Title of Thesis

Study on Tactile Spatial and Temporal Processing in Human Somatosensory System using Behavioral Experiment and Event-related Potentials

2018 September

Yang Liu

The Graduate School of

Natural Science and Technology

(Doctor's Course)

OKAYAMA UNIVERSITY

Abstract

Individuals are often surrounded by stimuli from various sensory modalities (e.g., auditory, visual, olfactory, somatosensory). The brain can screen available information from multiple senses and integrate them to better perceive the external environment, shaping and guiding our behaviours. The somatosensory system is a part of the sensory nervous system. The somatosensory system is a complex system of sensory neurons and pathways that responds to changes at the surface or inside the body. Tactile signals are sensed by mechanoreceptors distributed over the elastic surface of the body, i.e., the skin. When the skin contacts an object, it is spatially deformed. As the skin or the body moves relative to the object, this deformation pattern is spatially shifted. This shift is the source of the brain's ability to know the location changes or movements of an object on the skin. Spatial and temporal factors are received separately and integrated in the human brain and, thus, provide a comprehensive understanding of the real world. Therefore, it is important to study integration across sensory modalities. However, the neural mechanism of spatial and temporal processing in human somatosensory system is not completely clear.

The main aim of this present thesis was to investigate the spatial and temporal processing in human somatosensory system by vibration stimulation through behavioral and electroencephalography (EEG) experiments.

The dissertation contains descriptions of the four experiments and a general discussion briefly introduced below.

Chapter 1 describes the concept of somatosensory system and the sense of touch. The previous studies of spatial and temporal processing in monkeys and humans have also been summarized hear. Additionally, the technique of electroencephalogram (EEG) and event-related potential (ERP) have been introduced. At last, the purpose and contents of the thesis are briefly described.

Chapter 2 describes a device which we developed a novel automatic vibrotactile patterns delivery capable of perform the tactile cognitive experiment. It can serve to determining the sensitivity of each finger that contributes to tactile spatial discrimination. To evaluate the performance of the device, we conducted a basic function test. The results indicated that the device can record reliable data and control the tactile pattern position precisely.

Chapter 3 introduces the first experiment, which measures vibration stimulation in human fingers by using behavioral measurements. This part aim to determine the spatial characteristics when the stimuli simultaneous presented on the different regions of the hand. We investigated tactile numerosity judgments and position report tasks by simultaneously presenting between 1 and 8 vibrotactile stimuli on the hand. The accuracy data from numerosity judgments task indicated that performance was poor when more than 3 stimuli were activated. And as the more stimulus presentation, the answer is smaller than the correct answer. Position report task indicated that the accuracies were changed when the tactile stimuli presented on different place and the increased of stimuli number also effected the accuracy. The results of the two experiments reported in this part demonstrate that people are to some extent able to discriminate between different numbers of tactile stimuli when multiple stimuli are activated simultaneously across the hand.

Chapter 4 describes the second experiment, in which we used a similar parameter to investigated the aging effect of vibrotactile stimulus counting abilities by behavioral measurements in youngers and older adults. In the present study, we asked 15 younger (mean age 22.7 ± 0.8 years) and 10 older (mean age 67.9 ± 5.1 years) subjects to perform a tactile stimulus numerosity task, and we recorded their response accuracy to investigate the effects of aging on vibrotactile stimulus counting abilities. The results showed that as the calculation trials increased, the accuracy rate decreased in both young and old groups (p < 0.05). In addition, in the older group, the decrease in the accuracy as the number of calculation trials increased was greater than that in the younger group. In other words, this decrease in the older group may be explained by a reduction in working memory capacity, which is directly caused by a decline in basic tactile cognitive ability.

Chapter 5 describes the third experiment. In the present ERP study, we modified the traditional spatial attention paradigm by adding the double stimuli with short interval (i.e., 10, 30, and 100 ms) conditions to approach how the somatosensory system processes the balance between excitation and inhibition. A total of five kinds of stimulation were used in the experiment which are single stimulus (one raised pin for 40 ms), standard stimulus (eight pins for 40 ms), interval 10 ms, 30 ms, 100 ms double stimuli. Subjects were asked

to pay attention to the instructed finger and detect whether the standard stimulus was presented to the finger. The results showed clear attention component of the single stimulus condition, but the suppression component of three interval conditions seem dominant in the somatosensory areas. In detail, we found that the strongest suppression effect in interval 30 ms condition, and the suppression and enhancement effects seem counterbalance for both of interval 10 ms and 100 ms conditions. This processing may allow the human easily to discriminate multi-stimulations on the same body part.

Chapter 6 conclusions of the dissertation and future challenges are put forward.

According to the current situation, future studies will focus on tactile spatiotemporal integration with ERP technique. I hope to find the neural mechanism of spatiotemporal integration and to provide important basis for the cognitive neuroscience in human.

Table of Contents

Abstract	I
Chapter 1 Introduction	1
1.1 The somatosensory system	2
1.2 The sense of touch	
1.3 Spatial and temporal processing on touch	
1.4 Related studies on touch	5
1.4.1 Related studies for vibrotactile	
1.4.2 Related studies for spatial and temporal processing	6
1.5 Event-related potentials (ERPs)	7
1.5.1 Electroencephalogram (EEG)	7
1.5.2 Event-related potentials (ERPs)	
1.5.3 Analysis method of ERPs data	9
1.6 The purpose of the present thesis	9
Chapter 2 Development and evaluation of vibrotactile stime	uli presentation
device	11
2.1 Background	
2.2 Device development	
2.3 Evaluation experiments	
2.3.1 Subjects	
2.3.2 Stimuli	
2.3.3 Position report task	
2.3.4 Result	
2.4 Discussion	
2.5 Conclusion	
Chapter 3 Tactile spatial processing in human somatosensor	y system using
behavioral experiments	22
3.1 Background	
3.2 Methods and apparatus	
3.2.1 Subjects	
3.2.2 Device and stimuli	
3.2.3 Experimental procedure	

3.2.3.1 The numerosity judgment task	
3.2.3.2 The position report task	
3.3 Results	
3.3.1 The numerosity judgment task	
3.3.2 Position report task	
3.4 Discussion	
Chapter 4 Tactile spatial processing and counting abilities in human so	omatosensory
system	34
4.1 Background	
4.2 Methods	
4.2.1 Participants	
4.2.2 Experimental equipment and stimuli	
4.2.3 Procedure and design	
4.3 Results	
4.3.1 The accuracy of the stimulus position judgement task	
4.3.2 The accuracy of the stimulus counting task	
4.4. Discussion	
4.4.1 Distribution of tactile receptive field	
4.4.2 The aging effect of working memory capacity	
4.5. Conclusions	
Chapter 5 Stimuli interval modulates the balance of brain activity i	n the human
primary somatosensory cortex: an ERP study	48
5.1 Background	
5.2 Methods	50
5.2.1 Participants	50
5.2.2 Material and procedure	50
5.2.3 EEG recording and data analysis	53
5.3 Results	
5.4 Discussion	
Chapter 6 General conclusion and future projections	59
6.1 General conclusions	60
6.2 Future projections	62
Appendix	63

I. Simple introduction of vibrotactile device	
II. Simple introduction of EEG apparatus	66
III. Simple introduction of primary somatosensory cortex	69
Publications	72
Acknowledgements	74
References	75

Chapter 1 Introduction

Summary

This chapter introduces the concept of somatosensory system and the sense of touch. The previous studies of spatial and temporal processing in monkeys and humans have also been summarized hear. Additionally, the technique of electroencephalogram (EEG) and event-related potential (ERP) have been introduced. At last, the purpose and contents of the thesis are briefly described.

1.1 The somatosensory system

The somatosensory systems inform us about objects in our external environment through touch (i.e., physical contact with skin) and about the position and movement of our body parts (proprioception) through the stimulation of muscle and joints. The somatosensory systems also monitor the temperature of the body, external objects and environment, and provide information about painful, itchy and tickling stimuli. The sensory information processed by the somatosensory systems travels along different anatomical pathways depending on the information carried. For example, the posterior column-medial lemniscal pathway carries discriminative touch and proprioceptive information from the body, and the main sensory trigeminal pathway carries this information from the face. Whereas, the spinothalamic pathways carry crude touch, pain and temperature information from the body, and the spinal trigeminal pathway carries this information from the face.

The somatosensory systems process information about, and represent, several modalities of somatic sensation (i.e., pain, temperature, touch, proprioception). Each of these modalities can be divided into sub-modalities, as shown in Table 1.1 (e.g., pain into sharp, pricking, cutting pain; dull, burning pain; and deep aching pain). Discriminative touch is also subdivided into touch, pressure, flutter and vibration. Each of these sensations (i.e., sub-modalities) is represented by neurons that exhibit modality specificity. That is, when a somatosensory neuron is stimulated naturally (e.g., by skin warming) or artificially (e.g., by electrical stimulation of the neuron), the sensation perceived is specific to the information normally processed by the neuron (i.e., warm skin). Consequently, a "warm" somatosensory neuron will not respond to cooling of the skin or to a touch stimulus that does not "warm" the skin. The somatosensory receptor and its central connections determine the modality specificity of the neurons forming a somatosensory pathway (Figure.1.1).

		-		
Modality	Sub Modality	Sub-Sub Modality	Somatosensory pathway(Body)	Somatosensory pathway(Face)
Pain	sharp cutting pain		Neospinothalamic	Spinal Trigeminal
	dull burning pain		Paleospinothalamic	
	deep aching pain		Archispinothalamic	
Temperature Touch	warm/hot		Paleospinothalamic	
	cool/cold		Neospinothalamic	
	itch/tickle&crude touch		Paleospinothalamic	
		touch		
	discriminative touch	pressure		
		flutter		
		vibration		
Proprioception		muscle length		Main Sensory Trigeminal
	position: static forces	muscle tension	Medial Lemniscal	
		joint pressure		
		muscle length		
	movement; dynamic forces	muscle tension		
		joint pressure		
		joint angle		

Table 1.1 The Sensory Modalities Represented by the Somatosensory Systems

In addition, tactile stimuli are external forces in physical contact with the skin that give rise to the sensations of touch, pressure, flutter, or vibration. We normally think of touch as involving minimal force on-or-by an object that produces very little distortion of the skin. In contrast, pressure involves a greater force that displaces the skin and underlying tissue. Time varying tactile stimuli produce more complex sensations such as object movement or object flutter (20 to 50 Hz) or vibration (100 to 300 Hz).

1.2 The sense of touch

In our daily life we place great emphasis on vision and hearing because they can make us more aware of the surroundings. However, sense of touch processing plays a key role in our surroundings, it can use short-term memory systems to extract stimuli from our daily activities. From the previous research "sense of touch" in fact comprises two distinct senses which were the cutaneous and kinesthesis senses.

Cutaneous sense receives sensory inputs from the receptors embedded in the skin and kinesthesis sense receives sensory inputs from the receptors within muscles, tendons and joints [1-3]. It should be noted that the sensory inputs are not only mechanical stimulations but also heat, cooling and various stimuli that produce pain. Sensations from these receptors are carried by nerves to the spine and then ascend to the brain using the spinothalamic pathway (Figure.1.1). While the anterior spinothalamic tract carries crude touch and pressure sensations, the lateral tract carries pain and temperature sensations.

Sensations reach the thalamus where the signals are sorted and processed before being relayed to the primary somatosensory cortex (SI) in the cerebral hemispheres.

The SI is located in the postcentral gyrus and contains a somatotopic organization of body representations. This area was the first cortical region to be shown to be involved in the perception of touch. These areas 3b and 1 of the SI are activated by all types of touch signals from the skin's mechanoreceptors, such as the indentation of the object-skin contact. In contrast, area of 2 of SI was significantly activated more by shape and surface curvature than roughness and object-skin contact.



Fig. 1.1 Somatosensory pathway. There is precise wiring between the periphery and the cerebral cortex. Through the long nerves- and relayed in the thalamus- all somatosensory information ends up at a particular site in the cortex.

1.3 Spatial and temporal processing on touch

We perceive the world around us through multiple senses. As we know, the hands are the basic tools which we interact with the world. They are the more important parts of the body and closely related to movements and perceptions. The fingertips, can be considered as the main somatosensory counterparts used for tactile perception. Tactile signals are sensed by mechanoreceptors distributed over the surface all through the body, such as the skin. When the skin or the body moves relative to the object, this spatially shifted is occurred on the skin [4]. The brain understands objects through this shift in the skin, including positional changes or movements. Recent studies shows that this type of spatiotemporal input pattern is considered to be detected by coincidence detectors with delay lines [5, 6], or spatiotemporal energy detectors [7].

In touch, there are two groups of sensory processing with different spatial and temporal characteristics [8-12] : Pacinian corpuscles (PC channel) and non-Pacinian (non-PC) channels. In fact, many studies have reported behavioral and neuronal evidence indicating that the non-PC channels are related to tactile movement/orientation detection [13-15]. And spatiotemporal integration of tactile inputs from different skin areas and body parts is an important function of the human sensory cortex [16].

1.4 Related studies on touch

1.4.1 Related studies for vibrotactile

Skin vibrations sensed by tactile receptors contribute significantly to the perception of object properties during tactile exploration and to sensorimotor control during object manipulation. Recent years, vibrotactile have been extensively studied in various fields.

Several studies have shown the analgesic effect of both tactile and vibratory stimuli in psychophysiological evaluation in healthy subjects [17, 18] and in chronic pain conditions [19, 20]. Additionally, an electrophysiological study with laser-evoked potentials demonstrated the attenuation of a vertex component by concurrently applied vibratory stimulation. Because these studies presented nociceptive and non-nociceptive stimuli simultaneously, cross-modal interaction most likely occurred in the spinal cord. On the contrary, recent somatosensory evoked potential (SEP) and magnetic field (SEF) studies [21, 22] have indicated a supraspinal mechanism in tactile-induced pain relief via experimental paradigms with concurrent bimodal inputs at the cortical level.

A number of studies used vibrotactile stimulus to investigated the neural mechanism of sustained spatial attention in somatosensory cortex. An electroencephalography (EEG) study using tactile spatial sustained attention to mechanical stimuli found that the earliest somatosensory component (P50) was significantly increased for attended stimuli [23]. In a simultaneous EEG-fMRI study, Schubert and colleagues [24] by means of Braille stimulation found significant effects of spatial-selective attention for the P50 and P100 for left and for the N80 for right tactile stimuli in SI.

