σ_E^2, calculated as the variance of E_i

3) The "systematic error (SE)" b^2, calculated as $(20 - m)^2$

Note: sum of online and offline variable error is the variance of VF force ($\overline{\sigma_X^2} + \sigma_E^2 = \sigma^2$) and the systematic error is the squared bias of VFF ($(20 - m)^2 = b_{FI}^2$).

The online and offline variable errors can be further defined as the sum of IFF variances, plus between-finger covariances: (Note that IFF varainces and covariances are used as coordination variables)

$$\overline{\sigma_X^2} = \overline{\sum \sigma_{x_i}^2} + \overline{\sum \sigma_{x_i} \sigma_{x_j}}$$

$$\sigma_E^2 = \sum \sigma_{e_i}^2 + \sum \sigma_{e_i} \sigma_{e_j}$$

where x_j is demeaned IF force of jth finger and ε_j is the IF force differences of jth finger between the means across time and mean across all time steps of 15 trials, n is the number of task fingers (n = 4) and the overhead bars indicate means over trials. The sum of IFF variances reflects the total amount of variability in the motor task, while the sum of IFF covariances reflects the total amount of error compensation (or error amplification). Note that negative covariance indicates that IFF acts to compensate each other errors (i.e., error compensation) while positive covariance is that IFF acts to amplify the VFF (i.e., error amplification). Here, we use the ratio of negation of IFF covariance to IFF variance as index of online and offline synergies, which reflect amount of error compensation (or error amplification) for given motor variability.

$$Syn(x) = \frac{-\overline{\sum \sigma_{x_i} \sigma_{x_j}}}{\sum \sigma_{x_i}^2}$$

$$Syn(e) = \frac{-\sum \sigma_{e_i} \sigma_{e_j}}{\sum \sigma_{e_i}^2}$$

The indices of synergy quantified above are mathematically equal to the motor synergy calculated in the previous studies as the normalized variance difference between in task-relevant space and task-irrelevant space using the uncontrolled manifold analysis.

5.3.5 Statistics

Paired t-test with Bonferroni correction was performed to compare the experimentally obtained *OMSE* to the *OMSE* predicted by the MLE along with variance and systematic error. A two-way repeated measures ANOVAs with factors

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Auditory Modality (3 levels: F, I, and FI) and *Uncertainty* (4 levels: low, mod-low, mod-high, and high) were used. The level of statistical significance was set at *p*=0.05. A Post-hot test with Bonferroni correction was performed to determine which feedbacks or/and levels of uncertainty exhibited significant difference. We used Greenhouse-Geisser correction for violation of sphericity. All independent variables were log-transformed to correct for a non-normal distribution using the log-modulus transformation methods [121], which allowed us to log-transform positive and negative values as follows:

$$T(x) = sign(x) \times \log(|x| + 1)$$

5.4 Results

5.4.1 Comparison of experimental data and MLE model

The *OMSE* from experimental data did not differ from the MLE at every level of uncertainty (High; p=0.381, Mod-High; p=0.59, Mod-Low; p=0.577, and Low; p=0.206), along with no significant differences in systematic error (High; p=0.367, Mod-High; p=0.093, Mod-Low; p=0.533, and Low; p=0.45). A significant difference between the VF variance from experimental and from the MLE at Mod-High uncertainty (p=0.019) was observed while no significant difference was observed at High (p=0.435), Mod-Low (p=0.844), and Low (p=0.123), (Figure 5.2c).

5.4.2 Effectiveness of auditory integration on performance

A two-way repeated measures ANOVA with Bonferroni's multiple comparisons *post hoc* test was used to compare motor performance (i.e., *OMSE*, *VE*,

and *SE*) for bimodal (i.e., IF) and unimodal (i.e., F or I) conditions across the different levels of uncertainty. A main effect of *Auditory Modality* on *OMSE* ($F_{1.119,9}$=7.728, *p*=0.017) *VE* ($F_{1.123,9}$=6.46, *p*=0.027) and *SE* ($F_{2,9}$=5.196, *p*=0.017), *Uncertainty* on *OMSE* ($F_{3,9}$=38.194, *p*<0.001) *VE* ($F_{3,9}$=59.539, *p*<0.001) and SE ($F_{1.601,9}$=13.431, *p*=0.001), *Auditory Modality* × *Uncertainty* interaction on *OMSE* ($F_{6,9}$=2.736, *p*=0.021) *VE* ($F_{6,9}$=2.831, *p*=0.018) and *SE* ($F_{2.58,9}$=1.723, *p*=0.195) was observed. In the comparison of motor performance as a function of auditory feedback conditions, the *OMSE* for bimodal condition collapsed across all feedback uncertainties were significantly lower than the *OMSE* for unimodal conditions (FI vs F; *p*=0.003, and FI vs I; *p*=0.007) (Figure 5.2a). The reduction of the *OMSE* for bimodal condition was mainly due to the reduction in the *VE* (FI vs F; *p*=0.007, and FI vs I; *p*=0.009). The *SE* for bimodal condition was not significantly lower than the *SE* for I conditions (FI vs F; *p*=0.031, and FI vs I; *p*=0.61). The Bonferroni's multiple comparison *post hoc* test revealed that the *OMSE* (FI vs F; *p*=0.002, and FI vs I; *p*=0.004) and *VE* (FI vs F; *p*=0.003, and FI vs I; *p*=0.007) for the bimodal condition was significantly lower than the *OMSE* and *VE* for the unimodal conditions at Mod-High uncertainty (Figure 5.2b). The SE for bimodal condition did not differ significantly as compared to the *SE* for unimodal conditions across all feedback uncertainties.
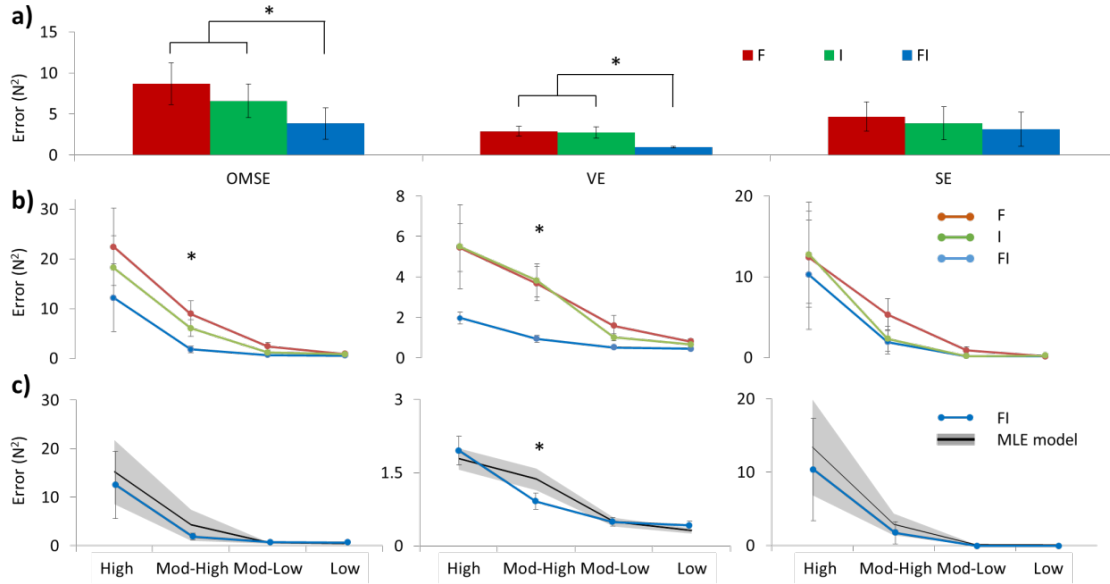
Figure 5.2. Multi-finger pressing performance measured by *OMSE*, *VE*, and *SE* under F (blue), I (red), and FI conditions (green) across feedback uncertainties. (a) *OMSE*, *VE* and *SE* for each of the conditions collapsed across all feedback uncertainties. (b) *OMSE*, *VE* and *SE* as a function of sensory modality and uncertainty. (c) The comparison of *OMSE*, *VE* and *SE* for bimodal condition calculated from MLE model and obtained from experiment. Collapsing across all uncertainties, *OMSE* for FI condition was significantly lower as compared for F or I condition alone (a). The reduction of the *OMSE* mainly resulted in the reduction of the *VE*. The *OMSE* and *VE* for the FI condition were significantly lower when compared to both the F condition and the I condition when performed under Mod-High uncertainty (a). The *VE* obtained from experimental data at Mod-High uncertainty significantly differed from the VE measured from MLE model. The asterisk indicates the significant level as $p<0.05$. Error bars represent s.e.m. across subjects.

