LOCALIZING TOUCH ON THE SKIN SURFACE AND IN EXTERNAL SPACE:
REVISITING THE SERIAL MODEL

by
Yuqi Liu

A dissertation submitted to the Faculty of the University of Delaware in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Psychology

Summer 2019

© 2019 Yuqi Liu
All Rights Reserved
LOCALIZING TOUCH ON THE SKIN SURFACE AND IN EXTERNAL SPACE:
REVISITING THE SERIAL MODEL

by

Yuqi Liu

Approved:

Robert Simons, Ph.D.
Chair of the Department of Psychological and Brain Sciences

Approved:

John Pelesko, Ph.D.
Dean of the College of Arts and Sciences

Approved:

Douglas J. Doren, Ph.D.
Interim Vice Provost for Graduate and Professional Education and
Dean of the Graduate College
I certify that I have read this dissertation and that in my opinion it meets the academic and professional standard required by the University as a dissertation for the degree of Doctor of Philosophy.

Signed: Jared Medina, Ph.D.
Professor in charge of dissertation

I certify that I have read this dissertation and that in my opinion it meets the academic and professional standard required by the University as a dissertation for the degree of Doctor of Philosophy.

Signed: Helene Intraub, Ph.D.
Member of dissertation committee

I certify that I have read this dissertation and that in my opinion it meets the academic and professional standard required by the University as a dissertation for the degree of Doctor of Philosophy.

Signed: Timothy J. Vickery, Ph.D.
Member of dissertation committee

I certify that I have read this dissertation and that in my opinion it meets the academic and professional standard required by the University as a dissertation for the degree of Doctor of Philosophy.

Signed: Matthew R. Longo, Ph.D.
Member of dissertation committee
I certify that I have read this dissertation and that in my opinion it meets the academic and professional standard required by the University as a dissertation for the degree of Doctor of Philosophy.

Signed:  

Amy Griffin, Ph.D.
Member of dissertation committee
ACKNOWLEDGEMENTS

Dr. Jared Medina for all the great support, guidance, and inspiration during my academic development.

My dissertation committee, Timothy Vickery, Helene Intraub, Amy Griffin, and Matthew Longo, for their insights and advice on this dissertation.

Dr. Robert Rafal for devoting time teaching me analyzing neuroimaging data.

Alexandria O’Neal, Kylie Wright, Cassidy Edmondson, and Erika Schemmel for help in data collection.

DS for dedicating time being such a great participant.

All the other graduate students in the Psychological and Brain Sciences department for creating a friendly environment.

The Psychological and Brain Sciences department for all the help and support.
DEDICATION

This manuscript is dedicated to

My parents, for their support and encouragement.

My friends, for their faith in me.

My husband, for his love and patience.
TABLE OF CONTENTS

LIST OF TABLES ............................................................................................................. x
LIST OF FIGURES .......................................................................................................... xi
ABSTRACT .................................................................................................................. xviii

Chapter

1  TACTILE LOCALIZATION AND BODY REPRESENTATIONS .........................1
   1.1  Primary somatosensory cortex .................................................................3
   1.2  Beyond the primary somatosensory cortex: higher-order body
        representations .........................................................................................6
       1.2.1  Body representations .....................................................................6
       1.2.2  An alternative model to the labelled-line hypothesis ..............7
       1.2.3  Information other than body size and shape .........................10
   1.3  Effects of body posture on tactile localization on the body ..............13
       1.3.1  A strictly serial model ...............................................................14
       1.3.2  Body posture modulates tactile detection .............................16
       1.3.3  Effects of body posture on tactile localization on the body ....17

2  INTACT TACTILE DETECTION YET BIASED TACTILE LOCALIZATION
   IN A HAND-CENTERED REFERENCE FRAME: A CASE STUDY ..............24
   2.1  Experiment 2.1.1 Assessing tactile detection ......................................29
   2.2  Experiment 2.2. Tactile localization ....................................................31
   2.3  Experiment 2.3. Investigation of spatial reference frame in tactile
        localization errors ......................................................................................36
        2.3.1  Experiment 2.3.1. Hand palm facing down ............................36
        2.3.2  Experiment 2.3.2. Hand palm facing up ..................................39
        2.3.3  Experiment 2.3.3. Hand palm facing down, rotated 90° .....42
   2.4  Experiment 2.4. Are the observed biases motor or perceptual? .......45

---

1The experiments in this dissertation are numbered in consistency with the chapter
numbers.
2.4.1 Experiment 2.4.1. Examining pointing ability of the ipsilesional hand........................................45
2.4.2 Experiment 2.4.2. Tactile localization with verbal response.........................................................47

2.5 Experiment 2.5. Landmark localization.................................................................50
2.6 General discussion.................................................................................................60

3 THE EFFECTS OF VISUAL-PROPRIOCEPTIVE CONFLICT ON TACTILE LOCALIZATION: INVESTIGATING NEUROLOGICALLY INTACT INDIVIDUALS.........................................................60

3.1 Experiment 3.1. Effects of visual-proprioceptive conflict on tactile localization ........................................64
3.2 Experiment 3.2. Controlling for the effects of hand position on tactile localization ....................................................75
3.3 Experiment 3.3. Controlling for the effects of gaze-proprioceptive spatial mismatch on tactile localization..............84
3.4 General discussion.................................................................................................93

4 EFFECTS OF FINGER POSTURE ON TACTILE LOCALIZATION.................104

4.1 Experiment 4 ..................................................................................................107
4.2 General discussion.................................................................................................123

5 NEURAL CORRELATES OF TACTILE LOCATION REPRESENTATIONS IN SOMATOTOPIC AND EXTERNAL SPACE.........................................................133

5.1 Experiment 5 ..................................................................................................136
5.2 General discussion.................................................................................................150

6 SUMMARY AND CONCLUSIONS.........................................................................158

6.1 Summary of the findings ..................................................................................158
6.2 Mechanisms of how external information influences tactile localization on the body surface.........................................................161
6.3 Neural correlates of integration of external information and somatotopic representation.........................................................163
6.4 Conclusion............................................................................................................164

REFERENCES .............................................................................................................165

Appendix

A DIFFUSION-WEIGHTED IMAGING ANALYSIS ON DS .................180
B  ADDITIONAL FIGURES AND ANALYSES ON EXPERIMENT 3.1 TO EXPERIMENT 3.3 ............................................................. 188
C  IRB APPROVAL .................................................................................................................................................. 193
LIST OF TABLES

Table 1. Tactile detection threshold on each hand, collected from two testing sessions.. 31
Table 2. Results from Fisher’s exact tests on cross-surface errors in Experiment 2.4.2. . 49
Table 3. Examples demonstrating the problem of leave-one-run-out in the current design......................................................................................................................... 144
LIST OF FIGURES

Figure 1. A schematic of the serial model for tactile localization. ........................................ 15

Figure 2. Stimulus locations in Overvliet et al.’s study (2011). The figure is taken from the original article. .......................................................................................................................... 18

Figure 3. Finger postures in Overvliet et al.’s study (2011). Figures are taken from the original article........................................................................................................................................... 18

Figure 4. Experimental conditions in Medina, Tame, & Longo’s study (2018). The figure is taken from the original article.......................................................................................................................... 21

Figure 5. T1-weighted image for DS. The red ellipses highlight the lesion location. ...... 29

Figure 6. Actual (black) and perceived (red) stimulus locations on the left (left panel) and right (right panel) hand.......................................................................................................................... 34

Figure 7. a. Hand posture in Experiment 2.3.1. DS was stimulated on the dorsum (filament in red) and palm surfaces (filament in blue) in the same block with the hand positioned palm facing down. b. Actual (black labels) and perceived stimulus locations in Experiment 2.3.1 for each surface. The palm surface is displayed as being viewed from the top, through the dorsal surface. Consistent with the filament colors in a., red labels are localization judgments for stimuli delivered on the dorsum surface, blue labels are localization judgments for stimuli on the palm surface. Labels on the edge of the hand outline are localization judgments made on the edge of the hand surface, between the dorsal and palmar surfaces. ........................................... 38

Figure 8. a. Hand position and posture during Experiment 2.3.2. b. Actual (black labels) and perceived stimulus locations in Experiment 2.3.2 for the palm and dorsum surfaces. The dorsum surface is displayed as being viewed from the top, through the palm surface. Consistent with the filament colors in a., red labels are localization judgments for stimuli delivered on the dorsum surface, blue labels are localization judgments for stimuli on the palm surface. Labels on the edge of the hand outline are localization judgments made on the edge of the surface. .................................................................................................................. 40
Figure 9. a. Hand position and posture during Experiment 2.3.3. b. Actual (black labels) and perceived stimulus locations in Experiment 2.3.3 for the dorsum palm surfaces. The palm surface is displayed as being viewed from the top, through the dorsum surface. Consistent with the filament colors in a., red labels are localization judgments for stimuli delivered on the dorsum surface, blue labels are localization judgments for stimuli on the palm surface. Labels on the hand outline are judgments made on the edge of the surface. 43

Figure 10. Illustration of the setup in Experiment 2.4.1. DS was asked to point to visual targets presented in different quadrants defined by a 4×3 grid. The grid lines are displayed only for illustration purposes. During the experiment, DS was not able to see the grid lines. 46

Figure 11. Actual (solid lines) and perceived (dashed lines) landmark locations on the left (left panel) and right (right panel) hand. Landmarks are connected by straight lines to display the hand shapes. 52

Figure 12. Illustration of the rubber hand illusion. The participant views a rubber hand (V), with the actual hand (P) hidden from the view. When the rubber hand and actual hand are stroked in synchrony, the participant felt the touch as on the rubber hand, and the hidden hand as shifting towards the rubber hand (Botvinick & Cohen, 1998). 61

Figure 13. Illustration of the mirror box illusion. With the hands on each side of the mirror, visual estimate (V) and proprioceptive estimate (P) regarding the hidden hand position are dissociated. 64

Figure 14. Manipulations in Experiment 3.1. Participants placed their right hand in front of the mirror, either 4” or 10” away from the mirror. The left hand was hidden behind the mirror, at either 4” or 10” from the mirror. The reflection of the right hand in the mirror (dashed outlines) looks like the hidden left hand. Dashed black lines indicate where the participants were viewing. A 9×9 dot grid (not seen by the participant) was drawn on the back of the hidden left hand (right panel). Of the 81 dots, only the nine dots in red were stimulated. 66

Figure 15. Predictions of the anchoring hypothesis. Within each visual estimate, tactile localization would be biased towards proprioceptive estimate in incongruent vs. congruent condition. Arrows illustrate the expected direction of tactile localization bias. 70
Figure 16. a. Medial-lateral localization bias in each condition in Experiment 3.1. Negative values denote lateral biases. Arrows denote the predicted direction of localization bias in visuo-proprioceptive mismatch conditions compared to the visuo-proprioceptively congruent conditions. b. Proximal-distal localization bias in each condition, with negative values denoting distal biases. Conditions are illustrated on the right side of each bar. Unless otherwise noted, error bars indicate 95% within-subjects confidence intervals (Cousineau, 2005). *: p < .05. **: p < .01. ***: p < .001.

Figure 17. Manipulations of hand positions in Experiment 3.2. Arrows in the Mirror conditions indicate predicted tactile localization bias directions. The null symbol in $V_0$ indicates no visual information.

Figure 18. a. Medial-lateral localization bias in each condition in Experiment 3.1. Negative values denote lateral biases. Arrows with different lengths indicate that the difference between $P_{14}V_9$ and $P_4V_9$ was predicted to be larger than the difference between $P_{14}V_0$ and $P_4V_0$. b. Proximal-distal localization bias in each condition, with negative values denoting distal biases. Conditions are illustrated on the right side of each bar.

Figure 19. Conditions in Experiment 3.3. The left hand was positioned at either 10” or 4” behind the mirror. An object (illustrated by the red rectangle) was positioned at either 4” or 10” in front of the mirror, with its mirror reflection at either congruent or incongruent position with the hidden hand.