1.4.2 Related studies for spatial and temporal processing

One of the ways to solve the spatiotemporal integration of systematically in tactile perception is sensory saltation [25, 26]: If two stimuli are presented at two different positions with a short delay, the perceived position of the first stimulus – the attractee – is mislocalised toward the position of the second stimulus – the attractant – and this mislocalisation increases with decreasing delays between the two stimuli.

Electrophysiological recording studies in monkeys indicate that neuronal receptive fields in S2 [27-29] and PV [27, 30, 31] are large, encompassing multiple digits or even the entire hand. Further, these receptive fields are often bilateral, including, for example, both the contra- and ipsilateral hand. Studies of neuroanatomical connections also show that, beside the local homotopic connections in the ipsilateral hemisphere, both S2 [31, 32] and PV [32-34] have dense bilateral connections.

In addition, another electrophysiological study in owl monkeys [35] selected paired skin sites and delivered pulses simultaneously (0ms delay) and onset asynchronies of 10, 30, 50, 100, and 500ms delay to investigated how temporal factors influence spatial interactions. This study indicated that the maximal suppressed of firing rates when stimulus onsets were 30-50 Ms. The owl monkeys used drugs to keep them in a sedative state in this study, in other words, this suppressed effect was under unattended condition.

Previous study of spatiotemporal integration at the human hand has been conducted to date: Warren, Santello, and Helms Tillery [36] presented tactile spatiotemporal patterns across fingertips and could demonstrate that when the tips of the second and fifth digit were stimulated with a delay of 100 ms, the stimulus presented to the second digit was reported to be perceived at the tip of the third digit in 20–30% of the trials. These findings

can be interpreted as indicating that spatiotemporal integration does occur over the range of several fingers.

1.5 Event-related potentials (ERPs)

1.5.1 Electroencephalogram (EEG)

Electroencephalography (EEG) is an electrophysiological monitoring method to record electrical activity of the brain. It is typically noninvasive, with the electrodes placed along the scalp, although invasive electrodes are sometimes used such as in electrocorticography. EEG measures voltage fluctuations resulting from ionic current within the neurons of the brain. In clinical contexts, EEG refers to the recording of the brain's spontaneous electrical activity over a period of time, as recorded from multiple electrodes placed on the scalp. Diagnostic applications generally focus either on eventrelated potentials or on the spectral content of EEG. The former investigates potential fluctuations time locked to an event like stimulus onset or button press. The latter analyses the type of neural oscillations (popularly called "brain waves") that can be observed in EEG signals in the frequency domain.

Figure 1.2 shows recorded EEG data. EEG recordings show the overall activity of the millions of neurons in the brain. The recording shows fluctuations with time that are often rhythmic in the sense that they alternate regularly. The EEG patterns change when external stimuli (such as sounds or pictures) are presented.



Figure 1.2 Recorded EEG data

1.5.2 Event-related potentials (ERPs)

An event-related potential (ERP) is the measured brain response that is the direct result of a specific sensory, cognitive, or motor event. More formally, it is any stereotyped electrophysiological response to a stimulus. The study of the brain in this way provides a noninvasive means of evaluating brain functioning. The transient electric potential shifts (so-called ERP components) are time-locked to the stimulus onset with the present trigger to marking the onset time (Figure 1.3). Each component reflects brain activation associated with one or more mental operations. Contrasting with behavioral measures such as response times, ERPs are characterized by simultaneous multi-dimensional online measures of polarity (negative or positive potentials), amplitude, latency, and scalp distribution. Therefore, ERPs can be used to identify and distinguish neural and psychological sub-processes involved in perceptual, motor, or cognitive tasks.



Figure 1.3 A waveform showing several ERP components, including the N100 (labeled N1) and P300 (labeled P3).

1.5.3 Analysis method of ERPs data

The ERPs elicited by the task-irrelative stimuli were analyzed. The data were band-pass filtered from 0.1 - 60 Hz during recording at a sample rate of 500 Hz. The data were divided into epochs, from -100 ms before to 500 ms after the stimulus onset, and baseline corrections were made against a -100 ms to 0 ms time interval before stimuli onset. Trials with horizontal eyeball movements (horizontal EOG amplitudes exceeding \pm 25 mV), vertical eye movements and eye blinks (vertical EOG amplitudes exceeding \pm 100 mV), or other artifacts (a voltage exceeding \pm 80 mV relative to baseline) were rejected automatically from the analysis. In addition, the data associated with a false alarm were excluded. The data were then averaged for each stimulus type, following digital filtering with a band-pass filter of 0.01 - 30 Hz, and the grand-averaged data were obtained across all participants for each stimulus type in each electrode.

1.6 The purpose of the present thesis

The main aim of this present thesis was to investigate the spatial and temporal processing in human somatosensory system by vibration stimulation through behavioral and electroencephalography (EEG) experiments.

Chapter 1 Introduces the concept of somatosensory system and the sense of touch. The

Chapter 1 Introduction

previous studies of spatial and temporal processing in monkeys and humans have also been summarized hear. Additionally, the technique of electroencephalogram (EEG) and event-related potential (ERP) have been introduced. At last, the purpose and contents of the thesis are briefly described.

Chapter 2 Describes a device which we developed a novel automatic vibrotactile patterns delivery capable of perform the tactile cognitive experiment. It can serve to determining the sensitivity of each finger that contributes to tactile spatial discrimination. To evaluate the performance of the device, we conducted a basic function test. The results indicated that the device can record reliable data and control the tactile pattern position precisely.

Chapter 3 Describes the tactile spatial characteristics in younger group. We developed a tactile vibration system for this study. The results show that the device can be short lasting tactile representations of stimuli presented in parallel across the hand. And through the tactile numerosity judgments and position report task, we found the spatial characteristics in youngers.

Chapter 4 Describes the tactile spatial characteristics in younger and older groups. We use the same experimental conditions as chapter 2 to investigated the efffects of aging on vibrotactile stimulus counting abilities.

Chapter 5 Describes the how short ISI modulates brain activity in human using ERP, and further investigated the diversity in different ISI conditions and in which stage that the diversity was presented.

Chapter 6 Present a general conclusion based on the findings of the three experiments. And the future challenges are also described.

Chapter 2 Development and evaluation of vibrotactile stimuli presentation device

Summary

Human have five senses which are visual, auditory, smell, touch and taste. The sense of touch is occurring when the skin contact with any object and human can percept the shape, temperature, vibration of the object. As well known, the spatial density of receptors located in the human skin differed of different parts such as index finger. Therefore, the sensitivity of each finger were differed from each other. In the present study, we developed a novel automatic vibrotactile patterns delivery device that is capable of perform the tactile cognitive experiment. It can serve to determining the sensitivity of each finger that contributes to tactile spatial discrimination. The primary device consists of eight piezo-electric units, slider, hand support and a controller. The device is controlled by a computer. To evaluate the performance of the device, we conducted a basic function test. The results indicated that the device can record reliable data and control the tactile pattern position precisely. Finally, ten young subjects consented to participate in the position discrimination tasks. The subjects were asked to detect the tactile stimuli and report the location. We found that index finger has higher accuracy of vibrotactile discrimination than the other fingers. Moreover, the sensitivity of distal phalanx part is higher than middle phalanx.

2.1 Background

According to the book of physiologist Weber (EH Weber, 1795-1878) of Germany who has been called the father of modern tactile research, tactile is only defined by the action of receptors in the skin (touch, pressure, temperature and cold). The types of the tactility, it is possible to distinguish between contact, pressure, motion, vibration, hardness, smooth and rough, but in actual fact tactility becomes a variety of combination.

Studies [37-39] on the perception of touch with cognitive psychology technique has been widely used. These results indicated that human have the ability to identify various things in our daily life by using only the sense of touch. The ability like this can be seen even in everyday life. For example, it is possible that what you want to take out such as lipstick, pen, card case and wallet contained in the bag, take out them by touch without looking at the inside. However, even if it able to identify an object only by touch (three-dimensional), two-dimensional is not possible to identify the product at a similar level to three-dimensional. Klatzky and colleagues [40] investigated the difference of the shape recognition by touch. They used two-dimensional depicted in a convex shape of the real objects from our daily life, such as scissors and glasses. The result reported that subjects were able to identify what they touched more than 70% of the real thing. However, in the convex stimulation of two-dimensional was depicted, subjects discriminated only less than 40%. Thus, the major difference is seen in the ability to discriminate from the differences of the amount of information obtained fundamentally in two-dimensional and three-dimensional.

The initiative of the human touch is issued from the human brain. From the hands and determines the shapes of the products. When we explore the outside world by hand, not only the superficial touch of skin, as well as proprioceptive organ located in muscle, tendon and joint and so on. These proprioceptive organs are activated by the hand or finger movements. This demonstrated that active tactile including kinesthetic as well as cutaneous sensation.

In the previous study, the cognitive psychology experiments using the vibration stimulus have reported the human characteristics of tactile position determination and stimulus number judgment [41, 42]. During the experiment, the subjects were asked to report the

number of tactile vibration stimulus that is presented to the body surface in the stimulus number judgment task. The result suggested that the accuracy decreased when the number of the stimulus was increased and all the stimulus of presentation number was underestimated. Moreover, the accuracy of stimulus decision task was higher than stimulus location decision task [43]. Counting the number of vibration stimulation to the body surface is very difficult for human [41, 42, 44], that suggested the "change blindness" may affect the perception of tactile vibration stimulus [45-47].

According to the previous research [48], we knew that when the vibrate stimuli frequency is below 8Hz, we can clearly feel the vibration of the subject is the up and down movement. And when the vibration stimuli frequency greater than 25 Hz, can appeared very obvious individual differences. In order to make the subject to feel clearly up and down movement stimuli and get rid of the significant differences of individuals, we develop equipment with 10Hz frequency in this study.

2.2 Device development

First, the system is safe for the subjects. Second, the system can present in a random order, a multitude of tactile patterns (e.g., 10 patterns at the same time) to a designated location. Third, the system can measure the difference between the subject's index finger and the other fingers, the sensitivity between the subject's distal phalanx and the middle phalanx of the finger.

The system of this study was shown in Figure.2.1. Send a twelve digits signal (for example: 001255010005) from the PC. This signal through the microcontroller (PIC16F88) is controlled by 64ch serial-to-parallel converter (HV507), the selection of the vibration stimulus presentation cell stimulation and the piezo-electric can be points of presented stimuli at any position on fingers.



Figure 2.1 Device system

Chapter 2 Development and evaluation of vibrotactile stimuli presentation device

As shown in Fig.2, the vibration stimulus is presented by the piezo-electric. The eight white cylinders were made by insulated organic plastic. When the tactile vibrotactile stimuli were presented, piezo-electric under the white cylinders were produced the vibrotactile stimuli press strength of the spots is 0.177N. Lead to upper points of presented stimuli start to vibrate. Subjects can feel the vibrations stimulus obviously. Because the white cylinders were insulated, so the subject was no having any pain arising from electric shock or the other tactile effects. As shown in Figure (b), two vibrotactile units were installed on the left and right side. Eight white cylinders were fixed form like the 2×4 array [49]. The distance between the upper and lower points is 2.4mm, and width is 4.8mm. The purpose of this design is that we can present the stimuli at both fingertips and second knuckle as same time.



Figure 2.2 (a) One sell of the piezo-electric device. (b)The distance of the piezo-electric device

Figure.2.3 showed the controller used in this system. In this figure, we used the USB cable connected to computer (a). Below the controller (b), there have a cable that used connected to the vibration stimulation prompts device. And this control device need a 5V DC power source (c).

Chapter 2 Development and evaluation of vibrotactile stimuli presentation device



Figure 2.3 Control device

The major component of the vibration stimulus device is shown in Figure.2.4. It consists of the piezo-electric device, slit for sliding and the hand plate. The slits in the fixed base of the piezo-electric device, the piezo-electric device can move in the direction of the arrow. This configuration allowed us to adjust the stimuli location for different individual to fit their hand size. And the length of the piezo-electric device is shown as Figure.2.5.



Figure 2.4 Device system

The subjects put the palm of right hand on the plate through the experiment (Figure.2.6). Adjust the position of the piezo-electric device consistent with the position of the finger for the subjects. By using elastic kept to the finger of right hand tightening with fixation unit in this way, is not to allow the finger to bend during the experiment. The vibration stimulation is controlled by the controller.



Figure 2.5 Distance of the device



Figure 2.6 Fixation unit for Hand

Chapter 2 Development and evaluation of vibrotactile stimuli presentation device

The photo of the experiment device is shown in Figure.2.7. The experiment was conducted in a normally illuminated room, with participants sitting on a chair. The control device received the signal and controlled by PC, through the piezo-electric device vibration stimulation is presentation.



Figure 2.7 The photo of the experiment device

2.3 Evaluation experiments

2.3.1 Subjects

Ten healthy subjects (mean age, 22.8 years; standard deviation 0.8 years) participated in this study with informed consent according to a protocol approved by the institutional review board of the National Institute of Mental Health. Subjects were tested at the right hand.

The subjects had no history of neurological or psychiatric disorders, neurological trauma, disabling medical conditions, or brain abnormalities as evidenced by MRI and had normal neurological examinations that were performed by a neurologist.

2.3.2 Stimuli

We used the experimental device as described above. The distal phalanx of the index finger named Id, the middle phalanx unit named Im; the distal phalanx of the middle finger named Md, the middle phalanx unit named Mm; the distal phalanx of the ring finger named Rd, the middle phalanx unit named Rm; the distal phalanx of the little finger named Ld, the middle phalanx unit named Lm. (Figure 2.8)



Figure 2.8 Definition of the places of presented stimuli

2.3.3 Position report task

This experimental task of vibration stimulus numbers 1 to 3 was presented at the right hand. Subjects were required to answer the stimulate prompt place ((Id was ①,Im was ②,Md was ③,Mm was ④,Rd was ⑤,Rm was ⑥,Ld was⑦,Lm was ⑧) between the delay periods, and we are beside the subjects to record the answer that subjects response to the vibration stimulus during the experiment. If the subjects did not answer within the delay periods, the answer is wrong to be considered. The tactile vibration stimuli using frequency 10Hz and the presented time is 500ms, delay periods between the vibration stimulus indication was used 3000ms ~ 5000ms shown as Figure.2.9.

By presenting at the same time more than the vibration stimulus, when one stimulus presentation number was 8 types, 2 was 28 types, 3 was 56 types stimulus was indicated.



Figure 2.9 Time chart of the task

2.3.4 Result

The mean percent correct of stimulus presentation location for each finger was shown as Figure.2.10. And the vertical axis was the accuracy rate of the stimulus presentation number, the horizontal axis shows the location of stimulus presentation, error bars represented the standard error of the percentage of correct. The black bar is one stimulus presented, grey bar is two stimulus presented, white bar is three stimulus presented.