To evaluate main contributors of performance enhancement on *VE*, we further calculated sub-performance component errors (i.e., VE_{ON}, VE_{OFF}) using the hierarchical variability decomposition model. We found a significant main effect of *Auditory Modality* on VE_{ON} ($F_{2,9}=6.354$, $p=0.008$) and VE_{OFF} ($F_{2,9}=4.584$, $p=0.025$), *Uncertainty* on VE_{ON} ($F_{3,9}=17.647$, $p<0.001$) and VE_{OFF} ($F_{3,9}=43.73$, $p<0.001$). No significant *Auditory Modality* × *Uncertainty* interaction on VE_{ON} ($F_{6,9}=1.011$, $p=0.428$) and significant interaction on VE_{OFF} ($F_{2.831,9}=3.08$, $p=0.048$) were observed.

The Bonferroni's multiple comparison *post hoc* test showed that only the VE_{OFF} for the bimodal condition was significantly lower than the VE_{OFF} for unimodal conditions at Mod-High uncertainty (FI vs F; $p=0.019$, and FI vs I; $p=0.011$) (Figure 5.3). The VE_{ON} for bimodal condition did not significantly differ from the VE_{ON} for unimodal conditions across all of uncertainties.
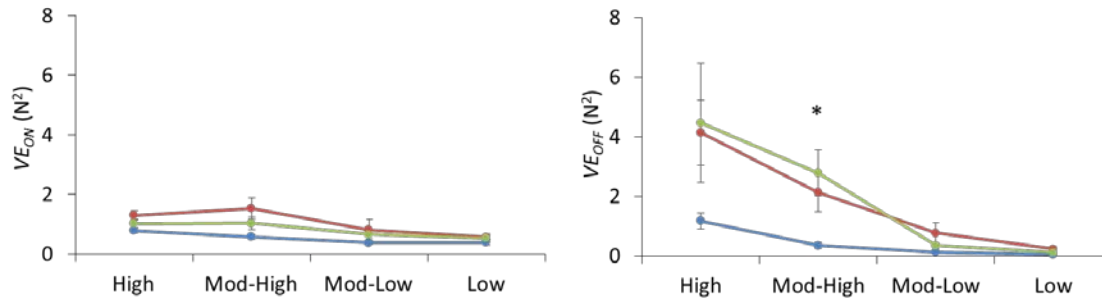
Figure 5.3. Online variable errors (VE_{ON}) and offline variable error (VE_{OFF}) under F (blue), I (red), and FI conditions (green) across feedback uncertainties. The VE_{OFF} for the FI condition were significantly lower when compared to both the F condition and the I condition when performed under Mod-High uncertainty. The asterisk indicates the significant level as $p<0.05$. Error bars represent s.e.m. across subjects.

5.4.3 Effectiveness of auditory integration on coordination

A two-way repeated measures ANOVA with Bonferroni's multiple comparisons *post hoc* test was used to compare motor coordination for bimodal (i.e., IF) and unimodal (i.e., F or I) conditions across the different levels of uncertainty. Index of online synergy (Syn_{ON}) and offline synergy (Syn_{OFF}) were used as a quantification of motor coordination. A significant main effect of *Sensory modality* on Syn_{ON} ($F_{2,9}=5.063$, $p=0.018$) and *Uncertainty* ($F_{3,9}=23.457$, $p<0.001$) were observed, but no significant *Auditory Modality×Uncertainty* interaction ($F_{6,9}=0.956$, $p=0.464$) was observed. The Bonferroni's multiple comparison *post hoc* tests revealed

that Syn_{ON} for the bimodal condition was not significantly lower than for all of unimodal conditions at any level of uncertainty. On Syn_{OFF}, we found a significant main effect of *Auditory Modality* ($F_{1.185,9}$=5.021, p=0.043), *Uncertainty* ($F_{3,9}$=21.774, p<0.001), and *Auditory modality×Uncertainty* interaction ($F_{6,9}$=2.744, p=0.021). The Bonferroni's multiple comparison *post hoc* tests revealed that Syn_{ON} for the bimodal condition was significantly lower than for all of unimodal conditions at any level of uncertainty (FI vs F; p=0.039, and FI vs I; p=0.034).
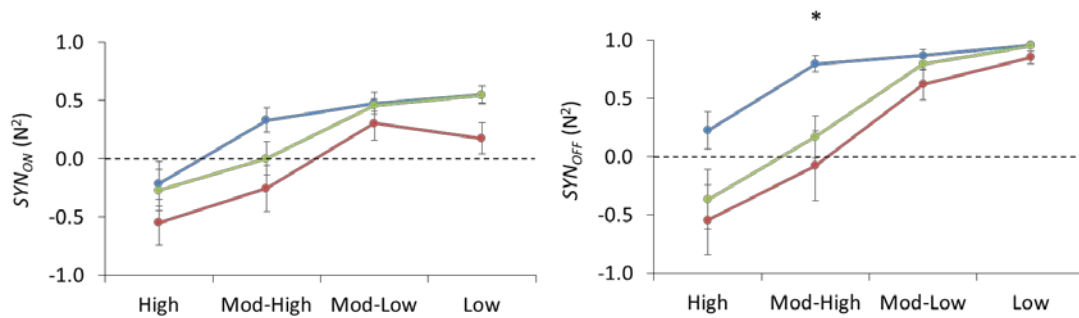
Figure 5.4. Indices of online synergy (Syn_{ON}) and offline synergy (Syn_{OFF}) under F (blue), I (red), and FI conditions (green) across feedback uncertainties. The Syn_{OFF} for the FI condition were significantly lower when compared to both the F condition and the I condition when performed under Mod-High uncertainty. The asterisk indicates the significant level as p<0.05. Error bars represent s.e.m. across subjects.