Figure 20. Conditions in Experiments 3.1 and Experiment 3.3 that were analyzed. Numbers on the top denote distance from the mirror. P, O, and V stand for proprioceptive hand position, object position, and visual hand position, respectively. Red arrows indicate predicted directional tactile localization bias induced specifically by visual-proprioceptive conflict relative to gaze-proprioceptive conflict.

Figure 21. a. Medial-lateral localization bias in the incongruent conditions in Experiments 3.1 and 3.3. Arrows indicate the direction of tactile localization bias when participants viewed a hand (Experiment 3.1) vs. object (Experiment 3.3). b. Medial-lateral localization bias in the congruent conditions in Experiments 3.1 and 3.3. Error bars are 95% CI calculated from the raw data.

Figure 22. One possible mechanism of the anchoring hypothesis. First, felt hand position ($F_{vp}$) is shifted onto the visual estimate (V) as a result of multisensory
integration (①). Consequently, touch on the actual hand (X on the P hand) is felt as on the mirror hand (X on the V hand), and externally localized at the visual position/felt hand position (②, \text{Touch(V)/Touch(Fp)}). Meanwhile, there is still a proprioceptive estimate of hand position (P), providing information that touch occurred further away from the visual estimate in external space (②, \text{Touch(P)}). Given two conflicting tactile location estimates, one anchored on a visually-defined location and one at a proprioceptively-defined location, tactile location estimate was biased away from the anchoring point, towards proprioceptive estimate (③). Finally, the external bias fed back to the skin surface, biasing tactile localization on the skin surface towards the proprioceptive estimate (④).

Figure 23. An alternative mechanism for the anchoring hypothesis. First, provided with a vivid visual hand (V) in a congruent orientation with the actual hand, representation of the peri-hand space shifts and centers on the viewed hand (①). As a result, touch is referred to the viewed hand (X on the V hand) and externally localized at the visual estimate of hand position (②, \text{Touch(V)}). Although touch is referred to the visual hand, given the spatial mismatch between visual and proprioceptive hand position estimates, the shift might not be complete and there might still be residual tactile information on the actual hand. This leads to an additional tactile location estimate defined by proprioceptive hand (②, \text{Touch(P)}). This proprioceptive-defined tactile representation biases tactile localization estimate away from the anchoring point (③), which then feed back to the skin surface, leading to tactile localization bias on the skin surface towards the proprioceptive estimate (④).

Figure 24. Illustration of the four conditions in Experiment 4. a. Condition 1: The hand was placed on the table with the fingers separated by 5 cm. b. Condition 2: The hand was placed on the table with the fingers separated by 5 mm. c. Condition 3: The hand was lifted, with only the index and ring finger placed to a lower plane, separated by 5 cm. d. Condition 4: The hand was lifted, with only the index and ring finger placed to a lower plane, separated by 5 mm.

Figure 25. Tactile localization accuracy for each finger during the staircase procedure, at intensities later used in the main experiment.

Figure 26. Response rate for each stimulated finger, collapsed across participants, for a. the All Fingers Close condition, b. the All Fingers Close condition and c., the difference between All Fingers Far and All Fingers Close condition. In a. and b., darker colors indicate higher response rate. Numbers in bold (i.e. along
the diagonal) are correct responses for the stimulated finger, i.e. accuracy. In c., darker yellow denotes more positive values, i.e. more responses in the All Fingers Far vs. All Fingers Close condition. Darker blue denotes more negative values, i.e. more responses in the All Fingers Close vs. All Fingers Far condition.

Figure 27. Average localization errors for each finger in each condition, calculated as the number of fingers. Positive values denote biases towards the pinky, negative values denote biases towards the index finger.

Figure 28. Response rate for each stimulated finger, collapsed across participants, for the a. Index-Ring Far condition, b. Index-Ring Close condition, and c., the Difference between the Index-Ring Far and Index-Ring Close conditions. In a. and b., darker colors indicate higher response rate. Numbers in bold (i.e. along the diagonal) are response rates on the stimulated finger, i.e. accuracy. In c., darker yellow denotes more positive values, i.e. more responses of each type in Index-Ring Far vs. Index-Ring Close. Darker blue denotes more negative values, i.e. less responses of each type in Index-Ring Far vs. Index-Ring Close. The red asterisk indicates that for stimuli on the index finger, more responses were made on the ring finger when the fingers were close vs. far, with p < .05.

Figure 29. Response rate for each stimulated finger, collapsed across participants, for a. conditions with all fingers in the same plane (All Fingers Far and All Fingers Close), b. with the index and ring finger on a different plane from the rest of the hand (Index-Ring Far and Index-Ring Close conditions), and c. the difference between the same plane vs. different plane conditions. In a. and b., darker colors indicate a higher response rate. Numbers in bold (i.e. along the diagonal) are response rate on the stimulated finger, i.e. accuracy. In c., darker yellow denotes more positive values, i.e. more responses of each type in different plane vs. Same plane. Darker blue denotes more negative values, i.e. less responses of each type in Different plane vs. Same plane. Bold numbers along the diagonal indicate changes in localization accuracy. The red asterisks indicate that across all stimulated fingers, more responses were made on the middle finger in the Different plane vs. Same plane conditions, p < .001.

Figure 30. Illustration of multi-voxel patterns associated with two experimental conditions. Each cell represents a voxel, with darker colors indicating higher amount of activation.
Figure 31. Manipulations in Experiment 5. Participants receive tactile stimulation on the tip of either the right index finger or ring finger, with the hand either palm facing up or facing down. Cells with the same background color contain conditions with the same external location (a. and d.: left; b. and c.: right).

Figure 32. Brain areas activated by tactile stimuli in test trials compared to baseline. Statistical maps are thresholded at FWE corrected p < .001. S1: Primary somatosensory cortex. SMA: Supplementary motor area. SPL: Superior parietal lobe. IFG: Inferior frontal gyrus. Pre-SMA: Pre-supplementary motor area. PMC: Premotor cortex. SFG: Superior frontal gyrus. IPL/PO: inferior parietal lobule/parietal-occipital region. S2: Secondary somatosensory cortex.

Figure 33. Clusters in contralateral primary somatosensory and premotor cortex that decoded tactile location in somatotopic space. Slices are shown in MNI coordinates.

Figure 34. Clusters that encoded tactile location in external space. Top: Anterior cingulate cortex. Bottom: Middle occipital gyrus. Slices are shown in MNI coordinates.

Figure A 1. Probabilistic tractography between the thalamus and S1 hand area in each hemisphere. M1 hand knob refers to the hand area in primary motor cortex as a landmark for visualization.

Figure A 2. Probabilistic tractography between the S1 hand area and S2 in each hemisphere. M1 hand knob refers to the hand area in primary motor cortex as a landmark for visualization.

Figure A 3. 3D view of probabilistic tractography from contralesional thalamus through the mirror lesion area. The thalamus is displayed in sagittal view for visualizing where the fiber tracts meet the thalamus in the anterior-posterior dimension. CS: central sulcus.

Figure A 4. Multi-slice view of the fiber tracts from the thalamus through the mirrored lesion mask in the left (contralesional) hemisphere, shown in FA values. The mirrored lesion mask is shown in green, and fiber tracts are shown in red. Yellow areas show overlap between the mirrored lesion mask and fiber
tracts, indicating where the fiber tracts went through the mirrored lesion area.

Figure A 5. Multi-slice view of the fiber tracts between the thalamus and the premotor cortex in ipsilesional (right) hemisphere, shown in FA values. ............... 186

Figure A 6. Multi-slice view of the fiber tracts between the premotor wirepoints mask and atlas-based thalamus mask in both hemispheres, shown in FA values. 187

Figure B 1. Average judgments for each target location in each condition in Experiment 3.1. Unless otherwise noted, bias bars indicate 95% within-subjects confidence intervals (Cousineau, 2005). The black dots represent actual stimulus locations. .......................................................... 188

Figure B 2. Average judgments for each target location in each condition in Experiment 3.2. The black dots represent actual stimulus locations. ...................... 189

Figure B 3. Average judgments for each target location in each condition in Experiment 3.3. The black dots represent actual stimulus locations. ...................... 190

Figure B 4. a. Proximal-distal localization bias in the incongruent conditions in Experiment 3.1 and 3.3. b. Proximal-distal localization bias in the congruent conditions in Experiment 3.1 and 3.3. Error bars are 95% CI calculated from the raw data. .................................................................................. 192
ABSTRACT

Upon receiving a tactile stimulus, the brain represents its location on the skin surface (e.g. on the index fingertip) as well as in external space (e.g. 10 cm to the right of my body midline). Prior literature proposed a serial model for these processes: The brain first localizes touch on the skin surface, then localizes touch in external space by combining the stimulus location on the skin surface with the current body position. Given that information regarding body position is utilized after a touch has been localized on the skin surface, the model predicts that perceived stimulus location on the body is not affected by body position. However, some studies provide evidence for the effect of body position on localizing touch on the skin surface, challenging the serial model. The central aim of this dissertation is to further test if information from external space influences tactile localization on the skin surface, using experimental investigations with both neurologically intact and impaired individuals. Evidence from these experimental investigations will provide a more complete understanding of how functional systems involved in tactile processing are organized.

Previous studies have reported brain-damaged individuals who substantially mislocalized touch on the body. However, whether tactile localization errors vary with body posture has not been systematically examined. Chapter 2 of this dissertation reports performance of a brain-damaged individual on tactile localization. The individual systematically and consistently mislocalized touch on the hand towards the left side of space relative to the hand long axis. Importantly, judgments on the skin surface varied with...
hand posture, biased towards the pinky when the contralesional left hand was palm facing
down, and towards the thumb when the hand was palm up. The data thus provide strong
evidence that hand posture influences tactile localization on the skin surface. These
findings also provide evidence that touch is represented in an external reference frame
specifically centered on the long axis of the hand.

Motivated by evidence from the brain-damaged individual, additional
investigations were performed on neurologically intact individuals to further examine if
tactile localization is influenced by external information. The experiments in Chapter 3
investigated tactile localization on the hand surface when there was a spatial conflict
between visual and proprioceptive estimates of hand position in external space. The results
showed that tactile localization judgments were consistently biased towards the direction
of the proprioceptive estimate, providing evidence that information from external space
influences where touch is perceived on the body. Potential mechanisms for the tactile
localization biases were discussed.

The experiment in Chapter 4 examined tactile localization across body parts, testing
tactile localization among fingers while manipulating the finger posture. The results did
not provide strong evidence that the distance between fingers influences tactile localization.
However, the distribution of localization error varied depending on whether all the fingers
were on the same plane, suggesting influences of relative finger elevation on tactile
localization. Finally, using multi-voxel pattern analysis, the neuroimaging study in Chapter
5 demonstrated distinct neural correlates for tactile location representations in external and
somatotopic reference frames. Overall, this dissertation provides strong evidence that
information from external space does influence tactile localization on the skin surface,
indicating that tactile localization is not a strictly serial process by which information flows from somatotopic representation to external representation in one direction. Rather, information from external space feeds back to somatotopic representation, influencing tactile location judgments on the skin surface.
Chapter 1

TACTILE LOCALIZATION AND BODY REPRESENTATIONS

In daily interactions with the environment, tactile sensations provide rich information about external objects regarding temperature, roughness, and size and shape. In addition, tactile information is integrated with information from other senses to form a coherent body representation. Understanding the mechanisms underlying tactile processing is important for several reasons. First, specifying the functional architecture of tactile processing is important for developing targeted rehabilitation for treating sensory deficits. Second, it develops our understanding of how sensory and motor information are integrated, processes that are crucial for actions and object manipulation. Finally, tactile information contributes to forming coherent representations of one’s body.