It has been seen that accuracy rate when stimulus number was 1 and 2, achieved a superior in the stimulus presentation place for each from the results of Figure.2.10. If you do repeat measures analysis of variance, there is a main effect on stimulus presentation number (F (7, 63) =23.6, p<0.001) and stimulus presentation location (F (7, 63) =8.33, p<0.001), and interaction in the accuracy rates and the stimulus presentation location (F (49,441) =4.23, p<0.001). By comparing the each of the stimulus presentation number, there is a significant difference between one stimulus and two to three stimulus, two stimuli and three stimuli. Also, compared to the stimulus presenting location for each, there was a significant difference between Id and Mm, Rm, Ld, Lm (p <0.05). Compared to the middle phalanx unit and the fingertip of hand, the accuracy rates on the fingertip was significantly higher than the middle phalanx unit of hand when the person who

presented a vibration stimulus (p < 0.05). Also, compared to stimulus presentation location and stimulus presentation number for each by chance level, there was no significant difference in Mm when stimulus presentation number was 3.



Figure 2.10 Accuracy rates every place of presented stimuli every numbers of presented stimuli of position report task

2.4 Discussion

There was no significant difference in accuracy rates (p = ns) with the stimulus position judgment task. This may suggest that there is no difference in difficulty to the task of answering the position of the vibration stimulus This result was consistent with conventional research [43].

The results also indicated that the accuracies were changed when the tactile stimuli presented on different place and the increased of stimuli number also effected the accuracy. The percentage of correct answers at the middle phalanx unit was lower than the fingertip, especially in Mm.

However, the accuracy of Im is significantly higher when stimulus presentation number is 8 in the same middle phalanx unit. It is inferred that there is a difference in function of humans' index finger and otherwise, or tactile information to the finger as being transmitted is preferred for more of the index finger has a higher information superiority [50-52].

Because the density of mechanoreceptors unit is high in index finger that it can exactly

recognized the stimulus. And in the middle phalanx unit can be predicted accuracy rates falls for density of mechanoreceptors unit is lower than the fingertip. There is no much difference in the density of mechanoreceptors unit in the middle phalanx unit and fingertips of the index finger in the Slowly Adapting I (SAI). Hence, Im suspected that accuracy rate is obtained as much as the tactile vibration stimulus of Id.

In addition, as the stimulus presentation number increased in Md and Rd, accident error of the accuracy rates was less than other stimulus presentation location. However, when the stimulus presentation number is low, there are many mistakes in Md and Rd. From this, index finger not only high on the information advantage, compared with other fingers, it also can obtain the information correctly.

2.5 Conclusion

In conclusion, we successfully developed a vibrotactile stimuli presentation device. All tactile research programs can adopt this method or system for the study of peripheral tactile. Moreover, we plan to continue the study to improve the tactile properties and convenience of the system.

Chapter 3 Tactile spatial processing in human somatosensory system using behavioral experiments

Summary

To investigate the tactile numerosity judgments and position report by simultaneously presenting, we asked human subjects to answer the number and the location of eight vibrations presented to different fingertips on right hand. In numerosity judgments task, we found that the accuracy of participants' responses decreased as the number of stimuli activated was increased. And as the more stimulus presentation, the answer is smaller than the correct answer. In position report task, we found that index finger has higher accuracy of vibrotactile discrimination than the other fingers. Moreover, the sensitivity of distal phalanx part is higher than middle phalanx.

3.1 Background

The somatosensory system is a complex sensory system. It has been shown in earlier studies that there are four different types of receptors in the glabrous skin area of the human hand [48]. It also comprises essential processing centers, or sensory modalities, such as proprioception, touch, temperature, and nociception. The haptic is including the ability to identify the weight, pressure and temperature, furthermore haptic could orientate the stimulus location [53]. For example, we can dissociate information about features of objects touched from knowledge of the spatial location of bodily contact [54]. And the flutter is primarily mediated by rapidly adapting cutaneous mechanoreceptors [55].

Studies [37-39] on the perception of touch with cognitive psychology technique have been widely used. Numerous researchers have used edge, grating, simple shapes or letter patterns to investigate tactile discrimination ability. Recent studies have used grating orientation as a measure of tactile spatial acuity on the fingers. The two-point threshold is probably the best-known method to evaluate the spatial resolution capacity of the skin [56, 57]. And it was also suggested that the two points threshold may not represent effective measures space vision [56, 58]. However, the most prominent alternative to the classical two-point threshold discussed in the literature is the grating orientation threshold(GOT) [59].

Klatzky and colleagues [40] investigated the difference of the shape recognition by touch. In a cognitive psychology study to explore the perceptual processing of shape recognition, it was found that people could identify 100 commonly used objects with almost 100% accuracy by touching alone when blind-folded, typically within only 2-3s per object [60]. And the tactile discrimination ability associated with active and passive touches suggested that the accuracy of shape discrimination by active touch was higher than that achievable by passive touch [61].

Several studies examined neurophysiological mechanisms of short-term memory through vibrotactile stimuli [62, 63]. Previous studies have demonstrated that people are generally quite poor at reporting the number of vibrotactile stimuli presented in their body surface [43]. In particular, when as few as three vibrotactile stimulus presented, the

percentage of error in counting the number becomes very high [64]. Such results have been interpreted by many authors as providing evidence for the existence.

In addition, through the two-point threshold and shape recognition, we knew that there are differences in the ability to identify the various parts of the hand. Therefore, in present study, we investigated tactile numerosity judgments and position report by simultaneously presenting between 1 and 8 vibrotactile stimuli on the hand. Our primary aim was to determine the influence when the stimuli simultaneous presented on the different regions of the hand.

3.2 Methods and apparatus

3.2.1 Subjects

Eleven healthy young subjects (mean age, 22.9years; standard deviation 0.9years) participated in this study with informed consent according to a protocol approved by the institutional review board of the National Institute of Mental Health. All of the subjects were tested at the right hand.

3.2.2 Device and stimuli

We used the experimental device as Figure.3.1 (a). The vibration stimulus is presented by the piezo-electric. The eight white cylinders were made by insulated organic plastic. When the tactile vibrotactile stimuli were presented, piezo-electric under the white cylinders were produced the vibrotactile stimuli press strength of the spots is 0.177N. Lead to upper points of presented stimuli start to vibrate. Subjects can feel the vibrations stimulus obviously. Because the white cylinders were insulated, so the subject was no having any pain arising from electric shock or the other tactile effects.

The place of stimulus presented is shown like Figure.3.1 (b). The eight places correspond to eight piezo-electrics. When the vibration stimulus presented multiple stimuli simultaneously, one stimulus has 8 styles, two stimuli has 28 styles, three stimuli has 56 styles, four stimuli has 70 styles, five stimuli has 56 styles, six stimuli has 28 styles, seven stimuli has 8 styles and eight stimuli presented at the same time has only one style.

A total of 255 trials 5 times in steps of presented.



Figure 3.1 Device system and the places of presented stimuli. Id: the distal phalanx of the index finger. Im: the middle phalanx of the index finger. Md: the distal phalanx of the middle finger. Mm: the middle phalanx of the middle finger. Rd: the distal phalanx of the ring finger. Rm: the middle phalanx of the ring finger. Ld: the distal phalanx of the little finger. Lm: the middle phalanx of the little finger.

The distance of the piezo-electric device is shown like Figure.3.2. two vibrotactile units were installed on the left and right side. Eight white cylinders were fixed form like the 2×4 array. The distance between the upper and lower points is 2.4mm, and width is 4.8mm. The purpose of this design is that we can present the stimuli at both fingertips and second knuckle as same time.



Figure 3.2 The distance of the piezo-electric device

3.2.3 Experimental procedure

3.2.3.1 The numerosity judgment task

In numerosity judgment task, multiple or single 10-Hz vibrotactile stimuli were presented in the right hand for 500 ms. In this experiment, we had 8 stimulus positions, there were 8 possibilities when one stimulus was presented, 28 when 2 were presented, 56 when 3 were presented, 70 when 4 were presented, 56 when 5 were presented, 28 when 6 were presented, 8 when 7 were presented, and only 1 when 8 were presented. A total of 255 stimuli were presented in the whole experiment. The time course of this task is showing in Figure. 3.3. All the vibrotactile stimuli were presented for 500 ms, and then there was a 3000- to 5000-ms delay time. In this time, subjects were instructed to answer the number of the stimulus (1 to 8) were presented at the same time and press a numerical key on a computer keyboard corresponding to the perceived number. All the stimulus numerosity judgment trials were repeated 5 times. One trial at least needed 3500 to $4500 \times 255 \times 5$ ms, or approximately 1.5 hours to 2.0 hours, to complete this experiment.

Chapter 3 Tactile spatial processing in human somatosensory system using behavioral experiments



Figure 3.3 Time chart of the numerosity judgment task

3.2.3.2 The position report task

In this experiment, multiple or single 10-Hz vibrotactile stimuli were presented in the right hand for 500 ms, and then the subjects reported the positions of the stimuli. In this experiment, since we presented multiple or single stimuli at the same time, the arrangement of the positions corresponding to different numbers of stimuli that needed to be calculated. Because we had 8 stimulus positions, there were 8 possibilities when one stimulus was presented, 28 when 2 were presented, 56 when 3 were presented, 70 when 4 were presented, 56 when 5 were presented, 28 when 6 were presented, 8 when 7 were presented, and only 1 when 8 were presented. A total of 255 stimuli were presented in the whole experiment. To make it easier for the subjects to report the locations, we referred to Id, Md, and so on as numbers (1, 2, etc.) for the volunteers (Figure. 3.1(b)). The time course of this position judgement task is showing in Figure. 3.4. All the vibrotactile stimuli were presented for 500 ms, and then there was a 4000- to 6000-ms delay time. In this time, subjects should report the numbers of the stimulated positions orally. All the subjects needed more time to name all position of the stimuli, which is why we included this longer delay time. In the prediction experiment, we found that 90% of the young group could correctly identify three or more positions. However, in the elderly group, all subjects could not correctly identify the positions of more than 2 stimuli presented at the same time. For this reason, we only randomly presented 1 to 2 stimuli in the elder group. All the stimulus position judgement trials were repeated 5 times. One trial at least needed 4500 to 6500×255×5 ms, or approximately 1.5 hours to 2.5 hours, to complete this experiment.


3.3 Results

3.3.1 The numerosity judgment task

The results of the numerosity judgment task are shown in Figure.3.5. And the vertical axis was the accuracy rate, the horizontal axis shows the number of stimuli presented, error bars represented the standard error of the percentage of correct.

This graph shows that the number of accuracies made by subjects when between 1 and 8 stimuli were presented increases with the number of stimuli presented in the fingertips. The mean percentages of accuracies in the numerosity judgment were submitted to a repeated measure analysis of variance (ANOVA) with the factor of numerosity (8 levels). This analysis resulted in a significant main effect [F (7, 63) =74.7, P<0.001], with the number of accuracies decreasing as the number of stimuli presented increased. Furthermore, compared to the chance level to each number of stimuli presented, there was a significant difference when the stimulus presentation number was $1\sim4(p<0.05)$.

Chapter 3 Tactile spatial processing in human somatosensory system using behavioral experiments



Figure 3.5 Time chart of the numerosity judgment task and Position report task

The relation between the number of stimuli presented and reaction times are shown in Figure.3.6. The vertical axis was the reaction times, the horizontal axis shows the number of stimuli presented, and error bars represented the standard error of the reaction times. This graph shows that reaction time is shorter when the stimulus presented fewer. The ANOVA confirmed that there was a significant main effect for the number of stimuli presented [F (7, 63) =22.3, P<0.001]. In addition, when compared with the number of stimulus presentation, there was a significant difference between the stimulus presentation number 3~8 and stimulus presentation 1(p<0.05), and between the stimulus presentation number 6 and stimulus presentation number 2, 3, 5(p<0.05).



Figure 3.6 Reaction times of the numerosity judgment task

The average number of each stimulus presentation answers is shown as gray plot in Figure.3.7. The vertical axis was the answer, the horizontal axis shows the number of stimuli presented, and error bars represented the standard error of the answer.

It can be seen that all of the subjects were underestimations of the stimuli presented. There was a main effect on repeated measures analysis of variance. By comparing the answer in the number of stimulus presentation, there was a significant difference besides the stimulus presentation number between $7 \sim 8(p < 0.05)$. In addition, comparing the correct answer with the answer to number each stimulus presentation, when the stimulus presentation above 3, the answer was significantly lower than the correct answers (p <0.05).



Figure 3.7 Compared answer with the correct answer of numerosity judgment task

3.3.2 Position report task

The results of the position report task are shown in Figure.3.8. The graph showed that the accuracy rate of the stimulus presentation in each location and the number of each stimulus presentation. All of vertical axis was the accuracy rates, the horizontal axis shows the number of stimuli presented, and error bars represented the standard error of the percentage of correct.

We found that the accuracy rate was higher when the stimulus number was 1 and 2 on each location from the results of Fig.6. The ANOVA revealed a significant main effect for the number of stimulus presented [F (7,63) =23.6, p<0.001] and the location of the stimulus presented [F (7,63) =8.33, p<0.001]. However, there was a significant interaction between the location of the stimulus presented and the accuracy rates [F (49,441) =4.23, p<0.001).



Figure 3.8 Accuracy rates every place of presented stimuli every numbers of presented stimuli of position report task

3.4 Discussion and Conclusion

The results of the two experiments reported here demonstrate that people are to some extent able to discriminate between different numbers of tactile stimuli when multiple stimuli are activated simultaneously across the hand. In experiment 1, RTs and accuracy rates for tactile enumeration judgments were linearly related to the number of stimuli (1 \sim 8) activated in all two experiments. The accuracy data from experiment 1 indicated that performance was poor when more than 3 stimuli were activated (see Figure 3.5). And as the more stimulus presentation, the answer is smaller than the correct answer (see Figure 3.7). This result was consistent with conventional research [42]. At first glance; the poor performance reported in experiment 1 might be interpreted as an inability of people to process simultaneously presented vibrotactile stimuli across the hand in parallel. However, the results of Gallace et al.'s study [46] also showed that participants do not base their numerosity judgments solely on the intensity of the stimuli presented.