5.5 Discussion

The purpose of the current study was to investigate the effectiveness of auditory integration on motor performance and coordination as uncertainty in the auditory feedback increases. Overall, we found that motor performance and coordination were enhanced with two auditory feedbacks (frequency and intensity) compared to unimodal feedback (either the frequency or intensity of auditory

feedback alone) across all of the level of uncertainties, with significance enhancement observed at the Mod-High uncertainty.

The Bayesian model has been used to interpret sensory integration mechanisms [7-15]. A fundamental feature of the Bayesian approach to sensory integration is the minimum variance. That is, motor variability (i.e., inverse of precision) is minimized when multiple sensory modalities are combined. The results from the current study show that the precision of performance was enhanced while the accuracy remained unchanged when the frequency and intensity of auditory modalities were combined, supporting the idea of the Bayesian approach to sensory integration.

The inverse effectiveness has been also proposed for the sensory integration, which states that multisensory stimuli are more likely or effectively integrated when the best unisensory response is relatively weak [122]. Although several neurological and behavioral studies found that the motor outcomes are followed by the inverse effectiveness [123-125], we found that the auditory integration was most effective at intermediate level of uncertainty, which is inconsistent with the inverse effectiveness rule.

Why is the auditory integration most effective at intermediate level of auditory uncertainty? It may be due to floor or ceiling effects. According to the floor effect, the performance reaches the minimum when the auditory information is most uncertain. As a result, the additional auditory modality information may not be beneficial to improve the performance. On the other hands, the ceiling effect indicates that the performance improves and reaches the maximum when the auditory

information is lest uncertain. The performance is reached at maximum level with uni-auditory modality. Thus, the enhancement of motor performance from auditory integration was not observed.

Online and offline controls of human movement have been intensively investigated in the field of motor control. Online control refers to the system's ability to control all degrees of freedom in order to achieve the goal in moment-to-moment basis while offline control reflects to the system's ability to reproduce the same motor outcomes in order to achieve equivalent motor outcomes to on trial-to-trial basis. The auditory integration leads to the improvement of the precision in offline control while no changes of the precision in online control. This indicates that auditory integration influences the offline control in order to reproduce the consistent motor outcomes.

One of the limitations of the current study is an assumption that a uniform prior distribution, meaning that no prior knowledge, exists. Prior knowledge is task specific knowledge that is achieved through experience with a particular task. According the Bayesian model, prior knowledge can be integrated with new sensory information obtained in order to achieve a more reliable estimate. Future research specifically on prior knowledge will enhance our understanding of the role of intra-auditory integration.

Another limitation of the current study includes our research only on the integration of congruent auditory feedbacks. Previous sensory integration studies have suggested humans integrate either congruent or incongruent multi-sensory modalities in order to enhance motor performance, following the Bayesian model; however, our experimental design did not include incongruent auditory feedback due

to different target force levels required for incongruent auditory feedback. According to the previous studies, force magnitude is associated with force variability [117-119]. In other words, the force variability can affect motor performance and potentially coordination as well. Our experiment did not involve incongruent auditory feedback in order to prevent adding additional complexity in the study design. However, the systematic investigation of incongruent auditory feedback would enhance our understanding on intra-auditory integration mechanism.

In conclusion, we investigated the effectiveness of auditory integration on the performance and coordination as level of uncertainty in the auditory feedback increases. We found that the Bayesian model is conserved in the auditory integration by demonstrating the precision of performance is enhanced when two auditory modalities are combined. Also, we found that the intra-auditory integration is maximally effective at intermediate level of uncertainty by improving the performance. Using the hierarchical variability decomposition model, the enhancement of the auditory integration resulted in enhancement of offline control by increasing synergistic actions among the individual finger during a constant force production task.

Chapter 6: The effect of auditory-motor learning on performance and coordination

6.1 Abstract

Two hypotheses have been proposed to interpret the mechanisms of the central nervous system (CNS) for achievement of sensorimotor learning. First, the specificity of learning hypothesis proposes that the enhancement of motor performance after practice is specific to the sensory information available during practice. Second, freezing hypothesis proposes that early state of learning, the CNS solves a redundancy problem imposed by numerous degrees of freedom by eliminating superfluous degree of freedom finding a unique solution. Here, we tested whether these two hypotheses are hold in auditory-motor learning. For experiments, two groups of subjects trained a constant finger force production task with frequency modality (F), or intensity modality (I). Each group performed a pre-test (10 trials), four blocks of training test (20 trials per block), and a post-test (10 trials per condition (F, I, and FI)). Motor performance and motor coordination was quantified using a previously developed variance decomposition analysis. In our results, the enhancement of performance and coordination after practice were observed with the auditory modality available through practice. Also, we found that variability of individual finger forces was reduced while multi-finger coordination remained unchanged through practice. Our results suggested that the auditory-motor learning develops specific to the auditory modality available through practice, supporting specificity of learning hypothesis. Furthermore, practice leads to the enhancement of performance by finding a unique solution, supporting the freezing hypothesis.

6.2 Introduction

Humans have the ability to learn a variety of motor skills such as playing a musical instrument, singing, dancing, etc. Learning motor skills is the process of consolidation between the sensory and the motor systems. The process of consolidation can be achieved by error detection from the sensory system and error correction to the motor system. This is also known as sensorimotor learning where the performance enhancement in the sensory-guided motor task through practice.

It has been proposed that the sensorimotor learning is achieved through sensory-modality-specific practice which has been known as the specificity of learning hypothesis [31]. For example, Proteau and his colleagues [126] investigated the effect of practice on visual feedback availability during a manual-aiming task. In their experiment, two group of subjects practiced reaching to a target with either a full-vision feedback, in which the target and hand were always visible, or with a target-only feedback, in which only the target was visible. After practice, motor performance for both groups was enhanced through practice. However, transferring from full-vision to target-only feedback in the full-vision group caused deterioration in motor performance. Since the first study of Porteau in 1987, the specificity of learning has been supported by a variety of manual-aiming tasks [127, 128] to gross motor tasks such as walking and weightlifting [129, 130].

Another view on the sensorimotor learning is based on Bernstein's postulation on the motor redundancy problem[3] in human movements [6]. Bernstein suggests that the CNS tends to freeze or eliminate the redundant degrees of freedom (DOFs) and

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[3] Motor redundancy problem states there are multiple ways to perform a particular task in order to achieve the goal-equivalent motor outcomes in human movement.

find a unique solution in early stages of learning, which is known as freezing hypothesis of motor learning [34]. Previous studies showed that variability of joint angles in a reaching task [35-37] and multi-finger forces in a pressing task [38] deceased with practice, supporting the freezing hypothesis.