First, specifying the functional architecture of tactile processing has implications in developing targeted treatments of sensory deficits. It can be especially beneficial given the report that around 50% of individuals suffering stroke have somatosensory deficits (Carey, Matyas, & Baum, 2018). For example, one question on tactile processing is how tactile detection and tactile localization are organized (Halligan, Hunt, Marshall, & Wade, 1995; Harris, Thein, & Clifford, 2004). If no dissociation was made between different processes, all tactile deficits could be treated the same way. However, by testing computational models and examining brain-damaged individuals, tactile localization is a separate but serial process to tactile detection (Harris et al., 2004; also see Chapter 2 below). This
indicates that there are mechanisms specific to tactile localization for which deficits could not be resolved by treatments designed to improve tactile detection. Along the same logic, specifying functional architecture of tactile processing can help accurate diagnosis of tactile deficits, from which targeted rehabilitation methods can be developed.

Second, precise object manipulation requires accurately representing tactile information. For example, to hold a cup of water, tactile information such as relative position between the cup and the fingers, and pressure from holding a cup, needs to be analyzed to determine an optimal grip strength. In one study using non-human primates (Xerri, Merzenich, Peterson, & Jenkins, 1998), after the monkeys became skilled at a small-object retrieval task, area 3b in the primary somatosensory cortex were lesioned. Interestingly, although the lesion was constrained in sensory cortex, the monkeys’ performance on the sensory-motor task decreased, indicating importance of tactile sensation in object manipulation. In humans, motor deficits were found in brain-damaged individuals who suffered pure sensory stroke (Smania, Montagnana, Faccioli, Fiaschi, & Aglioti, 2003). In addition, measures of tactile deficits have been associated with motor deficits (Umeki et al., 2018). These findings demonstrate a tight coupling between somatosensory and motor functions. Therefore, studying the mechanisms of tactile processing is important for specifying how tactile and motor information are integrated, as well as understanding motor deficits.

Finally, tactile information contributes to body representations. An example demonstrating this is the rubber hand illusion (Botvinick & Cohen, 1998). When one’s hidden hand is stroked in synchrony with a visible rubber hand, individuals reported feeling the rubber hand as their own hand as well as their hidden hand shifting towards the rubber
hand. This indicates that integration of visual and tactile input informs the brain where a body part is and which body part to incorporate to one’s self. In a different study, participants perceived their body parts as enlarged after anaesthesia, providing evidence for influences of tactile information on body size representation (Gandevia & Phegan, 2004). These findings demonstrated the importance of touch in forming coherent body representations. For this reason, specifying the mechanism of tactile processing facilitates an understanding of how a coherent body representation is formed.

This dissertation focuses on the problem of tactile localization on the skin surface. This chapter first reviews studies that give rise to a serial model in tactile localization, focusing on processes from primary somatosensory cortex to percepts on the skin surface. Then findings against the serial model will be discussed, focusing on the effects of body posture on tactile localization on the skin surface. This then leads to further investigations of the serial model presented in later chapters.

1.1. **Primary somatosensory cortex**

Neurons in primary somatosensory cortex (S1) have receptive fields on the skin surface. Penfield & Boldrey (1937) first documented that stimulating neurons in the postcentral gyrus elicited cutaneous sensations at certain locations. Interestingly, representations in S1 have a general topographic organization, such that body parts that are anatomically close are represented by adjacent cortical areas. Using microelectrode mapping methods, studies have provided more detailed cortical maps for monkey hands in S1 (specifically Brodmann area 3b), showing topographic representations for the palm
surface from digit 1 to digit 5, and from the fingertips to the palm area (Merzenich et al., 1983; 1984; Xerri et al., 1998).

Certain aspects of tactile perception might reflect characteristics of S1 representations. First, Weber’s illusion (Weber, 1834/1996) documented that the distance between two tactile stimuli is perceived as longer on the skin surface that has larger cortical representations in S1 (e.g. hand vs. arm). The size of S1 representations of different body parts are highly distorted relative to their anatomical size. For example, hand representations are larger than arm representations. Accordingly, neurons representing the hands have smaller receptive fields than neurons representing the arm, resulting in higher spatial acuity for the hands versus arms. Weber’s illusion was explained as resulting from such differences in cortical magnification and tactile acuity (Cholewiak, 1999). Second, studies have found that on the hairy surface of the hand, distances between tactile stimuli are perceived as longer when the stimuli were along the medial-lateral hand axis versus the proximal-distal hand axis (Longo & Haggard, 2011; Fiori & Longo, 2018). These effects were at least partially attributed to the findings that receptive fields for the hairy surface are oval-shaped with the long axis along the proximal-distal axis of the limb, resulting in lower spatial acuity and shorter perceived tactile distances along the proximal-distal axis versus the medial-lateral axis (Longo & Haggard, 2011; Miller, Longo, & Saygin, 2016).

What are the implications of the correspondence between tactile perception and S1 organization for mechanisms of tactile localization? One hypothesis is that there is a fixed point-to-point mapping between which neurons are active in S1 and the location of perceived sensation (labelled-line hypothesis; Lotze, 1885). However, this hypothesis is problematic for a number of reasons. For example, the labelled-line hypothesis does not
explain reorganization after brain damage. If there is a fixed point-to-point correspondence between S1 and the skin surface, damage to S1 would result in loss of somatosensation. However, there is evidence that individuals with damage to S1 are still able to detect and/or localize tactile stimuli (Rapp, Hendel, & Medina, 2002; Halligan, Hunt, Marshall, & Wade, 2008; Birznieks, Logina, & Wasner, 2012), suggesting reorganization of somatosensory functions into other brain areas (see also Xerri, et al., 1998). These findings indicate that the mapping between neural activity and perception is not fixed. After reorganization, the perceptual consequence of activity in the new cortical territory changed from the previous function to somatosensory perception, indicating additional processes that properly interpret neural activity and then map to perception.

Second, studies have shown increased cortical representation in S1 for the reading finger in Braille readers (Pascual-Leone, 1993) and for the left hand in string players (Elbert et al., 1995), indicating that the representation of the excessively used body parts can take over cortical territory from other body parts. The labelled-line hypothesis would predict that when the neurons with reorganized receptive fields are activated by stimulating the excessively used body parts, individuals would feel touch in the body parts that these new neurons used to represent. However, no such mislocalizations have been reported or seen in daily life, suggesting that the mapping between neural activity and perceived stimulus locations has changed in tandem with cortical reorganization.

In summary, although tactile perception reflects characteristics of S1 representations at some level, S1 representations alone do not fully account for perception. Intermediate processes are needed to interpret information from S1 and map to perceived stimulus locations on the skin surface. In testing healthy and brain-damaged individuals,
studies have found that these intermediate processes rely on how the brain represents the body. In the following section, I will review literature on different types of body representation, along with the role of these body representations in tactile localization.

1.2. Beyond the primary somatosensory cortex: higher-order body representations

1.2.1. Body representations

In testing patients on sensory and motor function, Head and Holmes (1911-1912) first introduced the idea that there are multiple body representations serving different functions. One of the body representations is a postural schema that represents body position in space before and after movements, and is constantly updated as the body moves. Since veridical information about body posture can always be obtained from vision, the concept of a postural schema focuses more on proprioceptive inputs when visual information is not available. In patients who could not recognize changes in limb posture after passive movements without vision, a postural schema was likely impaired. Accordingly, when presented with a tactile stimulus, these patients may be able to tell where on the skin surface they were touched, yet were unable to localize the touch in external space. From these cases it was concluded that a postural schema is essential for determining stimulus locations in external space. In addition to localizing touch in external space, making movements also requires information about current body position. In individuals deprived of sensory and proprioceptive inputs after brain damage, the ability to precisely control body movements can be impaired even when visual information is available (Cole & Paillard, 1995; Medina, Jax, Brown, & Coslett, 2010).
In addition to a postural schema, another body representation was proposed. This refers to a representation of the skin surface utilized for localizing touch on the body surface. This was based on the observations that after cortical lesions, patients were able to detect a touch but were unable to report its location on the skin surface. The detailed attributes of this superficial schema were not clearly described by Head & Holmes. In fact, there are debates on the terms and categorizations on this concept (e.g. de Vignemont, 2010; Longo, Azañón, & Haggard, 2010). Despite the ambiguity of the term, the idea that the brain localizes touch to the skin surface by referencing a body representation, instead of directly reading from neural activity, provides an alternative to the labelled-line hypothesis. In the next few sections I will discuss properties of this representation (or category of representations) inferred from tactile perception.

1.2.2. An alternative model to the labelled-line hypothesis

As discussed earlier, S1 representations alone are not sufficient for localizing touch on the skin surface. Multiple aspects of tactile perception indicate the need for additional processes between S1 activation and perception. One study made the idea explicit by studying tactile distance perception (Taylor-Clarke, Jacobsen, & Haggard, 2004). As reviewed earlier, tactile distances are perceived as longer on skin surfaces that have larger cortical representations in S1. However, differences in perceived tactile distances between skin surfaces were only 10% of differences in the size of cortical representation between different skin surfaces, indicating that information from S1 is already corrected before leading to tactile perception. An analogy used in the article relates to visual object perception: Although the fovea is cortically overrepresented, objects presented in fovea are
not perceived as substantially larger than objects presented peripherally, indicating rescaling of cortical representation. As for tactile perception, the authors hypothesized that cortical distortion is corrected by mapping information from distorted maps in S1 to a more veridical representation of the body size and shape. To the test this hypothesis, the authors created visual illusions such that the hand appeared to be half the actual size and the forearm double the actual size. Consistent with this prediction, after viewing the shrank hand and enlarged arm for an hour, tactile distances on the hand were less likely to be perceived as longer than on the arm, providing evidence for the effects of perceived body size and shape on tactile perception (also see Kennett, Taylor-Clarke, & Haggard, 2001).

In addition to visually-altered body size and shape, tactile perception was also affected by proprioceptively altered body size and shape (de Vignemont, Ehrsson, & Haggard, 2005). With an individual blindfolded, vibrating the biceps and triceps tendon elicits the perception that the arm is extending and flexing respectively, even though the arm is physically static. In the experiment, blindfolded participants held their left index finger with the right index finger and thumb, while the right triceps or biceps tendon was vibrated. On the one hand, the right arm was perceived as extending or flexing. On the other hand, tactile sensations from the fingertips informed the brain that the fingers were in contact. The brain would interpret the conflict between proprioceptive and tactile information as the left index finger elongating when the right biceps were vibrated, and shrinking when the right triceps were vibrated. Critically, it was found that when the left finger was perceived as elongated, tactile distances on the index finger were also perceived as longer. Given that changes in perceived size of the index finger affected perceived tactile
distance, these findings provided evidence that a representation of body size and shape is utilized in tactile perception.

Based on these and other findings, a serial model of tactile localization was proposed (Medina & Coslett, 2010; 2016; Longo, Azañón, & Haggard, 2010). Instead of S1 activation directly leading to perception, information from S1 representations is mapped to a higher-order body representation for determining stimulus location on the skin surface. After this step, stimulus location on the skin surface is combined with a body posture representation to determine stimulus location in external space. In the model discussed by Medina & Coslett (2010; 2016), the higher-order body representation is termed a body form representation, and represents body shape and size. In contrast, other models use the term “superficial schema” for the higher-order representation in tactile localization, and argue that a representation of body size and shape is only used for judging metrics/distances of tactile stimuli (Longo et al., 2010). Nevertheless, it was not specified what a “superficial schema” represents and how it differs from a body form representation. In addition to body size and shape, studies have identified other information that contributes to tactile localization, which will be discussed in Section 1.2.3.

This serial model (Medina & Coslett, 2010; 2016; Longo et al., 2010) also provides explanations for the lack of mislocalization after use-dependent plasticity. In one-finger Braille readers and musicians, cortical areas in S1 that represent the excessively-used body parts increased in size, indicating that some neurons that used to represent other body parts are now activated when the excessively used body parts are stimulated. Importantly, there have been no reported mislocalizations after such cortical reorganization, indicating that activation of these new neurons now leads to perception in the excessively used body part,
as opposed to body parts that they used to represent. One possibility is that when reorganization occurs, mapping from neural activation to the body form representation changes in tandem such that activation of these neurons now remaps to the excessively used body part in a body form representation, leading to veridical perception of the stimulus location. One possible neural mechanism could be that the cortico-cortical projection between S1 and the brain area that represents body form altered along with reorganized receptive field in S1 neurons, leading to unchanged tactile location perception.