The results of experiment 2 indicated that the accuracies were changed when the tactile stimuli presented on different place and the increased of stimuli number also effected the accuracy. The percentage of correct answers at the middle phalanx unit was lower than the fingertip, especially in Mm (see Figure 3.8). However, the accuracy of Im is significantly higher when stimulus presentation number is 8 in the same middle phalanx unit. It is inferred that there is a difference in function of humans' index finger and otherwise or tactile information to the finger as being transmitted is preferred for more of the index finger has higher information superiority.

Because the density of mechanoreceptors unit is high in index finger that it can exactly recognized the stimulus. And in the middle phalanx unit can be predicted accuracy rates falls for density of mechanoreceptors unit is lower than the fingertip. There is no much difference in the density of mechanoreceptors unit in the middle phalanx unit and fingertips of the index finger in the Slowly Adapting I (SA I). Hence, Im suspected that accuracy rate is obtained as much as the tactile vibration stimulus of Id.

In addition, as the stimulus presentation number increased in Md and Rd, accident error of the accuracy rates was less than other stimulus presentation location. However, when the stimulus presentation number is low, there are many mistakes in Md and Rd. From this, index finger not only high on the information advantage, compared with other fingers, it also can obtain the information correctly.

Although many crucial details remain to be elucidated, all findings presented here point toward a model for the neural basis of tactile working memory. Our results offer the clear evidence for the presence of short lasting tactile representations of stimuli presented in parallel across the hand.

Chapter 4 Tactile spatial processing and counting abilities in human somatosensory system

Summary

Numerosity shares a common cognitive representation in the brain, as it does not depend on what sensory inputs, including vision and touch, are used. Recent studies have focused on visual numerosity ability, and their findings suggest that humans can count below four stimuli very well. However, few studies in the tactile domain have used tactile numerosity judgment tasks to observe stimulus counting ability, and it is still unclear how aging influences this ability. In the present study, we asked 15 younger (mean age 22.7±0.8 years) and 10 older (mean age 67.9±5.1 years) subjects to perform a tactile stimulus numerosity task, and we recorded their response accuracy to investigate the effects of aging on vibrotactile stimulus counting abilities. The results showed that as the calculation trials increased, the accuracy rate decreased in both young and old groups (p < 0.05). In addition, in the older group, the decrease in the accuracy as the number of calculation trials increased was greater than that in the younger group. In other words, this decrease in the older group may be explained by a reduction in working memory capacity, which is directly caused by a decline in basic tactile cognitive ability.

4.1 Background

People can dissociate information about features of objects touched from their knowledge of the spatial location of bodily contact. When we recognize objects, we first perceive the shape, temperature, hardness, material property, etc., of the surface of the object that touches our fingers. Johnson and Hsiao reported that the skin sensations, such as the size, shape and material of the object are transferred from the receptors of the epidermis to the central nervous system [44, 65]. In the process of recognition, the skin structure and the position of the mechanical receptacle have a great influence on tactile information processing [48]. The mechanical receptors of fingers have different densities in different areas. In addition, the abilities of all creatures, not only humans, vary with age. Machinery receptors decrease with age, leading to a decline in spatial recognition ability.

Tactile numerosity judgments in healthy younger people have been widely researched [41-43, 66]. These studies ask subjects to count the number of simultaneous stimuli. The study of visual numerosity judgments shows that people can quickly and correctly calculate the following four stimuli [67]. Subjects can accurately estimate up to two different voices, and their performance will decline as the number of speakers increases [68]. The error rate in counting the number of tactile stimuli becomes very high when three vibrotactile stimuli are presented, and most of the time, performance falls to the level of chance when four or more stimuli are presented [64, 69].

With age, the major sensory systems undergo varying degrees of decline, making older persons less able to cope with environmental demands. This aging phenomenon can be seen in various ways. Frequently, aging manifests as a decrease in memory and athletic ability [70]. The impacts of age-associated changes in the sensory function of the hands, which can be dramatic and substantial in older persons [71]. Experiments on aging effects have been conducted in thickness discrimination experiments and angle discrimination experiments [72, 73]. In the angle discrimination experiments, there were differences in the results between young and elderly subjects, but in the thickness discrimination experiment, there was no difference.

The discrimination threshold decreases with age, but it is unclear whether the information processing ability of the working memory, such as the ability to count

vibrotactile stimuli, decreases. Therefore, two experiments were carried out in this study. Experiment 1 was a stimulus position judgment experiment, in which we investigated how many tactile stimuli could recognize by older subjects. As a result, we found that older people could not distinguish between more than two stimulation sites. Therefore, based on the above criteria, 1 to 2 randomly located stimuli were used for experiment 2 (stimulus counting experiment) in the young and old groups. In experiment 2, we found that the older group not only had a reduced ability to discriminate spatial location, but as the number of calculations increased, their accuracy became significantly lower than the younger group, and they even lost the ability to make correct calculations. In this report, we describe the aging effect on discriminating spatial location and the effect of working memory on stimulus number calculation.

4.2 Methods

4.2.1 Participants

Fifteen healthy younger (mean age 22.7 ± 0.8 years) and ten healthy older volunteers (mean age 67.9 ± 5.1 years) volunteers participated in this study. All participants had normal or corrected-to-normal vision and were right-handed. The participants had no neurological/psychiatric disorders and no hearing problems. The experimental protocol was approved by the Ethics Committee of Okayama University. All healthy, older participants passed the Mini Mental State Examination (MMSE). Their demographic information is shown in Table 4.1 and Table 4.2.

Name	Age	MMSE	Dominant hand
G.M	24	-	Right
M.Y	22	-	Right
Y.M	24	-	Right
G.R	23	-	Right
H.Y	23	-	Right
H.Y	22	-	Right
M.S	22	-	Right
T.J	22	-	Right
N.R	22	-	Right
A.Y	24	-	Right
O.T	22	-	Right
N.Y	23	-	Right
K.A	23	-	Right
K.S	22	-	Right
K.N	23	-	Right

Chapter 4 Tactile spatial processing and counting abilities in human somatosensory system

Table 4.1 Demographic information of the younger group

Table 4.2 Demographic information of the older group

Name	Age	MMSE	Dominant hand
K.M	63	30	Right
S.S	70	30	Right
I.T	80	29	Right
K.A	66	30	Right
H.H	70	30	Right
Y.H	63	30	Right
A.S	65	30	Right
S.K	64	30	Right
U.T	69	30	Right
Y.T	69	30	Right

4.2.2 Experimental equipment and stimuli

Figure.4.1 depicts the stimulation system in this study. Visual stimuli were presented by a notebook PC (ThinkPad T430, Lenovo) on a 17-inch monitor (Mitsubishi, 1920*1080).

Chapter 4 Tactile spatial processing and counting abilities in human somatosensory system

At the same time, the vibrotactile stimuli (Piezo-electric device, KGS, Japan) from the braille stimulator in Figure. 4.1 were controlled by the PC and presented to the subjects. In the figure, eight Piezo-electric devices were fixed on the table. To fit on each subject's palm, all the distances of the vibrotactile stimuli were adjustable. To keep the fingers unbent during this experiment, their whole finger was fixed by magic tape onto a board as shown in Figure. 4.1. The vibrotactile stimuli used in this experiment had a frequency of 10 Hz, and the presentation time was 500 ms. The position of the vibrotactile stimuli is shown in the black circle in Figure. 4.2. The distal phalange of the index finger was named Id, and its intermediate phalange was named Im; these phalanges of the middle finger were named Md and Mm, respectively; those of the ring finger were Rd and Rm; and those of the little finger were Ld and Lm.



Figure.4.1 Stimulation apparatus and placement of stimuli



Figure.4.2 Definition of the places of presented stimuli

4.2.3 Procedure and design

4.2.3.1 Stimulus position judgement task

In this experiment, multiple or single 10-Hz vibrotactile stimuli were presented in the right hand for 500 ms, and then the subjects reported the positions of the stimuli. In this experiment, since we presented multiple or single stimuli at the same time, the arrangement of the positions corresponding to different numbers of stimuli that needed to be calculated. Because we had 8 stimulus positions, there were 8 possibilities when one stimulus was presented, 28 when 2 were presented, 56 when 3 were presented, 70 when 4 were presented, 56 when 5 were presented, 28 when 6 were presented, 8 when 7 were presented, and only 1 when 8 were presented. A total of 255 stimuli were presented in the whole experiment. To make it easier for the subjects to report the locations, we referred to Id, Md, and so on as numbers (1, 2, etc.) for the volunteers (Figure. 4.2). The time course of this position judgement task is showing in Figure. 4.3. All the vibrotactile stimuli were presented for 500 ms, and then there was a 4000- to 6000-ms delay time. In this time, subjects should report the numbers of the stimulated positions orally. All the subjects needed more time to name all position of the stimuli, which is why we included this longer delay time. In the prediction experiment, we found that 90% of the young group could correctly identify three or more positions. However, in the elderly group, all

subjects could not correctly identify the positions of more than 2 stimuli presented at the same time. For this reason, we only randomly presented 1 to 2 stimuli in the elder group. All the stimulus position judgement trials were repeated 5 times. One trial at least needed 4500 to 6500×255×5 ms, or approximately 1.5 hours to 2.5 hours, to complete this experiment.



Figure. 4.3 Time chart of stimulus position judgement task

4.2.3.2 Numerosity counting task

In this experiment, we also used the same stimulus system and the same position of the right hand in both groups. However, only 1 or 2 vibrotactile stimuli were used, meaning that only single or double 10-Hz vibrotactile stimuli were presented to the right hand for 500 ms. This method was performed because of the results of the stimulus position judgement task (Figure. 4.4), which showed that when the number of stimuli was more than three, all participants' accuracy dropped to approximately 50%. To achieve a balanced difficulty in this experiment, we used a number of vibrotactile stimuli that would yield a correct rate of greater than 75%. When a single tactile stimulus was given, the position had 8 possibilities. With double stimuli, we used the 12 pairs that had a correct rate of more than 75% in experiment 1. Thus, a total of 20 types of tactile stimulation were used in this experiment. At the same time, as the tactile stimuli were presented, 2 types of visual cue stimuli were added in this numerosity counting task. As shown in Figure. 3.4, when the first green circle was presented, the subject needed to remember the number of stimuli in the first stimulation, and when the second green circle was presented, the subject needed to add the first and second numbers, and so on. When the red circle was presented, one stimulus counting trial was finished, and the subjects needed to report the final sum of this trial. The visual and tactile stimuli were presented for 500 ms,

followed by a 500- to 1000-ms delay time. The interval between two trials (ITI) was also 5500 to 6000 ms (random) because subjects needed more time to add the numbers. In one trial, a green circle was randomly presented 2, 4, 6, 8, 10, or 12 times at the same time as the tactile stimulation, and then the red stimuli appeared, at which time the subjects needed to give the final sum of this trial as accurately as possible. To get a stable average result, all the stimuli types were repeated 10 times.



Figure. 4.4 Time chart of the stimulus counting task

4.3 Results

4.3.1 The accuracy of the stimulus position judgement task

The results of the stimulus position judgement task in young and old groups are shown in Figure.4.5. From these results, it seems that the accuracy rate of stimulus numbers 1 and 2 was high for each position in the younger group (solid square). The ANOVA in the younger group showed that a main effect was found in the number of presented stimulus (F (7, 63) = 23.6; p <0.001) and position (F (1, 9) = 23.8; p <0.001). There was an interaction effect (F (7, 63) = 4.3; p <0.05) between position and accuracy rate, but no interaction effect (F (3, 27) = 2.6; p =0.14) between finger and position. There was a significant difference (p <0.05) in accuracy between 3 and 4 to 5. There were also significant differences (p <0.05) between Id and Mm, Rm, Ld, and Lm. The accuracy rate was significantly higher (p <0.05) when a vibrotactile stimulus was presented on the fingertip than on the middle phalanx.

ANOVA of the older group showed a main effect in the number of presented stimuli (F (1, 10) = 23.4; p <0.001) and position (F (7, 70) = 7.4; p <0.05). There was no interaction effect (F (7, 70) = 2.6; p =0.14) between the number of presented stimuli and position.



Figure.4.5 Accuracy rates on every place for the number of presented stimuli in the position judgement task. Solid squares are the younger group; empty squares are the older group. The horizontal axis is the number of stimuli presented, and the vertical axis is the accuracy rate. Error bars represent the standard error (SE) of their correct answers.

4.3.2 The accuracy of the stimulus counting task

When we compared each number of calculations, in the younger group, the accuracy rate of trials in which they had to add fewer numbers was significantly higher than the accuracy rate of trials in which they had to add more numbers (p < 0.05). When they had to sum fewer than 6 numbers, all volunteers' accuracy rates were higher than 85%, but when they had to add more than 10 numbers, a sharp decrease in the accuracy rate was found. Even the younger people could not calculate the numbers easily if more than 10 were added.

Chapter 4 Tactile spatial processing and counting abilities in human somatosensory system



Figure.4.6 Accuracy rates of the stimulus counting task in the younger group. The horizontal axis is the number of calculations, and the vertical axis is the accuracy rate. Error bars represent the standard error of their correct answers.

The accuracy rate in the number calculation task in the older group is shown in Figure.4.7. All the accuracy rates were lower than those in the younger group. More obviously, when the number of calculations was more than 10, the overall correct rate of the elderly was less than 30%. In other words, the older group could not complete the tactile recognition or number calculation. In the post hoc p test, some significant differences were found in this group. As in the younger group, the accuracy when adding 2 numbers was significantly higher than that when adding 8, 10 or 12 numbers (p <0.05). However, this decreasing trend did not end here; we also found significant differences between the 4-number condition and the 8-, 10- and 12-number conditions (p<0.001). Surprisingly, we also found a significant difference between the 2-number condition and the 4-number condition, showing that the older group decreased in accuracy much faster than did the younger group.



Figure.4.7 Accuracy rates of stimulus counting task in the older group. The horizontal axis is the number of calculations, and the vertical axis is the accuracy rate. Error bars represent the standard error of their correct answers.



Figure.4.8 Accuracy rates of stimulus counting task in the younger and older groups. The solid squares are the younger group, and the empty squares are the older group; the thin dotted line is the prospect of the younger group, and the thick dotted line is the prospect of the older group. The horizontal axis is the number of calculations, and the vertical axis is the accuracy rate. Error bars represent the standard error of their correct answers.