In the previous work, we have demonstrated that motor performance and coordination could be enhanced when both frequency and intensity of auditory information were utilized by the central nervous system (CNS) as compared to the frequency and intensity only conditions. The frequency and intensity are the most salient features contributing to the perception of pitch and loudness in sound [52, 99], respectively. Our study showed that the integration of multiple auditory modalities enhanced motor performance by improving the precision through increased synergistic actions between fingers (i.e., error compensation between motor effectors resulting in enhancing motor performance). Here, we tested how practice affects motor performance and coordination in the context of the integration of multiple auditory modalities.

The current study was to investigate the effect of auditory-motor learning on the performance and coordination during a multi-finger constant force production task. Our hypotheses are two-fold. First, according to the specificity of learning hypothesis, we expected that the enhancement of motor performance and coordination after practice is specific to the auditory modality available through practice. Second, according to the freezing hypothesis, we expected that the variability of individual finger forces would be reduced after practice, resulting in the enhancement of motor performance.

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6.3 Methods

6.3.1 Participant

Twenty-three right-handed volunteers (11 males and 12 females; 20 to 29 years of age) participated in the study. Participants were also free of neurological disorders, psychiatric disorders, speech-language disorders, and motor impairments. No participant had more than one year of musical training. Participants provided written informed consent. All procedures were approved by the University of Maryland College Park Institutional Review Board.

6.3.2 Experimental setup

Force data were collected using a 6 degree of freedom load cell (ATI Nano 17) at a sampling frequency of 1,000 Hz with data acquisition hardware (National Instruments DAQ- card-6024E) using a custom program written with Labview (National Instruments Labview 8.2). This program manipulated the frequency and intensity of an auditory signal played to the subjects via a headphone (Bose AE2) using a dual channel function generator (Agilient 33522A). To ensure that frequency response characteristics [110] of the headphone were minimized, we calibrated the auditory signal to produce a constant intensity across all frequencies. Calibration was performed in a soundproof room by manipulating frequency from 20 to 10,000 Hz in 1 Hz increments and normalizing intensity at each increment.

Figure 6.1. Experimental setup. The subjects sit and place their right hand finger tips on the sensors, wearing the headphones (a). The subject is asked to produce 20N with four fingers while the reference and the tracking force the subject produce are provided as an auditory feedback. Reference tone (i.e., auditory feedback for reference force) (b in red) is a sinusoid signal with a constant frequency of 1000 Hz and intensity of 70 dB to left ear while tracking tone (i.e., auditory feedback for the tracking force) (b in green) is a sinusoid signal determined by three feedback conditions; Frequency condition (F): the frequency of the tracking tone changed depending on the deviation of the subject's sum of finger forces from 18 N, with a constant intensity of 70 dB, 2) Intensity condition (I): the intensity of the tracking tone changed depending on the deviation of the subject's total finger force from 18 N, with a constant frequency of 1000 Hz, and 3) Frequency & Intensity condition (FI): both the frequency and intensity of the tracking tone changed depending on the sum of finger forces.

6.3.3 Behavioral task and auditory feedback condition

Participants sat, wearing headphones, with their head in a chin rest. Their right

hands were placed on the load cells (Figure 6.1). Participants were instructed to

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produce an isometric force of a reference force by pressing the sensors with 2nd to 5th digits, and to sustain the force consistently for 20 seconds. The reference forces were determined by 18 N for male and 15 N for female, which showed their averaged 20% maximum voluntary force. During the task, the reference force was provided as an auditory signal, a sinusoid signal with a constant frequency and intensity (i.e., reference tone), played to the subject's left ear via the headphones. The frequency and intensity of the reference tone were selected as 1000 Hz and 70 dB in order to minimize the influence of binaural beats [111]. A second auditory signal corresponding to the force generated by the participant was provided as a sinusoid signal (i.e., tracking tone) to their right ear. Tracking tone properties were defined by three feedback conditions:

1)   Frequency condition (F): the frequency of the tracking tone changed depending on the deviation of the subject's sum of finger forces from a target force, with a constant intensity of 70 dB.

2)   Intensity condition (I): the intensity of the tracking tone changed depending on the deviation of the subject's total finger force from a target force, with a constant frequency of 1000 Hz.

3)   Frequency & Intensity condition (FI): both the frequency and intensity of the tracking tone changed depending on the sum of finger forces.

Participants were instructed to match the tracking tone to the reference tone with background noise of 40 dB SPL. The changing in frequency and intensity per Newton were set as 24Hz/N and 1.2dB/N where the intra-auditory integration was most effective (Chapter 5).

6.3.4 Data analysis

The VFF for trial i, $y_i(t)$, was modeled as the sum of three components:

$$y_i(t) = X_i(t) + E_i + m$$

where $X_i(t)$ is the demeaned VFF for trial i, m is the mean VFF after averaging over all timesteps of all 15 trials, and E_i is the difference between the mean VFF for trial i and m.

OMSE as index of motor performance was partitioned into three error components as performance variables using the hierarchical variability decomposition (HVD) model [22]:

4) The "online variable error (VE_{ON})" $\overline{\sigma_X^2}$, calculated as the averaged variance of $X_i(t)$

5) The "offline variable error (VE_{OFF})" σ_E^2, calculated as the variance of E_i

6) The "systematic error (*SE*)" b^2, calculated as $(20 - m)^2$

The online and offline variable errors can be further defined as the sum of IFF variances, plus between-finger covariances: (Note that IFF varainces and covariances are used as coordination variables)

$$\overline{\sigma_X^2} = \overline{\sum \sigma_{x_i}^2} + \overline{\sum \sigma_{x_i} \sigma_{x_J}}$$

$$\sigma_E^2 = \sum \sigma_{e_i}^2 + \sum \sigma_{e_i} \sigma_{e_j}$$

where x_j is demeaned IF force of jth finger and ε_j is the IF force differences of jth finger between the means across time and mean across all time steps of 15 trials, n is the number of task fingers (n = 4) and the overhead bars indicate means over trials. The sum of IFF variances reflects the total amount of variability in the motor task,

while the sum of IFF covariances reflects the total amount of error compensation (or error amplification). Note that negative covariance indicates that IFF acts to compensate each other errors (i.e., error compensation) while positive covariance is that IFF acts to amplify the VFF (i.e., error amplification).