### 1.2.3. Information other than body size and shape

In the original model, the body form representation primarily contains information about body size and shape (Medina & Coslett, 2010; 2016). In addition to size and shape, studies have identified other information that is represented during tactile perception, including boundaries between body parts, knowledge of body structure, and anatomical body features. The relationship between these types of information and the body form representation is unknown: They might be separate body representations that jointly contribute to tactile localization, or they might be represented in a broad body representation. This proposal focuses more on what information is being used, rather than defining and categorizing body representations.

Patient studies provide evidence that a body structural representation might be important for tactile localization. A body structural representation is a visual-spatial description of the relative position of body parts on the body surface (Buxbaum & Coslett, 2001; Sirigu et al., 1991; Schwoebel & Coslett, 2005). For example, the hand and foot are not directly connected on the body surface. Unlike a body posture representation of current
body position in space, this structural representation is not affected by current sensory and motor information, and hence remains invariant when the body moves (e.g. the hand and foot are structurally not connected even if they are touching each other). Evidence for a representation of body structure comes from a single case who demonstrated a dissociation between knowledge of body structure and the body schema (Buxbaum & Coslett, 2001). The patient had deficits in tasks requiring knowledge of relative body position (e.g. could not point to his own body part named by the experimenter or shown in pictures), yet could reach and grasp accurately, indicating impaired body structure knowledge with an intact body posture representation.

In one study, a principle components analysis was conducted on performance from a group of brain-damaged individuals (N=70) on a battery of sensory and motor tasks (Schwoebel & Coslett, 2005). Consistent with a dissociation between a body structural representation and posture representation, performance on tasks involving an on-line representation of body posture (e.g. hand action) displayed different variances with tasks requiring knowledge of body structure (e.g. judging which of the pictured body parts is most closely connected with a target body part). Importantly, performance on a tactile localization task where patients pointed on a mannequin where they were touched co-varied with performance on the body structure tasks, indicating that representing body structure and tactile localization involve common processes (also see Schwoebel, Coslett, & Buxbaum, 2001 for a case study).

Although patient studies provide evidence for a body structural representation in tactile localization, there are caveats in interpreting these findings. First, co-occurrence of deficits in a body structural representation and tactile localization does not necessarily
indicate a causal relationship between these deficits. It is also likely that there are common processes whose impairment would lead to deficits in both tasks. Second, impairments in tactile localization in patients might be task-dependent, as opposed to purely sensory. In studies demonstrating correlated deficits in body structure knowledge and tactile localization, patients were asked to point to a mannequin where they felt the touch (Schwoebel & Coslett, 2005; Schwoebel, Coslett, & Buxbaum, 2001). This process requires mapping one’s own body parts to a mannequin with the knowledge of the body structure. It is likely that the patients had deficits in such explicit mapping processes, instead of identifying the stimulated location per se.

Finally, one study provided evidence that anatomical body features are represented during tactile localization (Badde, Roder, & Heed, 2019). Participants were presented with two stimuli close in time on two of the four limbs, and reported on which limb they felt the first stimulus. Intriguingly, participants reported limbs that were not stimulated (phantom sensations), with the reported limb sharing limb type (i.e. hand vs. foot), anatomical body side (i.e. left hand and foot versus right hand and foot), or anatomically-defined external hemispace (e.g. limbs that are currently on the right side when the right hand was stimulated, regardless of where the right hand is) with the actually stimulated limb. These findings indicate that the brain encodes locations on the skin surface based on body features. Nevertheless, it is worth noting that participants reported phantom sensations in only about 10% trials when making motor responses with the limb they were to report, and dropped to about 5% when they made verbal responses. Therefore, the contribution of body features identified in the study may not be prominent in normal situations, and part of its effects might be on stimulus-motor response mapping.
In summary, prior literature proposed that information from S1 is mapped to a representation of body size and shape before giving rise to perceived tactile locations on the skin surface (Medina & Coslett, 2010; 2016). Other than body size and shape, there is evidence that representations of relative position of body parts on the body surface (structural representation) and body features such as limb type and anatomical limb side are also referenced during tactile localization on the body.

The studies reviewed so far demonstrated the influence of information from the body surface on tactile localization on the skin surface. In other words, these studies did not consider influences of the current body position in external space on tactile localization. Indeed, in a strict serial model (Medina & Coslett, 2010; 2016; Longo et al., 2010), the brain first determines stimulus locations on the skin surface, then combines this location with a body posture representation to localize touch in external space. Given that a postural representation is used after tactile localization on the skin surface, the serial model implies that perceived stimulus locations on the skin surface are not influenced by body posture. However, there have been mixed findings regarding this prediction. In the next section, I will first discuss the serial model on tactile localization, then review studies investigating the influence of body posture on localizing touch on the skin surface, which potentially change the serial model.

1.3. Effects of body posture on tactile perception: Revisiting a serial model

This section is committed to a discussion and evaluation of the serial model, focusing on the model prediction that tactile localization on the skin surface is not affected
by body posture in external space. In doing this, I will review studies that investigate the effect of body posture on tactile localization on the skin surface.

Two terms will be used frequently in this section: somatotopic frame of reference and external frame of reference. In a somatotopic frame of reference, locations are represented on the skin surface regardless of body movement in space. For example, the center of the forehead is always the same location on the skin surface regardless of head orientation. An external frame of reference refers to the category of reference frames that are not somatotopic and centered on different body parts, e.g. trunk-centered, gaze-centered, hand-centered, etc. This contrasts with another type of frame of reference that centers on external objects (allocentric frame of reference; Schwoebel et al., 2001). As the body moves, the same location in a somatotopic frame of reference would change its position in external frames of reference. For example, as the right hand moves from the right side of the body to the left side, locations on the right hand skin surface change from the right to the left in a trunk-centered frame of reference.

1.3.1. A strictly serial model

Figure 1 shows a schematic of the serial model of tactile localization (Medina & Coslett, 2010; 2016). To annotate, when a touch is presented, tactile information is relayed from receptors on the skin surface to a location in S1 that represents the stimulated body part. Information from S1 is then mapped to a body form representation for localizing the touch on the skin surface. The stimulus’ location on the skin surface is then combined with a body posture representation to determine the stimulus location in external space, a
process that is referred to as tactile remapping (e.g. Azañón, Camacho, & Soto-Faraco, 2010).

As shown in Figure 1, the serial model involves strict one-way information flow from somatotopic space to external space. Since body posture is utilized after the stimulus has been localized in somatotopic space, the model implies that tactile localization on the skin surface is not affected by body posture. Consistent with this prediction, perceived stimulus locations on the hand dorsum did not differ whether the hand was placed straight (i.e. fingers pointing forward) or rotated 90° (Mancini, Longo, Iannetti, & Haggard, 2011). Nevertheless, other studies have showed that body posture affects tactile perception on the skin surface, which are discussed in the following sections.

Figure 1. A schematic of the serial model for tactile localization.
1.3.2. Body posture modulates tactile detection

Before discussing the effects of body posture on tactile localization, I will first review evidence that encoding tactile information varies with body posture. Individuals with tactile extinction can detect a single unilateral stimulus, but fail to report the contralesional stimulus when bilateral stimuli are presented simultaneously (tactile extinction). A critical question is in which frame of reference “contralesional” and “ipsilesional” are defined. In testing a group of patients, two stimuli were simultaneously presented on the ulnar and radial side of the ipsilesional wrist, with the ipsilesional hand palm facing up or down (Moscovitch and Behrmann, 1994). If tactile extinction in these patients is a deficit in coding stimuli in somatotopic space, participants would always fail to respond to the same tactile stimuli (e.g. the ulnar stimulus) regardless of hand posture. Alternatively, if tactile extinction occurs in an external frame of reference, in this case defined by the wrist midline, participants would always miss the tactile stimulus on the contralesional side of the space relative to the wrist midline. In 11 patients with extinction on either the right or left side, the missed stimuli were always on the contralesional side of the wrist midline in external space (left-right vs. radial-ulnar), providing evidence that these patients had deficits in tactile detection in an external frame of reference centered on the long axis of the wrist. More recent studies found decreased extinction on the contralesional hand when the hand was moved to the ipsilesional hemispace relative to body midline and/or crossed over the ipsilesional hand, indicating that tactile information is represented in trunk-centered frame of reference and a frame of reference that encodes the relative position between the two hands (Aglioti, Smania, & Peru, 2006; Moro, Zampini, & Aglioti, 2010).
These findings demonstrate representation of tactile stimuli in multiple frames of reference. However, they do not necessarily indicate that body posture directly affects somatosensory processing. Tactile extinction has been interpreted as a deficit in which attention cannot be allocated to both contralateral and ipsilateral stimuli at the same time (Critchley, 1949; Moscovitch and Behrmann, 1994). Therefore, tactile extinction in a specific frame of reference indicates attentional deficits in a frame of reference, while somatosensory processing itself could still be intact. To address the question of if body posture influences somatosensory processing per se, I will discuss studies on tactile localization in the following section.

### 1.3.3. Effects of body posture on tactile localization on the body

One approach to studying the effects of body posture on tactile localization is investigating if tactile localization is affected by the relative distance between body parts. For example, studies have investigated if spatial proximity between the fingers affects the accuracy in discriminating which finger is stimulated. In one study, participants were asked to localize a stimulus to one of 30 target locations – 3 targets on each fingertip (Figure 2), with fingers placed together or apart (Figure 3; Overvliet, Anema, Brenner, Dijkerman, & Smeets, 2011). If proprioceptive information affects tactile localization, participants would be more accurate when the fingers were separate versus touching each other. Specifically, placing the fingers together would selectively increase mislocalization on the spatially adjacent fingers. The authors found that placing the fingers together decreased overall localization accuracy. However, there was no interaction between finger distance and error type -- placing the fingers together equally increased errors of all types instead of
specifically increasing mislocalization to the adjacent fingers. These findings were explained as overall improved discriminability between the fingers when the fingers are placed apart. Because the fingers are typically close to each other in daily life, the brain might not specifically analyze the distance between any two adjacent fingers, but the overall separation across all the fingers. Nevertheless, it was still not explained by what mechanism spatial separation affects tactile localization among fingers.

![Figure 2](image1.jpg)

**Figure 2.** Stimulus locations in Overvliet et al.’s study (2011). The figure is taken from the original article.

![Figure 3](image2.jpg)

**Figure 3.** Finger postures in Overvliet et al.’s study (2011). Figures are taken from the original article.

In contrast, studies of brain-damaged individuals showed that placing the fingers together specifically increased localization errors to the adjacent fingers. In a patient with potential deficits in representing fine-grained proprioceptive information, tactile
Localization on the fingers of the contralesional left hand was more accurate when fingers were placed apart (by 4 cm) versus close together (0.5 cm apart; Coslett, 1998). Importantly, when the fingers were spatially grouped such that the index and middle finger were placed together, and the ring finger and pinky were placed together, mislocalization was more likely to occur on fingers within group versus across group. Given that the patient might have deficits discriminating finger locations in external space, these findings suggest that individual finger position in external space is referenced during tactile localization given particular brain damages. In contrast to findings from Overvliet et al.’s study (2011), finger position had no effects on tactile localization in two control patients, bringing up the question of whether it is a common mechanism to reference body posture when localizing touch on the body.