In Figure.4.8, we compare the stimulus counting results directly between the two groups. ANOVA showed a main effect (F (5, 110) = 28.4; P <0.001) of the number of calculations in the two groups. An interaction effect (F (5, 110) = 3.7; p <0.05) between group and number of calculations was found. To distinguish between tactile cognitive

abilities and individual multiple counting capabilities, we also calculated the prospect line related to the aging effect of the tactile cognitive abilities. As shown in Figure.3.8, the thin dotted line is the prospect of younger group, and the thick dotted line is the prospect of the older group. In the younger group, the accuracy of adding 10 and 12 numbers was significantly different (p < 0.05) from the younger prospect line. In contrast, the accuracy of all conditions had no significant difference between the prospect line and the accuracy in the older group. These results show that the calculation ability and tactile cognition of the elderly group were significantly lower than those of the young group.

4.4. Discussion

4.4.1 Distribution of tactile receptive field

From the accuracy of the tactile position judgement task, Mm, Rm and Lm had difficulty feeling the stimuli. In particular, Lm had almost no sense of stimulation, whereas Id and Im had the highest accuracy, suggesting that the different finger positions have different tactile receptive field densities [45, 73, 74]. The percentage of correct answers was lower in the middle section than in the fingertips, especially in Mm, Rm and Lm. An increase in the stimulus presentation number in Mm, Rm, and Lm yielded a correct answer rate that was no better than chance. However, Im had a significantly higher accuracy of answers than chance, even with stimulus presentation number 8. From this result, we infer that there is a difference in function between the index finger and others or that the tactile information to the finger is transmitted with priority because the index finger has higher information superiority. This finding would be in line with those of previous studies [45, 74] showing that since the index finger has a high density of machine receiving units, it more accurately recognizes stimuli.

The older group had a lower tactile cognitive performance in the position judgement task, although the cognitive performance of the index finger was stronger than that of other fingers in both groups. When some other stimuli were given near the Id, they had no impact on the perception of Id. In contrast, when this happened in other areas, such as Md or Rd, there was a decline in the accuracy of the two places. However, as shown in the older group's results, when other stimuli were shown at the peak of the index finger, the subjects immediately had a high level of wrong answers. These results suggest that the high-density tactile receptive field of the index finger has been degraded by cognitive skills due to age [75, 76].

4.4.2 The aging effect of working memory capacity

There was no significant difference between the prospect line and number of calculations in the older group (Figure.4.8). In contrast, a higher number of calculations had an effect in the younger group. There are two possible explanations for this difference. First, we speculate that compared with the younger group, the capacity of working memory in the older group had decreased greatly. Olesen and Westerberg (2004) showed that the when the targets numbered more than 8, although healthy younger subjects still could not make a correct judgment, suggesting that working memory is not infinite, there was a definitive capacity, and when more than 8 targets needed to be remembered, none of the subjects obtained the right answer [77]. In this study, all the younger subjects had more correct responses when the number of calculations was less than 8. However, in the older group, when the number was more 6, none of the subjects calculated the right answer, and the accuracy was 50%. The reason for this result may be that the working memory capacity of the elderly was decreased, eventually leading to a lower accuracy. Second, we hypothesized that the decline in working memory was influenced by basic tactile cognition in the older group. The result of the stimulus position judgement task showed a much lower accuracy. It can be conjectured that older subjects could not correctly judge the location when the stimulus became double, so that they could not count them correctly. Once the number of calculations was over 2, the positive accuracy rate of the older group dropped to 50%. Our hypothesis is supported by the result that there was no significant difference between the prospect line and the accuracy. Relative to hypothesis 1, we are more inclined to hypothesis 2, i.e., that the working memory of older people is reflected in the basic tactile perception in the older group.

4.5. Conclusions

In this study, we carried out two experiments to distinguish the aging problems in

tactile-based cognition. The phenomenon of a rapid reduction in working memory capacity due to the decrease in basic touch-cognitive ability of older persons was observed. In other words, the decline in working memory function in older subjects is directly caused by a weakening of basic cognitive ability.

Chapter 5 Stimuli interval modulates the balance of brain activity in the human primary somatosen sory cortex: an ERP study

Summary

Neuron excitation and inhibition occur in the brain at the same time, and brain activation reflects changes in the sum of excitation and inhibition. This principle is well established in the lower level sensory system, including vision and touch, based on previous animal studies. However, it is unclear how the somatosensory system processes the balance between excitation and inhibition. In the present ERP study, we modified the traditional spatial attention paradigm by adding double stimuli with short intervals (i.e., 10, 30, and 100 ms). All seventeen subjects were asked to participate in the experiment. Five types of stimulation were used in the experiment: a single stimulus (one raised pin for 40 ms), standard stimulus (eight pins for 40 ms), and double stimuli with intervals of 10 ms, 30 ms, and 100 ms. Subjects were asked to pay attention to a particular finger and detect whether the standard stimulus was presented to the finger. The results showed a clear attention component in the single stimulus condition, but the suppression components of the three interval conditions seemed to be dominant in the somatosensory areas. In particular, we found the strongest suppression effect in the ISI30 condition (interval of 30 ms) and that the suppression and enhancement effects seemed to be counterbalanced in both the ISI10 and 100 conditions (intervals of 10 ms and 100 ms). This type of processing may allow humans to easily discriminate between multiple stimuli on the same body part.

5.1 Background

Spatial attention to auditory [78, 79] or visual stimuli [80, 81] was modulated, and the evoked potentials were generated in the primary auditory or visual cortices. For the somatosensory system, studies have been conducted using fMRI and event-related potentials (ERPs) in humans [24, 82, 83], and they found that attention enhances activity in the primary somatosensory cortex (SI) when using a single stimuli. Animal studies [35, 84, 85] used double stimuli to show that the second stimulus suppresses the response to the first stimulus. This suggests that the spatiotemporal interaction modulates the response magnitude in human SI. However, it remains unclear how the balance between attentional enhancement and double asynchronous stimulation suppression is maintained.

Many previous studies about the effects of spatial-selective attention found that attentional effects occur in the early stage, but they did not find modulation of SEP components generated in S1. Some ERP studies used a mechanical tactile stimulus and also found a contralateral N80 component by sustained attention and a bilateral P100 component by spatial attention in the early stage [23, 86, 87]. Other electroencephalography (EEG) studies using tactile spatial sustained attention to mechanical stimuli found that the earliest somatosensory component (P50) was significantly increased for attended stimuli [23]. In a simultaneous EEG-fMRI study, Schubert and colleagues [24] used Braille stimulation and found significant effects of spatial-selective attention for the P50 and P100 for left and for the N80 for right tactile stimuli in SI. Other ERP and SEP studies of mechanical tactile stimuli [62, 88-90] showed that mid-latency components such as N140 and P200 amplitudes were enhanced in response to tactile stimuli presented to the attended hand.

In addition, an electrophysiological study in owl monkeys [35] selected paired skin sites and delivered pulses simultaneously (0 ms delay) with onset asynchronies of 10, 30, 50, 100, and 500 ms delay to investigate the effects of varying the temporal proximity of stimuli. This study indicated that maximal suppression of firing rates occurred when the stimulus onsets were 30-50 ms. The owl monkeys were sedated in this study, so the suppressed effect was observed under unattended conditions.

It is unclear how paired stimuli are presented by mechanical underlying processes of

attention and temporal processes in the human somatosensory cortex. Thus, we hypothesized that enhancement and suppression occur as follows in the human somatosensory areas: 1) the enhancement effect of sustained spatial attention is stronger than the suppression effect of paired stimulation. 2) the suppression effect of paired stimulation is stronger than the enhancement effect of sustained spatial attention. 3) the enhancement effect of sustained spatial attention. 3) the suppression effect of sustained spatial attention and the suppression effect of paired stimulation exist at the same time.

The present experiment was designed to determine whether sustained spatial attention enhancement or paired stimulation suppression affect neurophysiological responses in human SI. We extended the work of previous studies to investigate the temporal dynamics of the neural response when mechanical tactile stimulation is delivered to the left or right index finger with attention focused on one hand at different inter-stimulus intervals. Participants were asked to focus their spatial attention on one hand (on a finger) for a number of tactile stimuli, and we instructed them to detect rare tactile target stimuli at the index finger of the attended hand. To achieve this aim, ERPs were computed in responses with tactile stimuli.

5.2 Methods

5.2.1 Participants

Nineteen undergraduate students were recruited as volunteers. Two participants were excluded from the statistical analysis because of low performance in further analysis. Seventeen participants (age range: 21-25; mean age: 22.5) remained in the sample. All participants with normal or corrected-to-normal vision were right-handed. They had no neurological/psychiatric disorders and no hearing problems. The experimental protocol was approved by the Ethics Committee of Okayama University.

5.2.2 Material and procedure

The experiment was conducted in a dimly lit, sound-attenuated room, with participants facing a computer screen (17 inch, LG, FLATRON) at a viewing distance of 60 cm.

Tactile stimuli were applied to the distal phalanx of the left or right index finger using a piezoelectric Braille stimulator (KGS, Saitama, Japan). Each stimulator had 8 individually controllable plastic pins, grouped in a 2×4 array. The diameter of each pin was 1.3 mm. The distance between pins was 2.4 mm. Using a custom built electrical drive, pins could be elevated from the resting position by 0.7 mm with a tactile force of 0.177 N/pin. The mechanical onset from the trigger to the highest position was approximately 38 ms, as measured by a high-speed camera, so we set the tactile stimuli presented time to 40 ms.

Tactile stimuli were included for the standard and target. The target was 8 pins and was presented only on the visual instructions side. The standard had one pin in the lower left or right when stimuli were presented to the left or right index finger. It was composed of single and double conditions. The temporal proximity of the double condition consisted of three different inter-stimulus intervals (10 ms, 30 ms and 100 ms). The inter-stimulus interval, or ISI, is the time interval between the first tactile stimulus offset and second tactile stimulus onset (Figure. 5.1.a).

Visual and tactile stimuli were presented by using Presentation software (Neurobehavioral Systems Inc., Albany, California, USA) outside the dimly room. Visual instructions for the left and right index fingers (each instruction angle is 5×7 °flat at 3.5 ° left or right the fixation) changed the red color presented at 300 ms at the beginning of each block. This required the participants to keep their attention on the left or right index finger in the block. A fixation (a white cross of 1.7×1.7 °of visual angle) located between both instructions (Figure. 5.1.b). The experiment comprised 16 separate sessions, consisting of 15 blocks (80% standard and 20% target) per session. Each session contained 4 experimental conditions: a single condition and double conditions (ISI10 condition, ISI30 condition and ISI100 condition).

(a) The kinds of tactile stimulation



(b) Illustration of left hand attended experimental procedure.



Figure 5.1 (a) The types of tactile stimulation; standard (1 pin) and target (8 pins). (b) Illustration of attended left hand. Visual instruction was 300 ms, participants were instructed to direct their attention to the left index finger until the next instruction appeared. Standard stimuli presented on the left hand as attended stimuli. Stimuli delivered to the other hand were unattended stimuli. 1500 ms after instruction, tactile stimuli were presented unilaterally to the left or right hand. Target was presented only on the left side, and the participant responded vocally when it was detected.

Figure.5.1b illustrates the experimental stimulation procedure for the attended left hand. Each block began with the visual instruction of 300 ms. After that, participants were instructed to keep their gaze focused on the central fixation cross and keep their attention on the left index finger until the next instruction appeared. They were required to respond vocally when the target stimulus was detected at the left index finger. Thus, participants had to direct their attention to the attended hand. A standard stimulus was presented to this hand as an attended stimulus. In contrast, stimuli delivered to the other hand were unattended stimuli. 1500 ms after the instruction, tactile stimuli (2 target, 8 standard) were presented unilaterally to the left or right hand. Visual instructions and tactile stimuli were given in a pseudorandom order. During the entire experiment,

participants were also instructed to avoid movement of the body, in particular the eyes and fingers.

5.2.3 EEG recording and data analysis

An EEG system (Brain Amp MR plus, Germany) was used to record signals through 28 electrodes mounted on an electrode cap (Easy cap, Herrsching Breitbrunn, Germany) as specified by the International10–20 System. All electrodes were referenced to the combined signals from the bilateral earlobe. A horizontal electrooculogram (HEOG) was recorded from the outer canthus of the left eye. Eye blinks and vertical eye movements were recorded from an electrode placed 1.5 cm below the left eye. The impedance of all electrodes was below 5 k Ω . The raw signals were digitized with a sample frequency of 500 Hz with a 60 Hz notch filter. The band pass of the amplifiers was DC to 250 Hz.

Brain Vision Analyzer software (version 1.05, Germany) was used to analyze the ERPs, which were averaged separately for each stimulus type offline. To remove the target stimulus, we analyzed only ERPs elicited by standard stimuli. The continuous EEG signals were segmented offline from 100 ms before to 500 ms after the tactile stimulus onset. Baseline corrections were made against the data from–100 ms to 0 ms. We rejected artifact trials in which the amplitude reached $\pm 80 \ \mu\nu$ from –100 ms to 500 ms, and we filtered the data with a band pass filter retaining frequencies between 0.01 Hz and 30 Hz. The data from each electrode were then averaged, and a grand average ERP was computed across all participants for each stimulus type.

For further analysis, the mean amplitude data were computed within the following time windows relative to stimulus onset: P50 (34-62 ms), N80 (64-92 ms), P100 (94-122 ms), N140 (124-172 ms), P200 (174-242 ms), P300 (244-342 ms). In each time window, the mean amplitude data were analyzed using repeated measures analyses of variance (ANOVAs) with 2 factors (attended vs. unattended) \times 4 conditions (single, ISI10, ISI30 and ISI100 conditions) and electrode (C3/4) separately. RStudio (Version 1.1.383) was used for all statistical analyses.

5.3 Results

Figure.5.2 shows the grand averaged waveforms for the single condition and double conditions (ISI10 condition; ISI30 condition and ISI100 condition). The electrode sites were C3/4, approximately overlying the contralateral SI. The black solid line represents the attended state, and the black dotted line represents the unattended. For single condition, attended stimuli elicited more positive than unattended state. The double conditions were set up as follows: ISI10 condition,

attended stimuli elicited close to unattended; ISI30 condition, unattended stimuli elicited more positive than attended; ISI100 condition, attended stimuli elicited nearly to unattended once again.





(B) Double condition

(A) Single condition



Figure 5.2 The grand averaged waveforms for (A) a single condition (a-b) and (B) double conditions: (c-d) ISI 10 ms; (e-f) ISI 30 ms; (g-f) ISI 100 ms. The electrode sites were C3/4 approximately overlying the contralateral SI. Black solid line: attended. Black dotted line: unattended. The red arrow marks the onset of the second stimulus. The shaded areas indicate the periods used for the point-wise running t-tests comparing attended to unattended for all participants (p < 0.05).