6.3.5 Statistics

A mixed analysis of variance (ANOVA) using repeated measures with within factors, *Test* (Pre-Test and Post-Test), *Auditory Modality* (3 levels: F, I, and FI) and between factor, *Group* (3 levels: F, I, and FI groups) was used. The level of statistical significance was set at *p*=0.05. A Post-hoc test was performed to determine which sensory modality or/and training group exhibited significant difference when ANOVA revealed any significant effects. All independent variables were log-transformed to correct for a non-normal distribution using the log-modulus transformation methods [121], which allowed us to log-transform positive and negative values:

$$T(x) = \ sign(x) \times \log(|x| + 1)$$

6.4 Results

6.4.1 Freezing hypothesis

OMSE and *SE* remained unchanged through practice for all groups. Although two-way repeated measures ANOVA revealed a significant main effect of *Test* on *OMSE* ($F_{1,20}$=7.796, *p*=0.011), along with no significant main effect of *Group*

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($F_{1,20}$=0.622, p=0.547) nor *Test × Group* interaction ($F_{2,20}$=0.067, p=0.935), post-hoc tests revealed no significant differences for all groups (F group; p=0.190, I group; p=0.102, and FI group; p=0.095). On *SE*, there was no significant main effect of *Test* ($F_{1,20}$=2.635, p=0.120), main effect of *Group* ($F_{1,20}$=1.333, p=0.286), nor *Test × Group* interaction ($F_{2,20}$=0.185, p=0.833). However, practice led to a significant decrement in *VE_{ON}* for all groups during the multi-finger pressing task. These observations have been confirmed with two-way repeated measures ANOVA which revealed a significant main effect of *Test* ($F_{1,20}$=20.962, p<0.001), but no significant main effect of *Group* ($F_{1,20}$=0.761, p=0.480) nor *Test × Group* interaction ($F_{2,20}$=0.227, p=0.799). Post-hoc tests revealed *VE_{ON}* for Post-test was significantly lower as compared to Pre-test for all groups (F group; p=0.012, I group; p=0.041, and FI group; p=0.008). Practice also led to a significant decrement in *VE_{OFF}* for I and FI groups. Two-way repeated measured ANOVA revealed that a significant main effect of *Test* ($F_{1,20}$=18.139, p<0.001), but no significant main effect of *Group* ($F_{1,20}$=0.436, p=0.652) nor *Test × Group* interaction ($F_{2,20}$=1.019, p=0.379). Post-hoc tests revealed *VE_{OFF}* for Post-test were significantly lower as compared to Pre-test for I (p=0.011) and FI groups (p=0.005).
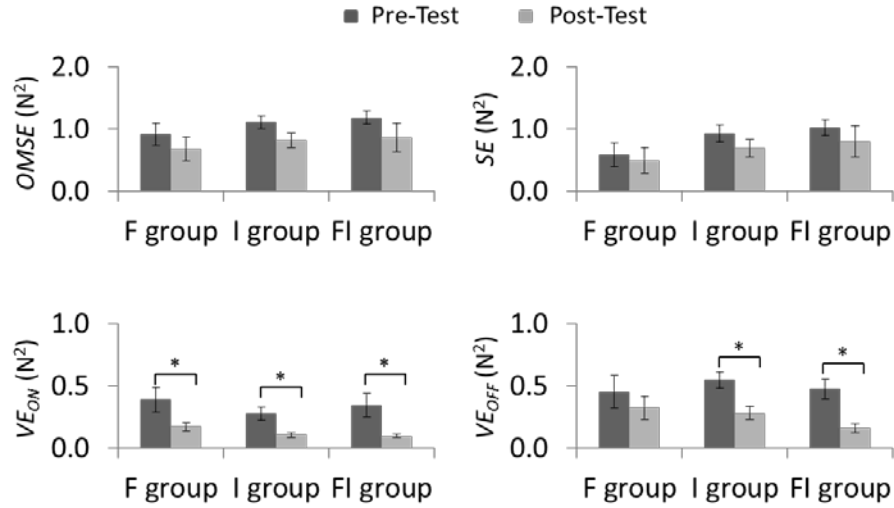
Figure 6.2. Multi-finger pressing performance measured by *OMSE*, *SE*, VE_{ON} and VE_{OFF} for Pre-Test and Post-Test. Two-way mixed ANOVA revealed that a significant main effect of *Test* (Pre-Test and Post-Test) on *OMSE*. Post-hoc test revealed that OMSE for all groups was no significant difference at Post-Test as compared to Pre Test (upper left panel). Using the HVD model, we further calculated *SE*, *VE* $_{ON}$ and VE_{OFF} of which the summation is equal to *OMSE*. SE remained unchanged between Pre-Test and Post-Test for all groups. However, VE_{ON} was significantly lower at Post-Test as compared to Pre-Test for both all groups (lower left panel. VE_{OFF} only for I and FI groups were significantly lower at Post-Test as compared to Pre-Test (lower right panel). The asterisk indicates the significant level as *p*<0.05. Error bars represent s.e.m. across subjects.

To evaluate the main contributors of the changes on VE_{ON} and VE_{OFF} variables through practice, we further calculated coordination variables (*Var*$_{ON}$, *Cov*$_{ON}$, *Var*$_{ON}$, and *Cov*$_{ON}$) using the HVD model. A two-way ANOVA with repeated measures revealed a significant main effect of *Test* on *Var*$_{ON}$ ($F_{1,20}$=24.473, *p*<0.001), *Cov*$_{ON}$ ($F_{1,20}$=5.021, *p*=0.037), *Var*$_{OFF}$ ($F_{1,20}$=13.837, *p*=0.001) and *Cov*$_{OFF}$ ($F_{1,20}$=4.507, *p*=0.046) was observed. Neither a significant main effect of *Group* on *Var*$_{ON}$ ($F_{1,20}$=1.138, *p*=0.340), *Cov*$_{ON}$ ($F_{1,20}$=0.528, *p*=0.598), *Var*$_{OFF}$ ($F_{1,20}$=0.429, *p*=0.657), and *Cov*$_{OFF}$ ($F_{1,20}$=0.207, *p*=0.815) nor *Test* × *Group* interaction on *Var*$_{ON}$ ($F_{1,20}$=0.158, *p*=0.855), *Cov*$_{ON}$ ($F_{1,20}$=0.722, *p*=0.498), *Var*$_{OFF}$ ($F_{1,20}$=0.265, *p*=0.770),

and Cov_{OFF} ($F_{1,20}$=1.434, p=0.262) was observed. Post-hoc tests revealed that Var_{ON}

(F group; p=0.007, I group; p=0.023, and FI group; p=0.006) was significantly lower

at Post-Test as compared to Pre-Test. Thus, the reduction of VE_{ON} for all groups was

mainly due to the reduction of Var_{ON}. Var_{OFF} for both F group (p=0.011) and I group

(p=0.005) were significantly lower at Post-Test as compared to Pre-Test, but Var_{OFF}

for FI group (p=0.187) was not significantly different. Cov_{OFF} for FI group (p=0.005)

was significantly lower at Post-test as compared to Pre-Test, but Cov_{OFF} for F