Other than studying errors in localizing a single stimulus, studies have investigated perception of two tactile stimuli and how it is affected by body posture. In one study, a patient was presented with two sequential tactile stimuli, one on the hand and one on the thigh (Schwoebel, Coslett, & Buxbaum, 2001). When asked to report if the stimuli were at the same location, the patient was correct in 75% of trials when the hand and thigh were separated by 20 cm, but was correct only on 31% of trials when the hand and thigh were separated by 4 cm. In theory, participant would report “different” as long as the tactile stimuli were localized to different body parts, regardless of the spatial distance. The finding that tactile discrimination was less accurate when the body parts were placed closer indicate that spatial distance between tactile stimuli might affect tactile perception on the skin surface.
Studies discussed above investigated tactile localization across body parts, for which one can manipulate the relative position. Are there effects of body posture on tactile localization on a continuous skin surface where the distance between locations is fixed? One study investigated tactile localization on the forearm in an arm-centered frame of reference (Sadibolova, Tame, & Longo, 2018). When the forearm rotates from a supine posture (i.e. with the volar surface facing up) to a prone posture (i.e. with the volar surface facing down), locations on the volar surface slide to the medial side (facing the body midline) as opposed to flipping to facing down. Interestingly, perceived stimulus locations also shifted medially when the forearm was in a prone versus supine posture, indicating that locations on the skin surface relative to the skeletal structure of the forearm (referred to as a “musculo-skeletal frame of reference” in the article) were taken into consideration during tactile localization.

As defined earlier, an external frame of reference is a category of spatial frames of reference centered on different body parts. One question is whether tactile localization is influenced by gaze position, with gaze being the center of an additional frame of reference (see Graziano, 2000 for evidence from non-human primates). In one study, participants placed their left hand behind a mirror that was aligned with the body midline, and the right hand in front of the mirror, making the reflection of the right hand look identical to the hidden left hand (Medina, Tame, & Longo, 2018). Tactile localization was tested on the back of the hidden left hand. The authors found significantly larger distal biases (e.g. towards the fingers) in tactile location when participants were looking at their actual right hand (“View Other Hand”, Figure 4c) versus the “left” hand in the mirror (“View Stimulated Hand”, Figure 4a) or an object in the mirror (“View Object”, Figure 4b),
concluding that tactile localization was affected by gaze direction. Nevertheless, the study did not dissociate what participants were looking at versus where participants were gazing in the View Other Hand condition (Figure 4c). It is thus possible that simply looking at a right hand, regardless of gaze direction, could drive those effects. Other studies also demonstrated different roles of gaze direction in tactile localization, with localization judgments shifting towards the location of gaze (Harrar & Harris, 2009; Pritchett & Harris, 2011; on the forearm) or opposite to the head/gaze direction (Ho & Spence, 2007, on the “frontal side of the waist”). In these studies, participants reported perceived stimulus locations by referring to external visual scales or judging if a visually presented mark was to the left or right of the perceived stimulus location, which involves transforming tactile locations on the skin surface to a scale-centered space. It is thus worth ruling out the possibility that gaze orientation might have affected transformations between frames of reference in making responses, instead of affecting tactile percepts per se. In summary, although there is some evidence that gaze orientation affects tactile localization, there are alternative explanations to be ruled out and it remains to be examined the exact role of gaze/head-centered representations in tactile localization.

Figure 4. Experimental conditions in Medina, Tame, & Longo’s study (2018). The figure is taken from the original article.
To summarize, this section discussed the serial model of tactile localization, focusing on the prediction that tactile localization on the skin surface is not affected by body posture. However, studies reviewed above demonstrated effects of body posture on tactile localization on the skin surface, potentially providing evidence against a serial model. Nevertheless, given the discrepant findings and potential alternative explanations, the evidence so far is not strong enough to fully reject a serial model. Given this gap, the first purpose of this dissertation is to further investigate whether proprioceptive information affects tactile localization on the skin surface. If proprioceptive information affects tactile localization, tactile localization would not be strictly serial with information flowing one-way from somatotopic to external space. The serial model would have to be revised to also allow information from external space to affect tactile localization in somatotopic space.

Three behavioral studies will be presented from Chapter 2 to Chapter 4 to address this question. Chapter 2 presents a single-case study investigating how changes in hand posture affected tactile localization in a brain-damaged individual. Localization judgments on the contralesional (left) hand varied dramatically with hand posture, clustering around the pinky when the hand was palm facing down, and around the index finger when the hand was palm facing up. These findings provide strong evidence that proprioceptive information modulates tactile localization on the body. Motivated by findings from the single-case study, Chapter 3 and Chapter 4 report experimental investigations on neurologically intact individuals, examining how proprioceptive information influences tactile localization. Using the mirror box illusion, Experiment 3 (Chapter 3) demonstrated that when visual and proprioceptive information regarding hand position are spatially
incongruent, tactile localization judgments on the hand were biased, providing additional evidence that external information affects tactile localization on the body. Whereas Experiment 2 and 3 studied tactile localization within body parts, Experiment 4 (Chapter 4) examined tactile localization across body parts, for which the relative position of tactile stimuli in external space vary with body posture. Specifically, participants were asked to localize touch to a finger on one hand with the distance between fingers manipulated. Results of this experiment are then discussed along with previous findings, which might suggest task-dependent effects of proprioceptive information on tactile localization among the fingers.

In addition to behavioral investigations, a neuroimaging study was conducted to address two questions. First, while it is widely confirmed that the primary somatosensory cortex represents tactile location in a somatotopic reference frame, little is known regarding which brain area represents touch in an external frame of reference. Second, if tactile localization on the skin surface is affected by external information, there should be brain areas in which the representation of tactile location on the skin surface is influenced by body posture. These areas would be potential neural correlates where information fed back from external space is integrated with somatotopic representations. A functional neuroimaging study combined with multi-voxel pattern analysis (MVPA) was performed to identify these brain areas.
Chapter 2

INTACT TACTILE DETECTION YET BIASED TACTILE LOCALIZATION IN A HAND-CENTERED REFERENCE FRAME: A CASE STUDY

Individuals with brain damage to somatosensory or related areas may demonstrate errors in localizing touch on the skin surface (Rapp, Hendel, & Medina, 2002; Birznieks et al., 2012, 2016; Anema et al., 2009). However, the influence of body posture on tactile localization has not been systematically tested in brain-damaged individuals. If information regarding body position is processed after localization on the body surface, as in the serial model, tactile localization on the body surface should not be influenced by body position. However, it is not clear if this is the case. This chapter reports an individual who made substantial errors in localizing touch on the hand surface, with perceived stimulus location on the skin surface strongly influenced by hand posture.

Along with testing the influence of hand posture on tactile localization, we examined in which frames of reference proprioceptive information could influence tactile perception. Individuals with tactile extinction fail to respond to contralesional stimuli relative to the wrist or hand midline (Moscovitch & Behrmann, 1994), indicating that tactile locations can be represented with regards to these body parts. Furthermore, studies

---

2 The case study was conducted on a brain-damaged individual we were testing and for whom we were planning on doing additional experiments for the proposal. However, he passed away and we cannot test him further. Here I briefly summarize data we have collected that are relevant to the questions discussed in this proposal. This will be expounded upon in the dissertation itself.
that manipulated hand posture (palms up versus down) have demonstrated that left and right can be encoded based on an external frame of reference (e.g. Moscovitch & Behrmann, 1994). There are two potential interpretations for these results. One is that stimulus locations can be encoded in a hand-centered reference frame, in which the midline is parallel to the long axis of the hand regardless of hand position relative to the body. For example, imagine an individual presented with bilateral tactile stimuli to the left wrist with the hand rotated 90° relative to the trunk midline. If the extinction operates in a hand-centered frame of reference, then the participant would fail to respond to the stimuli that are farther from the viewer in external space, but still leftward in a hand-centered frame of reference. A second possibility is that these stimuli are encoded based on the relative position of the two stimuli (see Aglioti et al., 1999; Medina & Rapp, 2008). In this frame of reference, left-right assignment is inherited from the body midline of the viewer, and any two stimuli are encoded based on the relative position of the two stimuli. In the aforementioned example with the hand rotated 90° relative to the trunk, an individual with tactile extinction in this frame of reference would not make errors, given that the two stimuli are parallel in this frame of reference. Previous studies of tactile extinction did not present individuals with tactile stimuli with the hand rotated 90°. From these studies, the evidence for hand-centered representations is unclear.

In addition to examining tactile localization, we also tested the individual’s tactile detection ability. Processing somatosensory information involves representing several aspects of the stimulus, including whether a stimulus was actually presented or not, the location of the stimulus on the skin surface, and its location in external space relative to the organism and its environment (Medina & Coslett, 2010; Longo, Azañón & Haggard,
2010). An important question for understanding tactile representations is the functional organization of these processes. Studies with brain-damaged individuals have provided evidence for a potential dissociation between tactile detection and tactile localization. There are multiple reports of brain-damaged individuals who could accurately detect tactile stimuli with substantial impairments in tactile localization, up to having no knowledge of stimulus location (Halligan et al., 1995; White, Davies, & Kischka, 2010; Birznieks, Logina, & Wasner, 2012; 2016, Rapp, Hendel, & Medina, 2002; Anema et al., 2009).

Three general models have been proposed for processing tactile detection and localization (see Harris, Thein & Clifford, 2004 for a discussion). First is a single process model in which tactile localization and detection processes are shared. Brain-damaged individuals who show dissociations between these processes suggest that these models are incorrect. Second, in a parallel processing model, tactile detection and localization are independent such that performance on one task does not affect the other. Third, in a serial processing model, tactile detection is performed first, after which sensory information is passed to a separate tactile localization process. The serial processing model hence predicts lower accuracy for localization than detection, and lower localization accuracy for missed versus detected stimuli. By studying participants’ ability to detect and localize tactile stimuli, Harris et al. (2004) found that behavioral data were most consistent with a serial processing model, indicating that detecting a tactile stimulus is necessary but not sufficient for localizing a tactile stimulus.³

³ One piece of evidence contradicting the serial model comes from cases of numsense, where individuals were able to localize tactile stimuli that they did not consciously detect (Paillard, Michel, & Stelmach, 1983; Rossetti, Rode, & Boisson, 1995, 2001). However, it is unclear whether these individuals truly did not detect the stimuli, or were being conservative in giving positive responses when they were unsure (see Medina & Coslett, 2017, for a discussion).
Despite evidence for a serial processing model, it is still unclear if tactile detection and localization are completely separate processes or involve common processes. All previous cases of brain-damaged individuals with tactile localization impairments have either mild to severe impairments in tactile detection, or incomplete evidence regarding their tactile detection abilities. For example, one patient who can detect tactile stimuli with no ability to localize (Halligan et al., 1995) could only detect 33% of all tactile stimuli. Patients in more recent studies of tactile localization also report mild impairments in tactile detection relative to their ipsilesional hand or age-matched healthy controls (Birznieks et al., 2012; 2016; White et al., 2010; Anema et al., 2009). The patients reported in Rapp et al. (2002) could reliably detect light taps delivered to their contralesional hand. However, their tactile detection thresholds were not tested systematically, hence it is unknown whether they were truly unimpaired at tactile detection. Given that tactile detection was either impaired or untested in these cases, there is no direct evidence from neuropsychological studies for a true dissociation of tactile detection and localization. Evidence for a strong dissociation between tactile detection and localization would ideally be cases in which individuals have normal tactile detection along with impaired tactile localization. In this manuscript, we report such a case.

Individuals with normal detection yet impaired localization can also inform mechanisms underlying tactile localization. With impairments in both tactile detection and localization in previous cases, errors in tactile localization could be caused by degraded quality of sensory input, or be related specifically to impairments in tactile localization separate from stimulus quality. It is thus difficult to infer mechanisms specific to the localization process from those patients. On the other hand, in individuals with completely
normal tactile detection yet impaired localization, errors in tactile localization would be solely due to impaired stimulus location representation. These error patterns can then be utilized to understand how the location of tactile stimuli is represented. In the individual reported in this chapter, tactile detection on the contralesional hand was within the normal range, despite substantial localization errors. Such dissociation indicates that the individual’s deficits were specific to representing the location of touch instead of general sensory noise, from which we could infer mechanisms specific to tactile localization.