Left column in Figure. 5.2 shows the EPRs elicited in four conditions by tactile stimulus presented on right index finger at contralateral electrodes (C3, Right hand). All subjects demonstrated a clear P45 component in their responses to tactile stimuli presented to the right index fingers. The mean amplitudes ANOVA of the P45 revealed a main effect [F (1,16) = 4.740; p < 0.05] of attention in C3, which was not accompanied by an attention × condition interaction; P100 revealed a main effect [F (1,16) = 6.175; p < 0.05] of attention in C3, which was not accompanied by an attention in C3, which was not accompanied by an attention in C3, which was not accompanied by an attention in C3, which was not accompanied by an attention in C3, which was not accompanied by an attention in C3, which was not accompanied by an attention in C3, which was not accompanied by an attention in C3, which was not accompanied by an attention in C3, which was not accompanied by an attention in C3, which was not accompanied by an attention in C3, which was not accompanied by an attention in C3, which was not accompanied by an attention in C3, which was not accompanied by an attention interaction. There was a main effect [F (3,16) = 3.230; p < 0.05] of conditions in C3 for the P300 component.

The right column of Figure. 5.2 shows the EPRs elicited in four conditions by a tactile stimulus presented to the left index finger at contralateral electrodes (C4, Left hand). The analysis of the left side for P45 revealed no main effect or interaction between attention and conditions, but there was an attention × condition interaction [F (3,16) = 2.989; p < 0.05] for N80, and a pairs-test found a significant difference between the attended and ISI30 condition (p < 0.05). There was a significant interaction between attention and conditions [F (3,16) = 6.589; p < 0.001] for P100; a pairs-test found the most significant difference between the unattended and ISI30 conditions (p < 0.001). No main effect was found in attention and conditions for N140 and P200; a main effect of conditions [F (3,16) = 2.809; P < 0.05] was found for P300.

Figure. 5.3 shows the mean amplitudes for the P45, N80 and P100 components. This result represents the attended minus unattended conditions on the left hand and right hand. Three components found the lowest amplitude of ISI30 condition in the left hand stimulus. The mean amplitudes of the P45 component, the main effect of P45 was significant in the attention [F (1, 16 = 6.14, p < 0.05]. Post hoc comparisons between the single and ISI30 conditions showed that most activation occurred at the C4 electrode (p < 0.05). In the N80 component, the interaction between attention and ISI was clear [F (3, 48) = 3.88, p < 0.05], and the mean amplitudes of the single and ISI10 conditions were significantly higher than the ISI30 condition (p < 0.05). ISI30 and ISI100 were also significantly different (p < 0.05). Similarly, these results are also limited to the C4 electrode (left hand). In the last component of the P100, there was no main effect or interaction at the C3 electrode, although an affect similar to the attentional main effect was found [F(1, 16) = 3.77, p = 0.07], but in the C4 electrode, an interaction effect between the attention and ISI was found clearly [F (3, 48) = 6.6, p < 0.05]. The mean amplitude of the single condition was higher than the ISI10 and ISI30 conditions (p < 0.01). Additionally, there was a significant difference between ISI30 and ISI100 (p < 0.05). For the right hand, there was no significant difference between conditions for P45, N80 and P100.



Figure 5.3 Mean amplitudes of attended minus unattended conditions on the left hand and right hand. The analysis time window for (a) P50 was 34-62 ms; (b) N80 was 64-92 ms and (c) P100 was 94-122 ms. Black line: left hand. Dotted line: right hand. *p < 0.05, **p < 0.01, ***p < 0.001.

5.4 Discussion and Conclusion

This study used double asynchronous stimulation to investigate the relationship between spatial attention enhancement and double asynchronous stimulation suppression of brain activity in human SI. Participants were asked to focus their spatial attention on one hand (on a finger) for a number of tactile stimuli, and we instructed them to detect rare tactile target stimuli at the index finger of the attended hand. In double stimulation conditions, as stimulus intervals were increased, a V-shaped effect was observed. We suggest that this occurs through attention enhancement and the double stimulation suppression effect.

We found the strongest suppression effect in the ISI30 condition, supporting a hypothesis from a previous study: spatiotemporal interactions modulate response magnitudes during paired stimulation. As was observed in monkeys, neural response intensity is generally suppressed by a preceding conditioning stimulus when the test stimulus occurs after a 30 or 50 ms delay. In this study, the ISI was very short, but all subjects were able to identify this interval very clearly. Without the attended condition, the first stimulus was the cue to the second stimulus [35]. Christian 2017 used double visual stimuli to investigate repetition suppression and suggested that stimulus-specific expectations about objects modulate LOC and propagate back to the earliest cortical station processing visual input. In this study, tactile input and visual input can explain this suppression phenomenon, which is due to repeated exposure to the same stimulus, which results in an attenuated brain response in cortical regions [91, 92]. We have extended the study of monkeys through this experiment, thus verifying that the double stimuli suppression effect in the human primary somatosensory cortex is the same as that of monkeys. When the ISI is 30 ms or 50 ms, the suppression effect is strongest. It fills the gap between spatial selective attention enhancement and double stimulation suppression in the human somatosensory cortex.

For a single condition, we found some ERP components in the contralateral hemisphere by comparing the unattended side significantly. The P50 and P100 components in the C4 electrode was significantly stronger on the attended side compared to the unattended side (Figure.5.2). An fMRI-EEG study used the braille stimulation to investigated the attentional effects on S1, and it found that left tactile stimulation (P50) was significantly enhanced by spatial-selective attention, suggesting that the attention enhances the sensory signal during its early passage in S1 [24]. This study also showed that P50 was the earliest component to be modulated by spatial-selective attention using braille stimulation similarity. Thus, the asymmetric effects of spatial selective attention for two sides can also be found in early and middle stages. For left stimuli, P50, P100 and P300 were found in the attended vs. unattended hand; but on the other side, only the P300 attentional effect was found in the attended vs. unattended hand. These asymmetric hemispheric activations may be explained by Mesulam's modality-unspecific model of spatial attention [93]. That is, higher-order areas in the left hemisphere control attention for events only on the right side, whereas the right hemisphere controls attention for both the left and right side. Both theories may explain the asymmetric attentional effects on the SEPs, leading to earlier (P50 and P100 only for left not for right stimuli) attentional modulation for left stimuli.

We found some attentional enhancement in the single condition only. In the double stimuli conditions, the attentional effect was partially decreased as the inter-stimulus interval increased. A previous study suggests that when the stimuli are double or more, the inhibition effect works from the first stimulus [35]. Additionally, the interval is very short (ISI 30 ms), but in the ISI10 condition, we did not observe any enhancement or suppression effect. There are two possibilities that explain these results: the interval may be too short, such that the subject cannot recognize the double stimuli and when the stimulus is changed to double, the suppression effect is activated much more strongly than the attentional enhancement effect. According to the interaction of spatial attention enhancement and double asynchronous stimulation suppression, when the enhancement and suppression effects are equal, there is no difference between attended and unattended in terms of the neurophysiological responses to double asynchronous stimulation (Figure. 5.2 and 5.3). We suggest a tentative explanation that may account for this finding: the attention enhancement and double asynchronous stimulation suppression effects decreased as the inter-stimulus interval increased. The stimulatory effect of attention is mutually competitive with the inhibitory effect of double stimulation. Moreover, the enhancement of spatial attention may be modulated by double stimulation suppression.

Chapter 6 General conclusion and future projections

Summary

This thesis has investigated the diversity of tactile spatial processing between younger and older adults; and investigated the diversity in different ISI conditions how ISI modulates brain activity in human. Additionally, the spatial and temporal processing has also been evaluated. In this chapter, our findings are summarized below. Further, some future projections are included.

6.1 General conclusions

The current thesis includes four experiment studies. The first experiments developed a novel automatic vibrotactile patterns delivery capable of perform the tactile cognitive experiment in future study. The second and third experiments investigated the vibration stimulation on human spatial processing in younger and older adults. The third experiment investigated the brain activity of temporal processing in human primary somatosensory cortex.

Chapter 2 describes a device which we developed a novel automatic vibrotactile patterns delivery capable of perform the tactile cognitive experiment. It can serve to determining the sensitivity of each finger that contributes to tactile spatial discrimination. To evaluate the performance of the device, we conducted a basic function test. The results indicated that the device can record reliable data and control the tactile pattern position precisely.

Chapter 3 describes the first experiment, which measures vibration stimulation in human fingers by using behavioral measurements. This part aim to determine the spatial characteristics when the stimuli simultaneous presented on the different regions of the hand. We investigated tactile numerosity judgments and position report tasks by simultaneously presenting between 1 and 8 vibrotactile stimuli on the hand. The accuracy data from numerosity judgments task indicated that performance was poor when more than 3 stimuli were activated. And as the more stimulus presentation, the answer is smaller than the correct answer. Position report task indicated that the accuracies were changed when the tactile stimuli presented on different place and the increased of stimuli number also effected the accuracy. The results of the two experiments reported in this part demonstrate that people are to some extent able to discriminate between different numbers of tactile stimuli when multiple stimuli are activated simultaneously across the hand.

Chapter 4 describes the second experiment, in which we used a similar parameter to investigated the aging effect of vibrotactile stimulus counting abilities by behavioral measurements in youngers and older adults. In the present study, we asked 15 younger (mean age 22.7 ± 0.8 years) and 10 older (mean age 67.9 ± 5.1 years) subjects to perform a tactile stimulus numerosity task, and we recorded their response accuracy to investigate the effects of aging on vibrotactile stimulus counting abilities. The results showed that as

the calculation trials increased, the accuracy rate decreased in both young and old groups (p < 0.05). In addition, in the older group, the decrease in the accuracy as the number of calculation trials increased was greater than that in the younger group. In other words, this decrease in the older group may be explained by a reduction in working memory capacity, which is directly caused by a decline in basic tactile cognitive ability.

Chapter 5 describes the third experiment. In the present ERP study, we modified the traditional spatial attention paradigm by adding the double stimuli with short interval (i.e., 10, 30, and 100 ms) conditions to approach how the somatosensory system processes the balance between excitation and inhibition. A total of five kinds of stimulation were used in the experiment which are single stimulus (one raised pin for 40 ms), standard stimulus (eight pins for 40 ms), interval 10 ms, 30 ms, 100 ms double stimuli. Subjects were asked to pay attention to the instructed finger and detect whether the standard stimulus was presented to the finger. The results showed clear attention component of the single stimulus condition, but the suppression component of three interval conditions seem dominant in the somatosensory areas. In detail, we found that the strongest suppression effect in interval 30 ms condition, and the suppression and enhancement effects seem counterbalance for both of interval 10 ms and 100 ms conditions. This processing may allow the human easily to discriminate multi-stimulations on the same body part.

6.2 Future projections

The current thesis utilize the behavioral experiment and the temporal solution of eventrelated potentials to investigate spatial and temporal characteristics on touch. The results suggest that spatial or temporal characteristics modulates the tactile processing differently, but partially overlapping. However, in daily life, humans are surrounded by information from multiple modalities, such as, visual, auditory, somatosensory, and so on. Information from spatial and temporal is the most important for understanding the real world. Spatial and temporal signals can be integrated in the human brain and provide a coherent cognition of the real world, which is called spatiotemporal integration. Therefore, future studies will focus on tactile spatiotemporal integration with ERP technique.

Another challenge is that the relationship between spatiotemporal integration and attention. By utilizing attention, it is possible to select stimuli from a multitude of sensory information to help the brain integrate useful and temporally coincident stimuli from various sensory modalities into coherent cognition. Conversely, because of its increased salience, an integrated multisensory stimulus can capture attention more efficiently in complex contexts. Recently, research associated with the interplay between multisensory integration and attention has blossomed in a spectacular fashion. To date, however, it is unclear under what circumstances and through what mechanisms multisensory integration and attention interact. Therefore, frameworks of the interactions between attention and spatiotemporal integration should have been proposed in the future.

Appendix

I. Simple introduction of vibrotactile device

The Braille stimulator was manufactured by KGS, Saitama in Japan (Figure A1). The white cylinders were made by insulated organic plastic. When the tactile vibrotactile stimuli were presented, piezo-electric under the white cylinders were produced the vibrotactile stimuli press strength of the spots is 0.177N. Lead to upper points of presented stimuli start to vibrate. Subjects can feel the vibrations stimulus obviously. Because the white cylinders were insulated, so the subject was no having any pain arising from electric shock or the other tactile effects.



Figure A1. The Braille stimulator


Figure A2. Electronic circuit of vibrotactile device

Tactile pin stroke		0.7[mm]	
Pitch between points		2.4[mm]	
Pitch between masses		4.0[mm]	
Tactile pin diameter		1.3[mm]	
Tactile pin pushing pressure		0.177[N]	
Operating ambient temperature		0~40[°C]	
Ambient humidity used		20~70[%]	
size	1 cell		6.4×16×68[mm]
weight	1 cell		about 6.2[g]
Power source	steady state200[V]	Per pin	8[µA](Max)
	steady state5[V]	Per pin	$4[\mu A](Max)$
	Operating 200[V]	Per pin	2[Hz]で65[µA]
	Operating 5[V]	Data transfer	fDATA=4[MHz]
		Per module	15[mA](Max)

 Table A1. Detailed explanation of braille sell

II. Simple introduction of EEG apparatus

The BrainAmp MR plus was manufactured by BrainProduct Inc., Germany. This amplifier is a compact solution for neurophysiology research that can be combined with other units within the same product family to cover a vast range of possible application areas. This fully portable solution can be used for standard EEG/ERP recordings and can also be placed inside of the MRI bore for simultaneous EEG/fMRI acquisitions.

Thanks to its 5 kHz sampling rate per channel, the BrainAmp can be used to record EEG, EOG, and EMG signals as well as evoked potentials with a frequency up to 1 kHz. The 16-bit TTL trigger input allows the detection of a large number of markers from visual, acoustic, electrical, magnetic or other stimulation modalities. The BrainAmps can be used both with passive and active electrodes offering a great degree of flexibility.

The 32 channel units can be stacked to expand the number of channels up to 256 and combined with the BrainAmp ExG to record EEG, EOG, EMG, ECG, GSR (Galvanic Skin Response) and many other types of bipolar and auxiliary signals.