(p=0.187) and I groups (p=0.187) were not significantly different (Figure 6.3). Thus,

the reduction of VE_{OFF} for I and FI groups was mainly due to the reduction of Var_{OFF}

while the reduction of VE_{OFF} for F group was mainly due to the reduction of Cov_{OFF}.
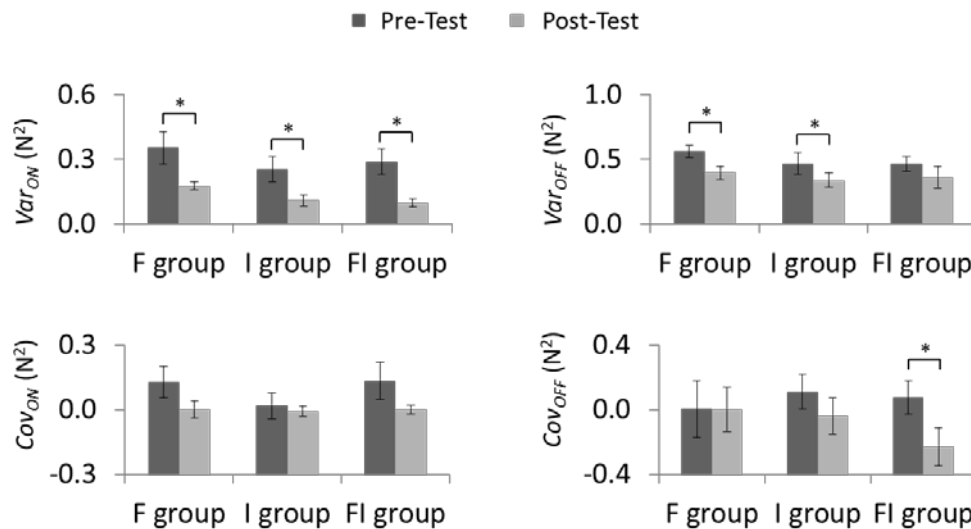
Figure 6.3. Multi-finger coordination measured by Var_{ON}, Cov_{ON}, Var_{OFF}, and Cov_{OFF} through practice. The bar graphs show the total variance and covariance among individual finger forces for F, I and FI groups between Pre-Test (dark gray) and Post-Test (light gray). A repeated-measures ANOVA was performed on the overall variance and covariance values to test if these values are different between Pre-Test and Post-Test. Var_{ON} for all groups F, I and FI groups showed a significantly lower at Post-Test as compared to Pre-Test, and Var_{OFF} for both F and I groups showed a significantly lower while Var_{OFF} for FI group showed no significant difference. Cov_{ON} for all groups showed no significant difference but Cov_{OFF} for FI group showed a significant different between Pre-Test and Post-Test. The asterisk indicates the significant level as p<0.05. Error bars represent s.e.m. across subjects.

6.4.2 Specificity of learning hypothesis

A two-way mixed ANOVA with repeated measures that revealed a significant main effect of *Auditory Modality* on *OMSE* ($F_{2,20}$=7.096, p=0.002) and *Auditory Modality* × *Group* interaction ($F_{4,20}$=3.586, p=0.014), but no significant main effect of *Group* ($F_{2,20}$=0.905, p=0.421) was observed. Post-hoc tests revealed that in F group, *OMSE* with I condition was significantly lower as compared to either F condition (p=0.011) or FI condition (p=0.037). *OMSE* with F condition was not significantly different as compared to FI condition (p=0.764). In I group, *OMSE* with F condition was significantly lower as compared to either I condition (p=0.041) or FI condition (p=0.003). *OMSE* with I condition was not significantly different as compared to FI condition (p=0.523). In FI group, *OMSE* with FI condition was significantly lower as compared to either F condition (p=0.004) or I condition (p=0.039). *OMSE* with F condition was not significantly different as compared to I condition (p=0.742) (Figure 6.4).
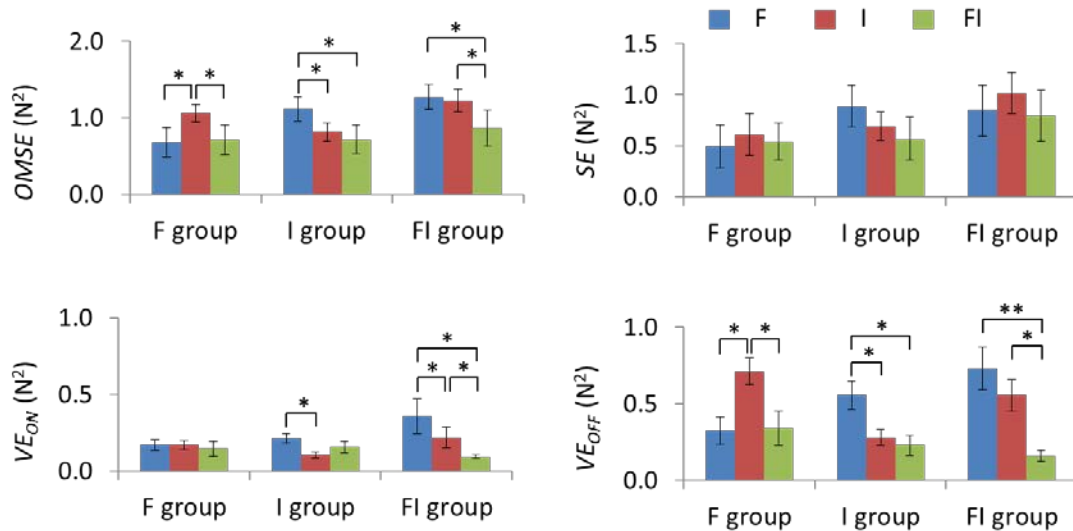
Figure 6.4. Multi-finger pressing performance after practice under three auditory feedback conditions measured by *OMSE*, *SE*, VE_{ON} and VE_{OFF}. Two-way mixed ANOVA revealed that a significant main effect of *Auditory Modality* on *OMSE*, and a significant *Auditory Modality* × *Group* interaction, but no significant main effect of *Group*. Post-hoc tests revealed that in F and I groups, *OMSE* was significantly lower with the auditory modality provided through practice as compared to the auditory modality not provided (F group; $p=0.011$ and I group; $p=0.041$) when F condition was compared to I condition. *OMSE* with bimodal (FI condition) was significantly lower as compared to the auditory modality not provided through practice (F group; $p=0.037$ and I group; $p=0.003$), but not significantly different as compared to the auditory modality provided (F group; $p=0.764$ and I group; $p=0.523$) (upper left panel). In FI group, FI condition was significantly lower than either F only ($p=0.004$) or I only condition ($p=0.039$). There were no significant differences between F and I conditions ($p=0.742$). Using the HVD model, the changes in *OMSE* as a function of auditory modalities was mainly caused by the changes in VE_{OFF}. Post-hoc tests revealed that VE_{OFF} in both F and I groups were significantly lower with the auditory modality provided through practice as compared to the auditory modality not provided (F group; $p=0.008$ and I group; $p=0.048$). VE_{OFF} with bimodal (FI condition) was significantly lower as compared to the auditory modality not provided through practice (F group; $p=0.008$ and I group; $p=0.003$), but not significantly different as compared to the auditory modality provided (F group; $p=0.862$ and I group; $p=0.677$) (lower right panel). VE_{OFF} in FI group was significantly lower with the auditory modality provided through practice as compared to the auditory modality not provided (F vs FI condition; $p<0.001$ and I vs FI condition; $p=0.007$). There was no significant difference between F and I condition ($p=0.227$). The asterisk indicates the significant level (* $p<0.05$ and ** $p<0.01$). Error bars represent s.e.m. across subjects.