Case History

At the beginning of our testing, DS was a 46-year-old right-handed male who suffered a subcortical infarct in the right hemisphere four years before the investigation. MRI revealed damage to the superior and anterior corona radiata (Figure 5). DTI showed that this lesion likely damaged pathways from the thalamus to superior frontal gyrus, including pre-supplementary motor area. Furthermore, DTI revealed intact pathways from the thalamus to the primary somatosensory cortex, and from the primary to secondary somatosensory cortex, in both hemispheres. See Appendix A for details of the DTI analyses.

The patient reported left-sided hemiparesis after the stroke, that subsided over time. In addition, he described signs of alien hand syndrome in his contralesional (left) hand a few months after the stroke. He described that the left hand would grasp objects and perform tasks without him realizing it. For example, when he was standing in front of the mirror, he would look up and find his left hand reaching for the soap. These signs of alien hand syndrome had subsided by our initial testing session. During our final experiments (five years after the initial testing), he did not demonstrate any obvious motor deficits on his hands.
2.1. Experiment 2.1. Assessing tactile detection

Given that his thalamus and primary somatosensory cortices were intact, along with the pathway from thalamus to S1 in the damaged hemisphere, we expected normal tactile detection on the contralesional hand. We therefore tested tactile detection threshold on both hands, with the ipsilesional hand as control. Tactile detection threshold was tested in two sessions that were five years apart.

Procedure

The patient was seated in front of a table with the tested hand placed on the table, aligned with body midline and palm facing up. There were two blocks in each testing session, one for each hand. The patient was asked to close his eyes throughout each block. Tactile detection threshold was measured by presenting Semmes-Weinstein monofilaments to the palmar side of the tip of the middle finger (North Coast Medical Inc., CA, USA). The monofilament set contains 20 intensities ranging from 0.008 to 300 g, which are then log-transformed to scales ranging from 1.65 to 6.65. A 2-down, 1-up staircase procedure
was used: Each block started with the thickest filament. If the patient detected the stimulus, the filament intensity was decreased by two scale levels for the next trial, otherwise the filament intensity was increased by one scale level. To differentiate hits from false alarms, catch trials where the experimenter would approach the patient’s hand with the filament without actually touching the hand were interspersed among actual trials. After each trial, the experimenter asked “Did you feel anything?” and the patient verbally responded Yes or No. We planned to stop the staircase procedures after 10 reversals and calculate detection threshold as the average intensity at all 10 reversals. However, due to experimenter error, we continued beyond 10 reversals on the tested blocks (see Table 1 for details). Given that the threshold estimate becomes more stable with more reversals, we report results from all trials below.

Results

We report tactile detection threshold on both hands tested in both investigations (Table 1), calculated as the average log-transformed scale across all trials where the direction (i.e. increasing or decreasing) of the staircase procedure reversed. False alarm rates are also reported.
Table 1. Tactile detection threshold on each hand, collected from two testing sessions.

<table>
<thead>
<tr>
<th></th>
<th>Left (contralesional) hand</th>
<th>Right (ipsilesional) hand</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Threshold (15 reversals)</td>
<td>False alarm rate (17 reversals)</td>
</tr>
<tr>
<td>Filament scale</td>
<td>2.45</td>
<td>0.14 (1/7)</td>
</tr>
<tr>
<td></td>
<td>2.46</td>
<td>0 (0/8)</td>
</tr>
</tbody>
</table>

|                | Threshold (14 reversals)  | False alarm rate (17 reversals) |
| Filament scale | 2.80                      | 0 (0/7)                      |
|                | 3.13                      | 0 (0/7)                      |

As shown in Table 1, in both sessions the left (contralesional) hand had no worse sensitivity than the right (ipsilesional) hand. Tactile detection thresholds below 2.83 are considered as normal (North Coast Medical Inc., CA, USA). In addition, in a large study using these filaments (N = 130, age 7-75 years, mean 41 years), detection thresholds ranged from 1.65 to 3.84, most frequently at 2.83 (Hage, van der Steen, & de Groot, 1995). Therefore, DS’s performance was well within the range of healthy individuals, demonstrating intact tactile detection.

2.2. Experiment 2.2. Tactile localization

Having found a normal tactile detection threshold on DS’s contralesional hand, we then tested his tactile localization ability. According to the serial processing model, tactile detection is necessary but not sufficient for tactile localization. It is therefore possible that DS has impaired tactile localization in spite of completely intact detection. More importantly, impaired tactile localization with normal detection would provide novel evidence that tactile detection and localization are completely dissociable processes.
**Procedure**

The tested hand was placed on the table, aligned with the body midline and palm facing down. For each hand, we used a filament that was two intensities above the hand’s threshold to ensure that stimuli were detectable. In cases where the detection threshold did not map to a filament, the closest thicker filament was considered as the threshold filament.

In each trial, the experimenter stimulated one of the 22 predetermined locations (Figure 6, black labels) on the hand dorsum with the patient’s eyes closed (as in Rapp et al., 2002). Then the patient opened his eyes and pointed to where he felt the touch using his untested hand. A second experimenter recorded the patient’s responses on a standardized hand illustration (hand drawings in Figure 6). In trials where the patient did not feel the stimulus, the locations were marked as missed.

We tested DS’s tactile localization during two separate sessions. In each session, two blocks were conducted on each hand with the order counter-balanced in an ABBA design. Within each block there were 22 trials, with one trial per location in a randomized order. In total four trials were tested for each location on each hand.

**Analyses**

Since single-case data can violate various assumptions in standard parametric statistics, we analyzed our data using permutation tests. In some cases, we were interested in whether DS’s localization judgments were biased in a particular direction. To examine this, we used one-sample permutation tests to examine if the bias for his localization judgments was significantly different from zero. To do this, we took the bias for each localization judgment and, in each permutation, randomly flipped the sign of each observation, with the assumption that observations would be randomly below or above zero.
under the null hypothesis. For comparing localization judgments across hands or experimental manipulations, we used permutation tests in which each permutation randomly shuffled the relationship between the localization judgment and tested hand/experimental condition. The actual mean localization bias was then compared to mean localization bias from each permutation, with the two-tailed permutation $p$-value being the percentage of permutation where the absolute mean bias was larger than the absolute actual mean bias.

Permutation tests were performed using a combination of the DAAG package in R (https://cran.r-project.org/web/packages/DAAG/DAAG.pdf) with 100,000 permutation iterations for each analysis.

Results

Actual and perceived target locations for each hand are shown in Figure 6. Overall, 15 out of 88 (17.0%) stimuli on the contralesional (left) hand and 24 out of 88 (27.2%) stimuli on the ipsilesional (right) hand were not detected. The detection rate did not differ between the two hands (Fisher’s exact $p = .146$). Trials in which tactile stimuli were not detected were excluded from subsequent analyses.
Next, localization biases were calculated as the difference between responses and actual locations in medial-lateral and proximal-distal directions. For both hands, negative values denote biases lateral to the body midline, i.e. towards the pinky, and proximal to the body, i.e. towards the wrist. As shown in Figure 6, perceived stimulus locations on the contralesional hand (left panel) shifted dramatically towards the pinky and wrist. One-sample permutation tests revealed a significant lateral ($p < .001$, $M = -19.3$ mm, $SD = 24.0$ mm) and proximal bias ($p < .001$, $M = -31.7$ mm, $SD = 29.3$ mm). For the control ipsilesional (right) hand (Figure 6, right), there was a slight but significant bias towards pinky, ($p < .001$, $M = -2.23$ mm, $SD = 4.95$ mm), and no significant bias in proximodistal direction ($p = .954$, $M = 0.41$ mm, $SD = 15.0$ mm). Two-sample permutation tests revealed significantly greater lateral and proximal biases on the left (contralesional) versus right hand ($ps < .001$).
Discussion

Despite normal tactile detection, we found large localization errors on his contralesional hand. Compared with his ipsilesional right hand, localization judgments for his left hand strongly clustered in the ulnar and proximal directions (Figure 6). To our knowledge, this is the first case that shows completely normal detection with impaired localization, providing strong evidence that tactile detection and localization are completely separate processes.

In addition to the contrast between tactile detection and localization, DS’s errors clustered on one side of the hand. One question regarding his tactile localization performance is the reference frame of his localization bias. One possibility is that this bias is somatotopic, such that DS will mislocalize towards the pinky regardless of hand position. However, tactile information can also be represented in one of many external frames of reference. A simple manipulation to examine this is changing hand position from palm down to palm up. If the bias is somatotopic and towards the ulnar side of the hand, then localization judgments will be biased towards the pinky regardless of hand posture. If his localization errors are based on an external representation, responses will be biased towards the left side of the hand, regardless of whether the hand is palm up or palm down. Furthermore, as noted earlier, one external frame of reference refers to a general category of representations in which left and right are assigned from the viewer, and are not yoked to the skin surface. If DS demonstrates localization biases in an external frame of reference, then other manipulations of hand position can be employed to further examine the type of representation involved in his deficit. These questions were addressed in Experiment 2.3.
2.3. Experiment 2.3. Investigation of spatial reference frame in tactile localization errors

We performed a series of experiments in a new testing session, manipulating hand posture to examine whether DS’s localization bias was in a somatotopic or external frame of reference. For time purposes, we only tested his contralesional (left) hand.

In addition, we tested both the hand dorsum and palm in the same block. In the brains of non-human primates, dorsum and palm surface representations in S1 are distributed differently: The surface of the palm is largely represented in continuous cortical areas whereas the dorsal surface is represented by smaller non-continuous cortical areas (Merzenich et al., 1984). It is therefore possible that representations of the dorsum and palm surfaces are differentially affected by brain damage. However, there is sparse evidence on how tactile localization performance on the two hand surfaces is affected after stroke, except for one study showing biases towards the hand center on both surfaces for two patients (Rapp et al., 2002). In Rapp and colleagues (2002), stimuli were only tested one surface at a time, not allowing for errors across the surfaces of the hand. We tested both dorsum and palm to examine if directional biases in DS are consistent across surfaces.

2.3.1. Experiment 2.3.1: Hand palm facing down

This experiment was performed to replicate the previous tactile localization pattern observed on the hand dorsum, and to examine what pattern would be observed after stimulating the palm (Figure 7a).

Procedure
The procedure was the same as in Experiment 2.2 except for the following differences. First, we only tested the contralesional (left) hand. Second, to test both the hand dorsum and palm, DS’s forearm was resting on a foam block such that we were able to stimulate the palm surface from below (Figure 7a). Finally, we used a clearly suprathreshold filament (scale of 5.18) to ensure tactile detection. We tested 22 locations on each hand surface, with one trial per location. All locations were tested in one block in randomized order. We were not able to test location X3 (at the base of the palm) as it was covered by the foam block. Accordingly, this location was not included in the analyses.

Results

Actual and perceived stimulus locations are shown in Figure 7b. Consistent with Experiment 2.2, overall there was a significant bias towards the pinky ($p < .001$, $M = -28.8$ mm, $SD = 25.5$ mm) and the wrist ($p < .001$, $M = -39.5$ mm, $SD = 33.1$ mm). Two-sample permutation tests did not reveal significant differences between the hand dorsum and palm in both mediolateral and proximodistal bias ($ps > .9$).

There were also trials where DS perceived tactile stimuli delivered to the dorsum surface as on the palm, and vice versa, which we term “cross-surface errors”. Overall, 1 out of 22 (4.5%) dorsum stimuli were perceived as on the palm, and 18 out of 21 (85.7%) palm stimuli were perceived as on the dorsum. A Fisher’s exact test revealed significantly more cross-surface errors for stimuli delivered to palm versus dorsum ($p < .001$).
Figure 7. a. Hand posture in Experiment 2.3.1. DS was stimulated on the dorsum (filament in red) and palm surfaces (filament in blue) in the same block with the hand positioned palm facing down. b. Actual (black labels) and perceived stimulus locations in Experiment 2.3.1 for each surface. The palm surface is displayed as being viewed from the top, through the dorsum surface. Consistent with the filament colors in a., red labels are localization judgments for stimuli delivered on the dorsum surface, blue labels are localization judgments for stimuli on the palm surface. Labels on the edge of the hand outline are localization judgments made on the edge of the hand surface, between the dorsal and palmar surfaces.