Figure A3. EEG amplifier of BrainAmp MR plus

Number of Channels per unit	32	
Max. Number of channels	128	
Reference Type	unipolar	
MR-compatibility	Yes (for scanners up to 4 Tesla)	
Bandwidth [Hz]	DC - 1000	
High Pass Filter [Hz]	0.016 / 10 s AC or DC switchable	
Low Pass Filter [Hz]	1000 / 250 switchable	
Input Noise [µVpp]	≤1	
Input Impedance [MΩ]	10 / 10000	
Input Measurement Ground / eference	Yes	
A/D-C [bit]	16	
A/D-Rate [Hz]	5000	
Max. Sampling Frequency [Hz]	5000	
Offset Compatibility [mV]	± 300	
Operating Range [mV]	selectable: ±3.2768; ±16.384; ±327.68	
Resolution [µV]	selectable: 0.1; 0.5; 10.0	
CMRR [dB]	≥110	
TTL Trigger Input [bit]	16	
Synchronized Digital Trigger Input [bit]	up to 16	
Max. Power Consumption [mA]	160	
Power Supply	rechargeable Battery	
Signal Transmission	optical	
PC Interface	PCI, USB 2.0	
Deblocking Function	Yes	
Blocking of Unused Channels	Yes	
Safety	Twin Fiber optical Transmission Protection Class II, Type BF IEC EN 60601 EMC tested, electrically safe	
Classification to MDD 93/42/EEC	Class IIa	
Dimensions H x W x D [mm]	68 x 160 x 187	
Weight [kg]	1.1	

 Table A2. Technical specifications of BrainAmp MR plus

The current thesis adapted 32 electrodes of this apparatus. The location and name of each channel that the present study was used is displayed in **Figure A4**.



Figure A4 The locations and names of each electrode

III. Simple introduction of primary somatosensory cortex

A somatosensory pathway will typically have three long neurons: primary, secondary, and tertiary (or first, second, and third).

- The first neuron always has its cell body in the dorsal root ganglion of the spinal nerve (if sensation is in parts of the head or neck not covered by the cervical nerves, it will be the trigeminal nerve ganglia or the ganglia of other sensory cranial nerves).
- The second neuron has its cell body either in the spinal cord or in the brainstem. This neuron's ascending axons will cross (decussate) to the opposite side either in the spinal cord or in the brainstem.
- 3. In the case of touch and certain types of pain, the third neuron has its cell body in the VPN of the thalamus and ends in the postcentral gyrus of the parietal lobe.

The primary somatosensory cortex is located in the postcentral gyrus, and is part of the somatosensory system. It was initially defined from surface stimulation studies of Wilder Penfield, and parallel surface potential studies of Bard, Woolsey, and Marshall. Although initially defined to be roughly the same as Brodmann areas 3, 1 and 2, more recent work by Kaas has suggested that for homogeny with other sensory fields only area 3 should be referred to as "primary somatosensory cortex", as it receives the bulk of the thalamocortical projections from the sensory input fields.

At the primary somatosensory cortex, tactile representation is orderly arranged (in an inverted fashion) from the toe (at the top of the cerebral hemisphere) to mouth (at the bottom). However, some body parts may be controlled by partially overlapping regions of cortex. Each cerebral hemisphere of the primary somatosensory cortex only contains a tactile representation of the opposite (contralateral) side of the body. The amount of primary somatosensory cortex devoted to a body part is not proportional to the absolute size of the body surface, but, instead, to the relative density of cutaneous tactile receptors on that body part. The density of cutaneous tactile receptors on a body part is generally indicative of the degree of sensitivity of tactile stimulation experienced at said body part. For this reason, the human lips and hands have a larger representation than other body parts.



Brodmann's cytotechtonic map (1909): Lateral surface Brodmann's cytotechtonic map (1909): Medial surface

Figure A5 The brain areas of primary somatosensory cortex

Publications

Journal Papers

 <u>Yang Liu</u>, Qiong Wu, Jiajia Yang, Satoshi Takahashi, Yoshimichi Ejima and Jinglong Wu. Effects of Aging on Vibrotactile Stimulus Counting Abilities[J]. International Information Institute, 21.07, 2018, pp.2071-2086.

International Conference Paper

- <u>Yang Liu</u>, Jiajia Yang, Yinghua Yu, Yoshinobu Inai, Jinglong Wu. Development and Evaluation of Vibrotactile Stimuli Presentation Device to Investigate Tactile Working Memory. *International Conference on Mechatronics and Automation (ICMA)*. 2013: 135-140.
- [2] <u>Yang Liu</u>, Yinghua Yu, Jiajia Yang, Yoshinobu Inai, Jinglong Wu. Ability to Recognize and Identify the Location of Vibration Stimulation on the Fingers. *International Conference on Mechatronics and Automation (ICMA)*. 2014: 1601-1606.
- [3] <u>Yang Liu</u>, Yinghua Yu, Jiajia Yang, Satoshi Takahashi, Yoshimichi Ejima, Jinglong Wu. Relationship between Spatiotemporal Integration of Tatile Information and Somatic Sensory Memory in Human Somatosensory Cortex: A Somatosensory Evoked Potentials (Seps) Study. *International Conference on Complex Medical Engineering (ICME)*. 2016.
- [4] <u>Yang Liu</u>, Jiajia Yang, Qiong Wu, Yinghua Yu, Hirofumi Shimamura, Yoshimichi Ejima, Jinglong Wu. Tactile Sensory Memory for the vibration stimuli presented on the fingers: an ERP Study. *International Conference on Complex Medical Engineering (ICME)*. 2017.
- [5] Ritsu Go, Jinglong Wu, <u>Yang Liu</u>, Yusuke Kuroda, Qiong Wu. Cognitive

Psychological Study on The Occurrence of Microsaccades in Visual Spatial Attention. *International Conference on Mechatronics and Automation (ICMA)*. 2018: 34-39.

[6] Qiong Wu, <u>Yang Liu</u>, Jinglong Wu, Ritsu Go. A Behavioral Study on Angle Discrimination and Sorting by Fingertip Touch. International Conference on Mechatronics and Automation (ICMA). 2018: 178-183.

Acknowledgements

Firstly, I would like to express my sincerely gratitude to Prof. Jinglong Wu for the continuous support during my Ph.D studies and related researches. Prof. Jinglong Wu helped me in all my research design and writing of this thesis. I could not complete my study of doctor course and finish this thesis successfully without his enlightening instruction, impressive kindness and patience. His diligence gives me power not only during my present PhD scours, but also in my future life. In addition, Prof. Wu also helps me also for my daily life, and let my life in japan much easier.

Secondly, I also want to express my sincerely gratitude to my supervisor Prof. Satoshi Takahashi. I got a lot of comments for Prof. Satoshi Takahashi during I make my study plan, conduct my experiments, write published papers and this thesis. During the PhD scours, Prof. Satoshi Takahashi also greatly supports me when I applied the scholarships.

Third, I would also like to express my sincere thanks to Prof. Yoshimichi Ejima and Jiajia Yang, who provided me a lot of comments during I write my papers. Without their precious support, it would not be possible to conduct this thesis successfully.

I also want to thank the rest of my thesis committee: Prof. Masanobu Abe, and Prof. Tokumi Yokohira for their insightful comments and encouragement, but also for the question which incented me to widen my research from various perspectives.

I also thank the students and staff in Wu lab. Without their cooperation, I cannot imagine how I could have finished my experiments. I sincerely thank all those who contributed to my experiment, my paper and my dissertation.

Finally, I extend my deep appreciation and dedicate this dissertation to my parents and my friends, especially to my husband, who have always supported and understood me.

References

[1] L. S. Loomis JM, "Tactual perception," *Handbook of perception and Human Performances*, vol. 2, 1986.

[2] B. M. Graziano MSA, "In How the Brain Represents the body," *Insights from Neurophysiology and Psychology*, pp. 136-157, 2002.

[3] S. K. Schultz, "Principles of neural science, 4th edition.," *American Journal of Psychiatry*, vol. 158, pp. 662-662, Apr 2001.

[4] S. Kuroki and S. Nishida, "Human tactile detection of within- and inter-finger spatiotemporal phase shifts of low-frequency vibrations," *Sci Rep*, vol. 8, p. 4288, Mar 9 2018.

[5] L. A. Jeffress, "A place theory of sound localization," *J Comp Physiol Psychol*, vol. 41, pp. 35-9, Feb 1948.

[6] J. P. van Santen and G. Sperling, "Elaborated Reichardt detectors," *J Opt Soc Am A*, vol. 2, pp. 300-21, Feb 1985.

[7] E. H. Adelson and J. R. Bergen, "Spatiotemporal energy models for the perception of motion," *J Opt Soc Am A*, vol. 2, pp. 284-99, Feb 1985.

[8] S. J. Bolanowski, Jr., G. A. Gescheider, R. T. Verrillo, and C. M. Checkosky,
 "Four channels mediate the mechanical aspects of touch," *J Acoust Soc Am*, vol. 84, pp. 1680-94, Nov 1988.

[9] R. S. Johansson, U. Landstrom, and R. Lundstrom, "Responses of Mechanoreceptive Afferent Units in the Glabrous Skin of the Human Hand to Sinusoidal Skin Displacements," *Brain Research*, vol. 244, pp. 17-25, 1982.

[10] M. Hollins, Delemos, K. A. & Goble, A. K, "Vebrotactile adaptation of a RA system: A psychophysical analysis," *Somesthesis and the Neurobiology of the Somatosensory Cortex*, 1996.

[11] M. Hollins and E. A. Roy, "Perceived intensity of vibrotactile stimuli: The role of mechanoreceptive channels," *Somatosensory and Motor Research*, vol. 13, pp. 273-286, 1996.

[12] M. Tommerdahl, K. D. Hester, E. R. Felix, M. Hollins, O. V. Favorov, P. M.

Quibrera, *et al.*, "Human vibrotactile frequency discriminative capacity after adaptation to 25 Hz or 200 Hz stimulation," *Brain Research*, vol. 1057, pp. 1-9, Sep 28 2005.

[13] K. O. Johnson, "The roles and functions of cutaneous mechanoreceptors," *Current Opinion in Neurobiology*, vol. 11, pp. 455-461, Aug 2001.

[14] E. P. Gardner and B. F. Sklar, "Discrimination of the Direction of Motion on the Human Hand - a Psychophysical Study of Stimulation Parameters," *Journal of Neurophysiology*, vol. 71, pp. 2414-2429, Jun 1994.

[15] J. A. Pruszynski and R. S. Johansson, "Edge-orientation processing in first-order tactile neurons," *Nature Neuroscience*, vol. 17, pp. 1404-1409, Oct 2014.

[16] Z. Zhu, E. A. Disbrow, J. M. Zumer, D. J. McGonigle, and S. S. Nagarajan, "Spatiotemporal integration of tactile information in human somatosensory cortex," *Bmc Neuroscience*, vol. 8, Mar 14 2007.

[17] F. Mancini, T. Nash, G. D. Iannetti, and P. Haggard, "Pain relief by touch: A quantitative approach," *Pain*, vol. 155, pp. 635-642, Mar 2014.

[18] D. Yarnitsky, M. Kunin, R. Brik, and E. Sprecher, "Vibration reduces thermal pain in adjacent dermatomes," *Pain*, vol. 69, pp. 75-77, Jan 1997.

[19] E. A. Roy, M. Hollins, and W. Maixner, "Reduction of TMD pain by high-frequency vibration: a spatial and temporal analysis," *Pain*, vol. 101, pp. 267-274, Feb 2003.

[20] R. Staud, M. E. Robinson, C. T. Goldman, and D. D. Price, "Attenuation of experimental pain by vibro-tactile stimulation in patients with chronic local or widespread musculoskeletal pain," *European Journal of Pain*, vol. 15, pp. 836-842, Sep 2011.

[21] K. Inui, T. Tsuji, and R. Kakigi, "Temporal analysis of cortical mechanisms for pain relief by tactile stimuli in humans," *Cerebral Cortex*, vol. 16, pp. 355-365, Mar 2006.
[22] E. Testani, D. Le Pera, C. Del Percio, R. Miliucci, A. Brancucci, C. Pazzaglia, *et al.*, "Cortical inhibition of laser pain and laser-evoked potentials by non-nociceptive somatosensory input," *European Journal of Neuroscience*, vol. 42, pp. 2407-2414, Oct 2015.

[23] R. Zopf, C. M. Giabbiconi, T. Gruber, and M. M. Muller, "Attentional modulation of the human somatosensory evoked potential in a trial-by-trial spatial cueing and sustained spatial attention task measured with high density 128 channels EEG," *Cognitive Brain Research*, vol. 20, pp. 491-509, Aug 2004.

[24] R. Schubert, P. Ritter, T. Wustenberg, C. Preuschhof, G. Curio, W. Sommer, *et al.*, "Spatial Attention Related SEP Amplitude Modulations Covary with BOLD Signal in S1-A Simultaneous EEG-fMRI Study," *Cerebral Cortex,* vol. 18, pp. 2686-2700, Nov 2008.

[25] F. A. Geldard and C. E. Sherrick, "The cutaneous "rabbit": a perceptual illusion," *Science*, vol. 178, pp. 178-9, Oct 13 1972.

[26] F. A. Geldard, "Sensory saltation: Metastability in the perceptual world," *New York: Lawrence Erlbaum Associates*, 1975.

[27] L. Krubitzer, J. Clarey, R. Tweedale, G. Elston, and M. Calford, "A Redefinition of Somatosensory Areas in the Lateral Sulcus of Macaque Monkeys," *Journal of Neuroscience*, vol. 15, pp. 3821-3839, May 1995.

[28] B. L. Whitsel, L. M. Petrucelli, and G. Werner, "Symmetry and connectivity in the map of the body surface in somatosensory area II of primates," *J Neurophysiol*, vol. 32, pp. 170-83, Mar 1969.

[29] S. R. Burton H, "Somatosensory cortex and tactile perceptions," *In Touch and Pain London: Academic Press*, 1996.

[30] H. X. Qi, D. C. Lyon, and J. H. Kaas, "Cortical and thalamic connections of the parietal ventral somatosensory area in marmoset monkeys (Callithrix jacchus)," *J Comp Neurol*, vol. 443, pp. 168-82, Feb 4 2002.

[31] E. Disbrow, E. Litinas, G. H. Recanzone, J. Padberg, and L. Krubitzer, "Cortical connections of the second somatosensory area and the parietal ventral area in macaque monkeys," *J Comp Neurol*, vol. 462, pp. 382-99, Aug 4 2003.

[32] L. A. Krubitzer and J. H. Kaas, "The organization and connections of somatosensory cortex in marmosets," *J Neurosci*, vol. 10, pp. 952-74, Mar 1990.