To evaluate main contributors to changes on *OMSE*, we further calculated sub-performance component errors (i.e., VE_{ON}, VE_{OFF}, and *SE*) using the HVD model. We found a significant main effect of *Auditory Modality* on VE_{ON} ($F_{2,20}$=6.813, *p*=0.003) and VE_{OFF} ($F_{2,20}$=10.984, *p*<0.001) and a significant *Auditory Modality* × *Group* interaction on VE_{ON} ($F_{4,20}$=3.090, *p*=0.026) and VE_{OFF} ($F_{4,20}$=5.790, *p*=0.001) were observed, but no significant main effect of *Auditory Modality* on *SE* ($F_{2,20}$=1.184, *p*=0.317) nor *Auditory Modality* × *Group* interaction on *SE* ($F_{4,20}$=1.082, *p*=0.378) was observed. There was no significant main effect of *Group* on VE_{ON} ($F_{2,20}$=0.732, *p*=0.493), VE_{OFF} ($F_{2,20}$=1.001, *p*=0.385), and SE ($F_{2,14}$=0.686, *p*=0.515). Post-hoc tests revealed that in F group, there were no significant differences across feedback conditions on VE_{ON} (F vs I; *p*=0.978, F vs FI; *p*=0.703, and I vs FI; *p*=0.629), but in I group, VE_{ON} with I condition was significantly lower than F condition (*p*=0.034), and in FI group, VE_{ON} was significantly different across feedback conditions (F vs I; *p*=0.015, F vs FI; *p*=0.001, and I vs FI; *p*=0.027).

In F group, VE_{OFF} with I condition was significantly lower as compared to F condition (*p*=0.008) or FI condition (*p*=0.008). VE_{OFF} with F condition was not significantly different as compared to FI condition (*p*=0.862). In I group, VE_{OFF} with F condition was significantly lower as compared to either I condition (*p*=0.048) or FI condition (*p*=0.003). VE_{OFF} with I condition was not significantly different as compared to FI condition (*p*=0.677). In FI group, *OMSE* with FI condition was significantly lower as compared to F condition (*p*<0.001) or I condition (*p*=0.007), but not significantly different between F condition and I condition (*p*=0.227) (Figure 6.4).
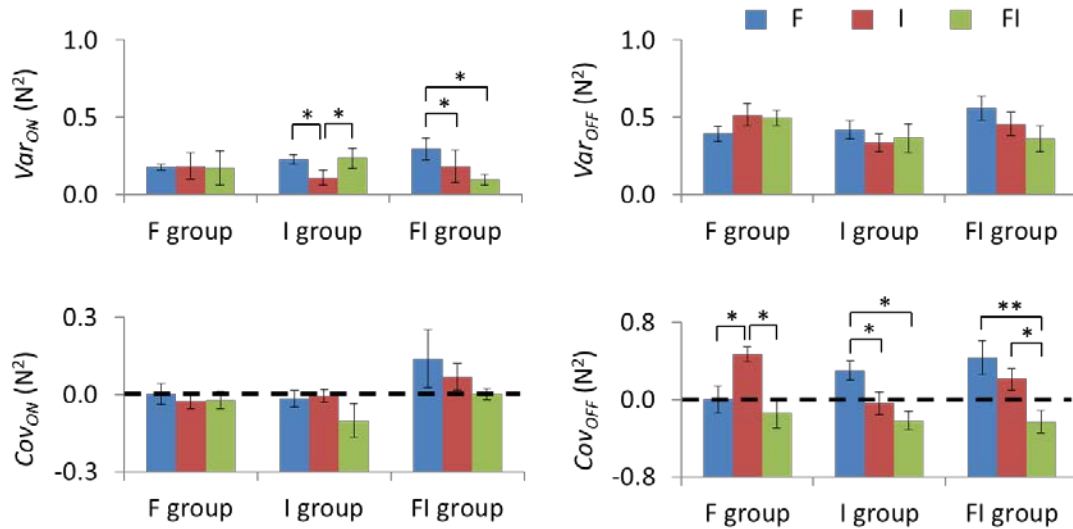
Figure 6.5. Multi-finger coordination after practice under three auditory modality conditions measured by Var_{ON}, Cov_{ON}, Var_{OFF}, and Cov_{OFF}. Var_{ON} and Var_{OFF} refer to the total variability of the system, and Cov_{ON} and Cov_{OFF} indicate the error compensation among individual finger forces if the values are negative (below the dashed line) or the error amplification if values are positive (above the dashed line). Var_{ON} in I group was significantly lower with I condition as compared to either F only ($p=0.009$) or FI condition ($p=0.017$). Var_{ON} in FI group was significantly lower with F condition as compared to either I only ($p=0.019$) or FI condition ($p=0.001$). Cov_{OFF} in both F and I groups was significantly lower with the auditory modality provided through practice as compared to the auditory modality not provided (F group; $p=0.018$ and I group; $p=0.025$) in the comparison of unimodal conditions (F or I condition). Cov_{OFF} with bimodal (FI condition) was significantly lower as compared to the auditory modality not provided through practice (F group; $p=0.001$ and I group; $p=0.006$), but not significantly different as compared to the auditory modality provided (F group; $p=0.417$ and I group; $p=0.238$) (lower right panel). In FI group, Cov_{OFF} with FI condition was significantly lower as compared to either F only ($p=0.001$) or I only condition ($p=0.011$). The asterisk indicates the significant level (* $p<0.05$ and ** $p<0.01$). Error bars represent s.e.m. across subjects.

In the coordination variables (Var_{ON}, Cov_{ON}, Var_{OFF}, and Cov_{OFF}), two-way mixed ANOVA with repeated measures revealed that a significant main effect of *Auditory Modality* on Var_{ON} ($F_{2,20}=4.269$, $p=0.021$) and Cov_{OFF} ($F_{2,20}=12.586$, $p<0.001$), along with a significant *Auditory Modality × Group* interaction Var_{ON} ($F_{4,20}=4.328$, $p=0.005$) and Cov_{OFF} ($F_{4,20}=3.717$, $p=0.012$). There were no significant main effect of *Auditory Modality* on Cov_{ON} ($F_{2,20}=3.153$, $p=0.054$) and Var_{OFF}

($F_{2,20}$=0.710, p=0.498), along with a significant *Auditory Modality × Group* interaction *Cov$_{ON}$* ($F_{4,20}$=0.772, p=0.550) and *Var$_{OFF}$* ($F_{4,20}$=2.759, p=0.051). There were no significant main effect of *Group* on *Var$_{ON}$* ($F_{2,20}$=0.052, p=0.949), *Cov$_{ON}$* ($F_{2,20}$=1.678, p=0.212), *Var$_{OFF}$* ($F_{2,20}$=1.678, p=0.212), and *Cov$_{OFF}$* ($F_{2,20}$=0.557, p=0.581). Post-hoc tests revealed that in F group, there were no significant differences across feedback conditions on *Var$_{ON}$* (F vs I; p=0.820, F vs FI; p=0.963, and I vs FI; p=0.809), but in I group, *Var$_{ON}$* with I condition was significantly lower than F condition (p=0.009), and in FI group, *Var$_{ON}$* with FI condition was significantly different as compared to either F only (p=0.019) or I only condition (p=0.001). In F group, *Cov$_{OFF}$* with I condition was significantly lower as compared to either F only (p=0.018) or FI condition (p=0.001), but not significantly different as compared to FI condition (p=0.417) (Figure 6.5). In I group, *Cov$_{OFF}$* with F condition was significantly lower as compared to either I (p=0.025) or FI condition (p=0.006). *Cov$_{OFF}$* with I condition was not significantly different as compared to FI condition (p=0.238). In FI group, *Cov$_{OFF}$* with FI condition was significantly lower as compared to either F (p=0.001) or I condition (p=0.011). *Cov$_{OFF}$* with F condition was not significantly different as compared to I condition (p=0.265).