Discussion

In this experiment, we replicated our previous finding that DS mislocalized tactile stimuli on the hand dorsum towards the pinky and the wrist. In addition, localization biases were consistent across the dorsum and palm surfaces.

First, there are multiple interpretations of DS’s localization errors in terms of which frame of reference they occurred. One possibility is that those biases occur in somatotopic space, such that errors would be towards the pinky regardless of hand position in space. Alternatively, those biases might occur in external space, such that they are on the left side relative to the hand proximodistal axis. On this assumption, tactile localization judgments
would be biased in the ulnar direction when the contralesional (left) hand is palm down, but would shift towards the thumb when placed palm up. We tested these possibilities in Experiment 2.3.2.

Second, one surprising and novel finding was that when stimuli could be presented to either surface, DS mislocalized the majority of stimuli that were delivered to the palm as on the dorsum. However, since the hand was positioned palm facing down, it is possible that DS made more dorsal responses because a) this surface was stimulated more in past experiments, and could be more likely to be stimulated or b) because of the relative ease in pointing to the dorsal surface. We further investigated these cross-surface errors in the following experiments.

2.3.2. Experiment 2.3.2: Hand palm facing up

Procedure

The procedure was the same as in Experiment 2.3.1 except that the contralesional (left) hand was placed palm facing up (Figure 8a). We did not test locations X1 and X3 on the dorsum because they were covered by the foam block. Accordingly, these locations were not included in the analyses.

Results

Actual and perceived stimulus locations are shown in Figure 8b. There was still a significant lateral \( p = .002, M = -13.4 \text{ mm}, SD = 25.6 \text{ mm} \) and proximal bias \( (p < .001, M = -39.3 \text{ mm}, SD = 38.8 \text{ mm}) \), but on the skin surface judgments shifted towards the thumb. Together with the results from Experiment 2.3.1, these results provide evidence for a bias that is not based on a somatotopic representation, but instead on some type of
external representation. Two-sample permutation tests between the dorsum and palm surfaces did not reveal significant difference in mediolateral ($p = .551$) or proximodistal biases ($p = .553$).

As in Experiment 2.3.1, there were cross-surface errors on both surfaces. Overall, 1 out of 20 (5%) dorsum stimuli were perceived as on the palm, and 15 out of 22 (68.2%) palm stimuli were perceived as on the dorsum; a significant difference in cross-surface errors for palm versus dorsum stimuli (Fisher’s exact $p < .001$). This is consistent with Experiment 2.3.1, indicating that cross-surface errors occurred in a somatotopic space and are not affected by hand posture.

Figure 8. a. Hand position and posture during Experiment 2.3.2. b. Actual (black labels) and perceived stimulus locations in Experiment 2.3.2 for the palm and dorsum surfaces. The dorsum surface is displayed as being viewed from the top, through the palm surface. Consistent with the filament colors in a., red labels are localization judgments for stimuli delivered on the dorsum surface, blue labels are localization judgments for stimuli on the palm surface. Labels on the hand outline are localization judgments made on the edge of the surface.
Discussion

In this experiment, we tested if DS’s tactile localization errors occur in a somatotopic or an external frame of reference. Across Experiment 2.3.1 and 2.3.2, we found that perceived stimulus locations always shifted to the left side in space relative to the hand proximodistal axis, demonstrating biases in an external hand-centered frame of reference. Our case indicated that errors in tactile localization on skin surface can occur in a non-somatotopic representation. Accordingly, judgments on skin surface varied with hand posture, towards the pinky when the hand was palm facing down (Experiment 2.3.1), and towards the thumb when the hand was palm facing up (Experiment 2.3.2), demonstrating a strong influence of proprioceptive information. We also replicated a finding from Experiment 2.3.1 that DS localized the majority of palm stimuli to the dorsum, even when the dorsum was facing down and less easy to point to, confirming that cross-surface errors were perceptual errors, with a bias towards sensing touch on the hand dorsum even when the palm was stimulated.

In Experiment 2.3.1 and 2.3.2, the contralesional (left) hand was aligned with the body midline. It was therefore unclear if the leftward biases were relative to the hand proximodistal axis (in a hand-centered frame of reference) or relative to the body midline (trunk-centered frame of reference). In addition, as discussed earlier, since the hand long axis has been aligned with the viewer’s perspective, it is unclear if the left-right was relative to a body part itself, or general left-right along the transverse axis with respect to the viewer. In Experiment 2.3.3, we addressed these questions by rotating the hand by 90 degrees towards the body, such that the hand-centered (defined by the hand proximodistal axis)
frame of reference was misaligned from trunk-centered (defined by body midline) frames of reference and the viewer’s perspective (Figure 9a). With the hand placed palm down, if previous localization errors were made on the left side specifically relative to the hand itself, i.e. relative to the hand proximodistal axis, we expect perceived stimulus locations to shift towards the pinky. If localization errors were made on the left side of a trunk-centered frame of reference or based on the viewer, we expect shifts towards the wrist.

2.3.3. Experiment 2.3.3: Hand palm facing down, rotated 90°

Procedure

The procedure was the same as Experiment 2.3.1, except that the contralesional (left) hand was rotated 90° such that the mediolateral hand axis was aligned with the body midline (Figure 9a). We did not test location X3 (base of the palm) because it was covered by the foam block. Location 2B on the dorsum was excluded from the analysis due to a recording error.

Results

Actual and perceived stimulus locations are shown in Figure 9b. To be consistent with Experiments 2.3.1 and 2.3.2, localization errors were still coded in the hand space, with negative values denoting biases towards the pinky and wrist. Overall, there was a significant bias towards the pinky ($p < .001, M = -29.0$ mm, $SD = 23.7$ mm) and wrist ($p < .001, M = -49.4$ mm, $SD = 33.8$ mm). No differences in mediolateral ($p = .371$) or proximodistal ($p = .109$) bias between the hand palm and dorsum surfaces were found.

As for cross-surface errors, overall 2 out of 21 (9.5%) dorsum stimuli were perceived as on palm, and 3 out of 21 (14.3%) palm stimuli were perceived as on dorsum.
There was no significant difference in cross-surface error rate between stimuli delivered to hand dorsum and palm (Fisher’s exact $p = 1$). These findings differ from Experiment 2.3.1 and 2.3.2, in which there were more cross-surface errors made on stimuli delivered to palm vs. dorsum, although the reason for such an improvement is not clear.

Figure 9. a. Hand position and posture during Experiment 2.3.3. b. Actual (black labels) and perceived stimulus locations in Experiment 2.3.3 for the dorsum palm surfaces. The palm surface is displayed as being viewed from the top, through the dorsum surface. Consistent with the filament colors in a., red labels are localization judgments for stimuli delivered on the dorsum surface, blue labels are localization judgments for stimuli on the palm surface. Labels on the hand outline are judgments made on the edge of the surface.
Discussion

When DS’s contralesional hand was rotated 90°, tactile localization judgments again shifted leftward relative to the hand proximodistal axis, regardless of which surface the responses were made, indicating that tactile localization errors occur in a hand-centered frame of reference instead of a trunk-centered or other external frame of reference. Taken together, Experiments 2.3.1 to 2.3.3 showed that perceived tactile stimulus locations on skin surface was strongly affected by proprioceptive information in external space. Specifically, tactile localization judgments shifted towards the left side of the hand itself, whether the hand was palm down (Experiment 2.3.1), palm up (Experiment 2.3.2) or rotated 90° (Experiment 2.3.3).

In these experiments, DS responded by manually pointing with his ipsilesional hand to his contralesional hand. Is it possible that the observed errors were based on a motor deficit, and not a perceptual deficit? First, even though the ipsilesional hand was unaffected by his stroke, there might still be gross deficits that cause errors in pointing movements. In addition, previous literature reported a case in which an individual was more accurate in localizing touch when pointing to a hand image versus pointing to his own stimulated hand (Anema et al., 2009), indicating that there could be errors specifically associated with pointing to one’s own body. We therefore ran two control experiments to test DS’s general pointing ability, as well as examining whether his tactile localization errors generalized to other response modalities.
2.4. Experiment 2.4: Are the observed biases motor or perceptual?

2.4.1. Experiment 2.4.1: Examining pointing ability of the ipsilesional hand

To test if the observed tactile localization biases were based on a motor deficit, we instructed DS to point to visual targets with his ipsilesional (right) hand, the hand with which he made pointing responses in Experiment 2.3. In addition, to examine if he had a deficit specific to pointing to body-related objects, we instructed DS to point to visual targets shown either in different quadrants drawn on a piece of paper or at different locations on a hand line drawing.

Procedure

DS was tested on pointing to different locations on the table in front of him. Each location was within one of twelve quadrants in a 4×3 grid, spanning -33.8 cm to 33.8 cm in transverse direction relative to the body midline and 5 cm to 55.7 cm in the proximodistal direction (Figure 10). This grid was not visible to DS. A laser pointer was mounted to a tripod. In each trial, DS was asked to close his eyes while the experimenter positioned the tripod-mounted laser pointer to aim within one of the quadrants. Then DS was asked to open his eyes and look at the laser dot for approximately 2 seconds. The laser pointer was then turned off and DS immediately pointed to where he believed the laser dot was with his ipsilesional right hand. A picture was taken on the position of the laser pointer as well as where DS pointed to code the distance between the pointed position and actual location of the visual target. Three trials were presented for each quadrant, with the specific target locations within the quadrant varying across trials.
In a second version of the experiment, the procedure was the same except for the following differences. First, we placed a standard hand drawing of the dorsum of the left hand in front of DS. For each trial, the laser dot was shown on one of the 22 locations (one trial per location) as in tactile localization experiments (there were no target positions labeled on the drawing), with stimulus presentation and localization judgments done in the same manner as in the first block. A second experimenter recorded the location of the pointing response on a different hand drawing.

![Figure 10. Illustration of the setup in Experiment 2.4.1. DS was asked to point to visual targets presented in different quadrants defined by a 4×3 grid. The grid lines are displayed only for illustration purposes. During the experiment, DS was not able to see the grid lines.](image)

**Results**

For pointing to visual targets in quadrants, we calculated the distance between the actual visual stimulus and the localization judgment in proximal-distal and medial-lateral directions respectively. Positive values denote errors towards the right and distal relative to the body. One-sample permutation tests were performed to examine if the pointing errors significantly differed from zero. There was a slight but significant bias towards the right
side of space \( (p = .047, M = 2.28 \text{ mm}, SD = 6.52 \text{ mm}) \). No significant proximal-distal errors were found \( (p = .166, M = 2.50 \text{ mm}, SD = 10.4 \text{ mm}) \). Since the tactile localization biases were to the left side of the proximodistal hand axis and proximal to the wrist, those biases were unlikely to be explained by general pointing errors in external space.

In addition, DS accurately pointed to all 22 locations on the hand drawing with no observable errors (i.e. his finger touched the target location on every trial). These findings provide additional evidence that the tactile localization errors could not be attributed as pointing errors.

### 2.4.2. Experiment 2.4.2: Tactile localization with verbal response

To examine if his tactile localization errors generalized to other response modalities, we had DS respond to tactile stimuli by verbally describing perceived stimulus locations.

**Procedure**

This experiment was done in three blocks, each with a different hand posture. In the first block, the contralesional (left) hand was placed palm facing down, aligned with the body midline (same as Experiment 2.3.1). In the second block, the hand was placed palm facing up, aligned with the body midline (same as Experiment 2.3.2). In the third block, the hand was placed palm facing down, rotated 90 degrees (same as Experiment 2.3.3).