[33] H. X. Qi, D. C. Lyon, and J. H. Kaas, "Cortical and thalamic connections of the parietal ventral somatosensory area in marmoset monkeys (Callithrix jacchus)," *Journal of Comparative Neurology*, vol. 443, pp. 168-182, Feb 4 2002.

[34] E. Disbrow, E. Litinas, G. H. Recanzone, J. Padberg, and L. Krubitzer, "Cortical connections of the second somatosensory area and the parietal ventral area in macaque monkeys," *Journal of Comparative Neurology*, vol. 462, pp. 382-399, Aug 4 2003.

[35] J. L. Reed, H. X. Qi, Z. Y. Zhou, M. R. Bernard, M. J. Burish, A. B. Bonds, *et al.*, "Response Properties of Neurons in Primary Somatosensory Cortex of Owl Monkeys

Reflect Widespread Spatiotemporal Integration," *Journal of Neurophysiology*, vol. 103, pp. 2139-2157, Apr 2010.

[36] J. P. Warren, M. Santello, and S. I. H. Tillery, "Electrotactile stimuli delivered across fingertips inducing the Cutaneous Rabbit Effect," *Experimental Brain Research*, vol. 206, pp. 419-426, Oct 2010.

[37] R. S. Johansson and G. Westling, "Roles of Glabrous Skin Receptors and Sensorimotor Memory in Automatic-Control of Precision Grip When Lifting Rougher or More Slippery Objects," *Experimental Brain Research*, vol. 56, pp. 550-564, 1984.

[38] C. K. C. Loo, L. A. Hall, D. I. Mccloskey, and M. J. Rowe, "Proprioceptive Contributions to Tactile Identification of Figures - Dependence on Figure Size," *Behavioural Brain Research*, vol. 7, pp. 383-386, 1983.

[39] R. L. Klatzky, J. M. Loomis, S. J. Lederman, H. Wake, and N. Fujita, "Haptic Identification of Objects and Their Depictions," *Perception & Psychophysics*, vol. 54, pp. 170-178, Aug 1993.

[40] S. J. a. K. Lederman, R. L., "Designing haptic interfaces for teleoperational and virtual environments: Should spatially distributed forces be displayed to the fingertip?," 1997.

[41] A. Gallace, H. Z. Tan, and C. Spence, "Numerosity judgments for tactile stimuli distributed over the body surface," *Perception,* vol. 35, pp. 247-266, 2006.

[42] A. Gallace, H. Z. Tan, and C. Spence, "Multisensory numerosity judgments for visual and tactile stimuli," *Perception & Psychophysics*, vol. 69, pp. 487-501, May 2007.

[43] A. Gallace, H. Z. Tan, P. Haggard, and C. Spence, "Short term memory for tactile stimuli," *Brain Research*, vol. 1190, pp. 132-142, Jan 23 2008.

[44] A. Gallace, H. Z. Tan, and C. Spence, "The body surface as a communication system: The state of the art after 50 years," *Presence-Teleoperators and Virtual Environments*, vol. 16, pp. 655-676, Dec 2007.

[45] A. Gallace, H. Z. Tan, and C. Spence, "Tactile change detection," *World Haptics Conference: First Joint Eurohaptics Conference and Symposium on Haptic Interfaces for Virutual Environment and Teleoperator Systems, Proceedings*, pp. 12-16, 2005.

[46] A. Gallace, Auvray, M., Tan, H.Z., Spence, C, "When visual transients impair tactile change detection: A novel case of crossmodal change blindness?," *Neuroscience Letters*, vol. 398, pp. 280-285, 2006.

[47] A. Gallace, H. Z. Tan, and C. Spence, "The failure to detect tactile change: a tactile analogue of visual change blindness," *Psychon Bull Rev*, vol. 13, pp. 300-3, Apr 2006.

[48] J. Lofvenberg and R. S. Johansson, "Regional Differences and Interindividual Variability in Sensitivity to Vibration in the Glabrous Skin of the Human Hand," *Brain Research*, vol. 301, pp. 65-72, 1984.

[49] R. Schubert, P. Ritter, T. Wustenberg, C. Preuschhof, G. Curio, W. Sommer, *et al.*, "Spatial attention related SEP amplitude modulations covary with BOLD signal in S1--a simultaneous EEG--fMRI study," *Cereb Cortex*, vol. 18, pp. 2686-700, Nov 2008.

[50] J. C. Bliss, H. D. Crane, P. K. Mansfield, and J. T. Townsend, "Information available in brief tactile presentations. NASA CR-623," *NASA Contract Rep NASA CR*, pp. 57-86, Feb 1967.

[51] J. C. Craig, "Vibrotactile pattern perception: extraordinary observers," *Science,* vol. 196, pp. 450-2, Apr 22 1977.

[52] J. Downar, A. P. Crawley, D. J. Mikulis, and K. D. Davis, "A multimodal cortical network for the detection of changes in the sensory environment," *Nat Neurosci*, vol. 3, pp. 277-83, Mar 2000.

[53] J. M. Loomis and C. C. Collins, "Sensitivity to shifts of a point stimulus: an instance of tactile hyperacuity," *Percept Psychophys*, vol. 24, pp. 487-92, Dec 1978.

[54] R. W. Van Boven, J. E. Ingeholm, M. S. Beauchamp, P. C. Bikle, and L. G. Ungerleider, "Tactile form and location processing in the human brain," *Proceedings of the National Academy of Sciences of the United States of America*, vol. 102, pp. 12601-12605, Aug 30 2005.

[55] W. H. Talbot, I. Darian-Smith, H. H. Kornhuber, and V. B. Mountcastle, "The sense of flutter-vibration: comparison of the human capacity with response patterns of mechanoreceptive afferents from the monkey hand," *J Neurophysiol*, vol. 31, pp. 301-34, Mar 1968.

[56] J. C. Craig, Johnson, K.O, "The two-point threshold: Not a measure of tactile spatial resolution," *Curr Dir Psychol*, vol. 9, pp. 29–32, 2000.

[57] S. J. Lederman and R. L. Klatzky, "Haptic perception: A tutorial," *Attention Perception & Psychophysics*, vol. 71, pp. 1439-1459, Oct 2009.

[58] K. O. Johnson and J. R. Phillips, "Tactile spatial resolution. I. Two-point

discrimination, gap detection, grating resolution, and letter recognition," *J Neurophysiol*, vol. 46, pp. 1177-92, Dec 1981.

[59] P. Bruns, C. J. Camargo, H. Campanella, J. Esteve, H. R. Dinse, and B. Roder,
"Tactile acuity charts: a reliable measure of spatial acuity," *PLoS One*, vol. 9, p. e87384,
2014.

[60] J. J. Yang, J. L. Wu, and J. P. He, "Programmable tactile pattern presentations operational under MRI to investigate neural mechanisms of tactile shape discrimination," *Journal of Neuroscience Methods*, vol. 201, pp. 17-26, Sep 30 2011.

[61] J. Gibson, "Observation on active touch," *Psychol Rev,*, vol. 69, pp. 477–91, 1962.

[62] T. Katus, S. K. Andersen, and M. M. Muller, "Maintenance of tactile short-term memory for locations is mediated by spatial attention," *Biological Psychology*, vol. 89, pp. 39-46, Jan 2012.

[63] J. A. Harris, I. M. Harris, and M. E. Diamond, "The topography of tactile working memory," *Journal of Neuroscience*, vol. 21, pp. 8262-8269, Oct 15 2001.

[64] K. J. Riggs, L. Ferrand, D. Lancelin, L. Fryziel, G. Dumur, and A. Simpson, "Subitizing in tactile perception," *Psychological Science*, vol. 17, pp. 271-272, Apr 2006.

[65] K. O. Johnson and S. S. Hsiao, "Neural Mechanisms of Tactual Form and Texture-Perception," *Annual Review of Neuroscience*, vol. 15, pp. 227-250, 1992.

[66] M. Auvray, A. Gallace, and C. Spence, "Tactile short-term memory for stimuli presented on the fingertips and across the rest of the body surface," *Attention Perception & Psychophysics*, vol. 73, pp. 1227-1241, May 2011.

[67] L. M. Trick and Z. W. Pylyshyn, "Why are small and large numbers enumerated differently? A limited-capacity preattentive stage in vision," *Psychol Rev*, vol. 101, pp. 80-102, Jan 1994.

[68] V. Camos and B. Tillmann, "Discontinuity in the enumeration of sequentially presented auditory and visual stimuli," *Cognition,* vol. 107, pp. 1135-43, Jun 2008.

[69] Y. Liu, Y. H. Yu, J. J. Yang, Y. Inai, and J. L. Wu, "Ability to Recognize and Identify the Location of Vibration Stimulation on the Fingers," *2014 Ieee International Conference on Mechatronics and Automation (Ieee Icma 2014)*, pp. 1601-1606, 2014.

[70] F. Tremblay, A. C. Mireault, L. Dessureault, H. Manning, and H. Sveistrup, "Postural stabilization from fingertip contact: I. Variations in sway attenuation, perceived stability and contact forces with aging," *Experimental Brain Research*, vol. 157, pp. 275-285, Aug 2004.

[71] F. Tremblay, A. Backman, A. Cuenco, K. Vant, and M. A. Wassef, "Assessment of spatial acuity at the fingertip with grating (JVP) domes: validity for use in an elderly population," *Somatosensory and Motor Research*, vol. 17, pp. 61-66, 2000.

[72] J. J. Yang, T. Ogasa, Y. Ohta, K. Abe, and J. L. Wu, "Decline of Human Tactile Angle Discrimination in Patients with Mild Cognitive Impairment and Alzheimer's Disease," *Journal of Alzheimers Disease*, vol. 22, pp. 225-234, 2010.

[73] K. T. John, A. W. Goodwin, and I. Dariansmith, "Tactile Discrimination of Thickness," *Experimental Brain Research*, vol. 78, pp. 62-68, 1989.

[74] A. B. Vallbo, K. A. Olsson, K. G. Westberg, and F. J. Clark, "Microstimulation of Single Tactile Afferents from the Human Hand - Sensory Attributes Related to Unit Type and Properties of Receptive-Fields," *Brain*, vol. 107, pp. 727-749, 1984.

[75] J. C. Stevens, "Aging and Spatial Acuity of Touch," *Journals of Gerontology*, vol. 47, pp. P35-P40, Jan 1992.

[76] F. Vega-Bermudez and K. O. Johnson, "Fingertip skin conformance accounts, in part, for differences in tactile spatial acuity in young subjects, but not for the decline in spatial acuity with aging," *Percept Psychophys,* vol. 66, pp. 60-7, Jan 2004.

[77] P. J. Olesen, H. Westerberg, and T. Klingberg, "Increased prefrontal and parietal activity after training of working memory," *Nat Neurosci,* vol. 7, pp. 75-9, Jan 2004.

[78] K. Alho, S. V. Medvedev, S. V. Pakhomov, M. S. Roudas, M. Tervaniemi, K. Reinikainen, *et al.*, "Selective tuning of the left and right auditory cortices during spatially directed attention," *Cognitive Brain Research*, vol. 7, pp. 335-341, Jan 1999.

[79] C. M. Karns and R. T. Knight, "Intermodal Auditory, Visual, and Tactile Attention Modulates Early Stages of Neural Processing," *Journal of Cognitive Neuroscience*, vol. 21, pp. 669-683, Apr 2009.

[80] T. Noesselt, S. A. Hillyard, M. G. Woldorff, A. Schoenfeld, T. Hagner, L. Jancke, *et al.*, "Delayed striate cortical activation during spatial attention," *Neuron*, vol. 35, pp. 575-587, Aug 1 2002.

[81] E. Macaluso, J. Driver, J. van Velzen, and M. Eimer, "Influence of gaze direction on crossmodal modulation of visual ERPS by endogenous tactile spatial attention," *Cognitive Brain Research*, vol. 23, pp. 406-417, May 2005.

81

[82] K. J. Meador, J. D. Allison, D. W. Loring, T. B. Lavin, and J. J. Pillai, "Topography of somatosensory processing: Cerebral lateralization and focused attention," *Journal of the International Neuropsychological Society*, vol. 8, pp. 349-359, Mar 2002.

[83] B. Forster and M. Eimer, "The attentional selection of spatial and non-spatial attributes in touch: ERP evidence for parallel and independent processes," *Biological Psychology*, vol. 66, pp. 1-20, Mar 2004.

[84] C. Braun, H. Hess, M. Burkhardt, A. Wuhle, and H. Preissl, "The right hand knows what the left hand is feeling," *Experimental Brain Research*, vol. 162, pp. 366-373, Apr 2005.

[85] K. Pilz, R. Veit, C. Braun, and B. Godde, "Effects of co-activation on cortical organization and discrimination performance," *Neuroreport*, vol. 15, pp. 2669-2672, Dec 3 2004.

[86] M. Eimer and J. Driver, "An event-related brain potential study of cross-modal links in spatial attention between vision and touch," *Psychophysiology*, vol. 37, pp. 697-705, Sep 2000.

[87] M. Eimer and B. Forster, "The spatial distribution of attentional selectivity in touch: evidence from somatosensory ERP components," *Clinical Neurophysiology*, vol. 114, pp. 1298-1306, Jul 2003.

[88] M. Eimer, B. Forster, A. Fieger, and S. Harbich, "Effects of hand posture on preparatory control processes and sensory modulations in tactile-spatial attention," *Clinical Neurophysiology*, vol. 115, pp. 596-608, Mar 2004.

[89] M. Eimer and B. Forster, "Modulations of early somatosensory ERP components by transient and sustained spatial attention," *Experimental Brain Research*, vol. 151, pp. 24-31, Jul 2003.

[90] B. Forster and H. Gillmeister, "ERP investigation of transient attentional selection of single and multiple locations within touch," *Psychophysiology*, vol. 48, pp. 788-796, Jun 2011.

[91] C. Utzerath, E. S. John-Saaltink, J. Buitelaar, and F. P. de Lange, "Repetition suppression to objects is modulated by stimulus-specific expectations," *Scientific Reports,* vol. 7, Aug 18 2017.

[92] K. Grill-Spector and R. Malach, "fMR-adaptation: a tool for studying the functional properties of human cortical neurons," *Acta Psychologica*, vol. 107, pp. 293-

321, Apr 2001.

[93] M. M. Mesulam, "Spatial attention and neglect: parietal, frontal and cingulate contributions to the mental representation and attentional targeting of salient extrapersonal events," *Philos Trans R Soc Lond B Biol Sci*, vol. 354, pp. 1325-46, Jul 29 1999.