6.5 Discussion

This study was designed to examine auditory-motor learning through the utilization of the specificity of learning hypothesis and the freeing hypothesis. We hypothesized that the enhancement of motor performance and coordination   after practice would be specific to the auditory modality available through practice, based

on the specificity of learning hypothesis [31]. We also hypothesized the variability of individual finger forces after practice would decrease, according to the freezing hypothesis [34].

Our results supported the specificity of learning hypothesis, showing that motor performance for all groups was enhanced (i.e., decrease in *OMSE*) with the feedback condition which is available through practice as compared to the feedback condition which is completely new to the performer. These results indicate that the CNS achieves the auditory-motor learning in a constant force production task, relying on the source of afferent information available. These results are consistent with the findings in previous studies about manual aiming [31, 131], and goal-directed locomotion [132, 133], both of which, suggest that the enhancement of motor performance is specific to the sensory information available through practice.

Interestingly, we found that in both F and I groups, motor performance was not significantly different with the feedback condition which is available through practice as compared to FI combined condition. In the previous study, we found that motor performance was enhanced with FI combined feedback during a constant force production task which supports the ideas utilized in the Bayesian integration [10-15]. Thus, one can expect that motor performance after practice are enhanced when the frequency and intensity modalities are utilized together by the CNS as compared to utilizing either the frequency or intensity modalities individually. On the other hands, according to the specificity of learning hypothesis, we expected that adding sensory information (i.e., auditory integration) would lead to a decrement in performance because sensorimotor representation developed specific to the sensory modality

available through practice; however, in the current study, motor performance with the auditory modality available through practice was not significantly different from with combined information (FI condition). These results are inconsistent with the prediction of the Bayesian model and the specificity of learning hypothesis. In our experimental design, the frequency and intensity of sound used as auditory feedbacks are the most salient features contributing to pitch and loudness, respectively. These two quantities have been hypothetically thought to be perceived independently [52, 99]. Thus, it may be possible for the CNS to be able to separate each modality in the combined afferent signal and to rely on the auditory modality developed to the auditory-motor presentation, leading to similar level of motor performance.

Using the HVD model, we found that motor performance was enhanced (i.e., decreased in *OMSE*) for the specificity of learning mainly due to improvement of precision in offline control (decreased in Var_{OFF}) by reduction of covariation among individual fingers. This indicates that the enhancement of motor performance, which is specific to the auditory modality available through practice, is achieved by increasing synergistic actions during repetitions of a particular motor task.

The second aim of the current study was to test the freezing hypothesis in the auditory-motor learning. The freezing hypothesis suggested by Bernstein states that at early stage of the learning, the CNS tries to solve the redundancy problem induced by redundant DOFs involved a particular action by reducing "working space" of DOFs and finding a unique solution. Our results supported the freezing hypothesis, by showing that the variability of individual finger forces decreased through practice in F and I groups, while covariation among individual finger forces remained unchanged.

This indicates that the CNS minimizes the "working space" of individual fingers with no changes of multi-finger synergy. These results was consistent with the finding in previous studies [38, 134] which investigated the effect of the motor learning on the changes in the patterns of multi-finger variability. In these previous studies, uncontrolled manifold analysis was used to quantify the variability, which allows quantifying the variability of the system into the task-relevant variability which affects the performance and the task-irrelevant variability which does not. We found that variability in task-relevant as well as task-irrelevant space decreased through practice, indicating that practice leads to the reduction of working space of individual fingers.

Humans use sound intensity level difference of both ears to localize the source of location, which is known as the interaural level difference (ILD) [135]. In our experimental design, the intensity condition is directly related to the ILD mechanism. In the current study, we found that I and FI groups enhanced motor performance by improving the precision in offline control through practice. This may indicate that the intensity of auditory information is more beneficial for improving the performance through practice due to ILD mechanism.

In conclusion, we found that the enhancement of motor performance and coordination after practice was specific to the intra-auditory modality available during practice, which supports the specificity of learning hypothesis. Practice leads to the enhancement of performance by the reduction of variability among multiple effectors in both online, supporting the freezing hypothesis.

Chapter 7: Conclusions

This dissertation investigated the mechanisms of intra-auditory integration for the control of multiple fingers during constant force production tasks, specifically regarding how the CNS utilizes multiple sources in auditory feedback, how the CNS deals with uncertainty in auditory feedback, and how the CNS adapts or learns a motor task using auditory feedback. The conclusions of the experiments presented in this dissertation are as follows:

We developed new analytical techniques for the linear decomposition of the overall variability in a redundant motor system in both online and offline control, along with the quantification of precision and accuracy in outcomes of a multi-effector motor system.

We found that intra-auditory integration enhanced motor performance and coordination. These findings support the idea of the Bayesian sensory integration where multiple sources of sensory information are integrated in statistically optimal fashion. In addition, our results provide evidence that the central nervous system integrates the frequency and intensity of auditory information to enhance the coordination of multi-finger.

We found that the intra-auditory integration is maximally effective at intermediate level of uncertainty by improving the performance. Using the hierarchical variability decomposition model, the enhancement of the auditory integration resulted in enhancement of offline control by increasing synergistic actions among the individual finger during a constant force production task.

We found that the enhancement of performance and coordination after practice was specific to the intra-auditory modality available during practice, which supports the specificity of learning hypothesis. Practice leads to the enhancement of performance by the reduction of variability among multiple effectors in both online, supporting the freezing hypothesis.

7.2 Future Directions

The results from this dissertation have identified a number of control mechanisms in auditory-motor integration. These results can be used to guide additional studies targeted at providing a better understanding of human control mechanisms. The following experiments are suggested as continuations of this dissertation research:

1. Investigating the effect of integration of incongruent auditory modalities on motor performance and coordination

2. Investigating the effect of integration of more than two modalities such as the frequency, intensity, and harmony of auditory information on motor performance and coordination

3. Investigating the effect of intra-visual integration on motor performance and coordination.

4. Investigating the effect of intra-auditory integration on performance and coordination during a dynamical task.

5. Investigating the role of motor dependent noise in the auditory information on the intra-auditor integration.

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