The procedure of each trial was the same as in Experiment 2.3, except that DS verbally described the perceived stimulus location instead of pointing to it. DS was instructed to report on which surface (dorsum, palm) he felt stimuli, as well as the location on the surface. For describing stimuli on the palm and dorsum, we encouraged DS to
reference the fingers when describing stimulus position along the mediolateral direction by referencing fingers. An example response to a stimulus presented on his left hand was “top side (i.e. dorsum), in line with ring finger and close to wrist”. A second experimenter recorded his verbal responses.

For time purposes and to reduce difficulties in verbally describing locations, we only tested distal and proximal segments of each finger on each surface. By doing this, we were able to calculate medial-lateral distance between judgments and actual stimulus locations by the number of fingers (see Analyses below). As a result, there were 10 trials on each surface and 20 trials in each block.

Analyses

Given that our primary question examined whether DS still demonstrate leftward biases relative to the hand proximodistal axis with verbal responses, we only analyzed tactile localization errors in mediolateral direction. Target and perceived locations were coded as 1 to 5 from thumb to pinky. If DS referred to a location between two fingers, that location was coded as the average finger number (e.g. 3.5 for locations between the middle and ring finger). In trials where DS reported feeling touch on the side of the hand, locations were coded as the number of the corresponding outer finger plus 0.5 (e.g. 5.5 for the side surface of the pinky). We then calculated distance in finger units between actual and perceived target locations. As with previous experiments, permutation tests were performed on localization errors. Trials in which DS did not specify a finger in his response (3 out of 60) were excluded in the analyses. It is worth noting that although we coded judgments in terms of fingers, in most cases DS perceived the stimulus as on the palm or dorsum areas of the hand.
**Results**

For all blocks, one-sample permutation tests revealed a significant bias towards the left side in space relative to the hand proximodistal axis \((p < .05)\). No significant difference between the palm and dorsum surface were found in any block \((p > .8)\). These results are consistent with DS’s tactile localization performance when he manually pointed to perceived tactile locations, indicating that the previous findings generalize to different response modalities, and could not be attributed as pointing errors. Finally, DS also made cross-surface errors when making verbal responses (Table 2), indicating that these errors were also perceptual.

<table>
<thead>
<tr>
<th>Block</th>
<th>Surface</th>
<th>Stimuli localized to</th>
<th>Fisher’s exact test comparing surfaces</th>
</tr>
</thead>
<tbody>
<tr>
<td>Block 1:</td>
<td>Palm</td>
<td>1/10</td>
<td>(p = 0.141)</td>
</tr>
<tr>
<td>Block 2:</td>
<td>Palm up</td>
<td>0/10</td>
<td>(p = 0.032)</td>
</tr>
<tr>
<td>Block 3:</td>
<td>Palm</td>
<td>0/10</td>
<td>(p = 0.211)</td>
</tr>
</tbody>
</table>

**Discussion**

In two experiments, we ruled out the possibility that DS’s tactile localization errors were due to a motor deficit. First, when pointing to remembered visual targets in quadrants with the right (ipsilesional) hand, DS showed overall rightward biases relative to the body. Given that the tactile localization biases were towards the left of the hand proximodistal axis, these biases are unlikely to be explained by motor pointing errors. Second, DS pointed accurately to remembered visual targets shown on a hand drawing, indicating that his
tactile localization biases could not be explained by pointing errors specific to body-related objects. Finally, Experiment 2.4 showed a similar pattern of localization errors when DS made verbal responses compared to manually pointing to perceived stimulus locations, indicating that his tactile localization errors reflected general perceptual biases instead of response errors.

So far we have shown that DS made tactile localization errors consistently to the left side in space relative to the hand proximodistal axis. One question is if DS showed similar biases in other behavioral examinations that might explain his tactile localization biases. Although the mechanism is unclear given limited data, we found that when asked to judge location of the left (contralesional) hand in external space, DS made similar proximal and lateral errors. We report data from a proprioceptive judgment task to provide complementary data on his deficits and use this to motivate potential explanations in the discussion.

2.5. Experiment 2.5: Landmark localization

As part of a battery of tests, we presented DS with the landmark localization task as in Longo & Haggard (2010). Although this task is typically used to examine biases within the hand, an overall shift in localization judgments in this task can also be used to examine his ability to represent body position in external space. Data were collected over two testing sessions.

Procedure

At the beginning of each block, DS’s tested hand was placed on the table, palm facing down and aligned with the body midline. To ensure that he did not move the hand
during a block, we placed rubber cylinders between his fingers and around his hand. A picture of the hand was taken to later code the actual position of the hand. The hand was then occluded under a white board (50 cm × 50 cm) suspended 10 cm above his hand. His forearm and shoulder were covered with a black fabric to prevent DS from inferring hand position based on visual information.

In each trial, the experimenter verbally said a landmark on the hand (i.e. tip of your middle finger), and DS responded using a pointer to identify the location on the white board that was directly above the perceived landmark. We then took a picture of the localization judgment and coded them offline (as in Medina & Duckett, 2017). We examined landmark localization at 10 positions (tip and knuckle of each finger), three trials per location in a block. Another picture of the hand was taken at the end of each block. Comparing pictures taken before and after each block confirmed that the hand did not move during each block.

Each hand was tested in two blocks in each testing session, ordered in ABBA design. The first session started with the left hand, and the second session started with the right hand.

Results

Distance between the actual and perceived location of the landmarks was coded in millimeters and then compared against zero using one-sample permutation tests (Figure 11). For both hands, negative values denote lateral (away from body midline) and proximal biases. For the contralesional (left) hand, there was a significant lateral \( (p < .001, M = -63.3 \text{ mm}, SD = 30.3 \text{ mm}) \) and proximal bias \( (p < .001, M = -51.5 \text{ mm}, SD = 42.4 \text{ mm}) \). For the right hand, there was a significant lateral bias \( (p < .001, M = -17.5 \text{ mm}, SD = 26.1 \text{ mm}) \), but no significant shift in proximodistal direction \( (p = .395, M = -2.40 \text{ mm}, SD = 30.8 \text{ mm}) \).
Two-sample permutation test showed significantly larger lateral and proximal biases ($p < .001$) in the left hand versus the right hand.

Figure 11. Actual (solid lines) and perceived (dashed lines) landmark locations on the left (left panel) and right (right panel) hand. Landmarks are connected by straight lines to display the hand shapes.

**Discussion**

In this experiment, we found significant lateral and proximal shifts in perceived landmark locations on the contralesional left hand. Importantly, the direction of his landmark judgments are consistent with the direction of his tactile localization bias in previously reported experiments. We discuss the implication of these consistent biases in the General discussion section below.

**2.6. General discussion**

We report the tactile detection and localization performance of a unique case whose performance informs us regarding models of tactile processing. First, DS demonstrated
normal tactile detection with highly impaired localization, providing novel evidence that tactile detection and localization are completely separate processes. Second, we found that on the contralesional hand, perceived stimulus locations on the skin surface were strongly affected by hand posture, biased towards the pinky when the hand was palm facing down, and towards the thumb when the hand was palm facing up. To our knowledge, this is the first reported case showing changes in tactile localization as a function of hand position. This finding provides evidence that localizing touch on the body does not only occur in somatotopic space, but also takes into account information from external space. Furthermore, DTI analyses showed that the pathway from thalamus to S1 in the damaged hemisphere was intact, consistent with his normal tactile detection and indicating that his tactile localization deficits were due to damage to additional pathways responsible for tactile localization.

A dissociation between detection and localization has been discussed in previous literature, in which patients reported not knowing or mislocalized stimulus locations for stimuli that they successfully detected (Halligan et al., 1995; Birznieks et al., 2012; 2016; White et al., 2010; Anema, 2009; see also Harris et al., 2004 for evidence from healthy individuals). However, in all these studies, patients had impaired tactile detection ability along with impaired tactile localization. With impairments both in detection and localization, these studies did not provide strong evidence that the two processes are completely dissociable. In contrast to previous cases, DS had deficits exclusively in tactile localization while having normal tactile detection threshold, providing strong evidence that the two processes are completely separable.
A clear dissociation between tactile detection and localization has important implications for mechanisms of tactile processing. First, deficits in tactile localization that are separate from detection imply mechanisms specific to spatial representation of tactile information. In previous reports of brain-damaged individuals, both tactile detection and localization were impaired (Halligan et al., 1995; Birznieks et al., 2012; 2015; White et al., 2010; Anema, 2009; see also Harris et al., 2004). Therefore, deficits in tactile localization could be partially due to increased sensory noise, making it difficult to isolate mechanisms specific to the localization process. With completely intact tactile detection in DS, it is clear that his deficits were specific to tactile localization itself, indicating specialized mechanisms for localizing touch that are separate from sensory noise. Second, whereas most previous cases suffered brain damage along pathways from thalamus to S1 (Halligan et al., 1995; Birznieks et al., 2012; White et al., 2010; Rapp et al., 2002), DS had an intact thalamocortical pathway, along with no parietal damage. This demonstrates that tactile localization deficits can be caused by lesions outside of the traditional thalamocortical pathway to S1, indicating the existence of additional pathways specific to tactile localization. Specifically, given that DS’s localization errors occurred in an external, hand-centered frame of reference, the additional pathway might be responsible for mapping stimulus location to skin surface based on this frames of reference (this will be discussed in more detail later in the discussion).

The second important finding is that DS’ tactile localization biases occurred in external space, always towards the left side based on the hand’s proximodistal axis. Critically, these biases were not likely motor response errors during pointing, as DS could accurately point to remembered visual targets, and demonstrated similar localization biases
when making verbal responses. In addition, since tactile stimuli in the experiments were far beyond his detection threshold, localization errors were unlikely due to sensory noise. These findings provide strong evidence that tactile localization on the skin surface does not only utilize information from somatotopic space, but also information regarding current body posture. Previous studies have also provided evidence that proprioceptive information is considered during tactile localization, such that the pattern of localization errors were modulated by body posture (Haggard, Kitadono, Press, & Taylor-Clarke, 2006; Riemer et al., 2006; Ho & Spence, 2007; Badde, Roder, & Heed, 2019). Taken together, these findings challenge the serial model of tactile localization, which states that the brain first localizes touch on the skin surface, then combines with proprioceptive information to localize touch in external space (Medina & Coslett, 2010; Longo et al., 2010). Since proprioceptive information is utilized after touch has been localized on the skin surface, the serial model does not predict effects of proprioceptive information on localizing touch on the body. Evidence for effects of proprioceptive information on tactile localization indicates that tactile localization processes are not strictly serial.

In addition to contrasting somatotopic versus external frames of reference, we also provide clear evidence that DS’s tactile localization errors occurred in an external frame of reference specifically centered on the hand proximodistal axis. Previous studies reported spatial representations centered on the hand proximodistal axis. For example, tactile extinction occurred for tactile stimuli on the contralesional side with regards to the wrist midline (Moscovitch & Behrmann, 1994), a reference frame that overlaps with the hand proximodistal axis in the current study. In addition, studies of the tactile Simon effect showed that participants were faster and more accurate in judging intensity of a tactile
stimulus when the stimulus occurred on the same side as the responding effector, with the side of tactile location defined relative to the hand proximodistal axis (Medina, Theodoropoulos, Liu, Reyes, & Gherri, 2019). However, since in these studies the hand/wrist proximodistal axes were always aligned with the viewer’s perspective, the “left” and “right” sides could also be assigned from the viewer’s perspective, but not relative to the hand/wrist axis per se. In the current study, by rotating the hand 90° and still observing localization biases towards the left side of the hand proximodistal axis, we confirmed that DS’s localization errors occurred specifically relative to the hand proximodistal axis, providing strong evidence for a hand-centered frame of reference in representing tactile locations.

DS’s behavioral results and lesion location also provide novel insights on the neural correlates of tactile localization. Using transcranial magnetic stimulation (TMS), previous studies found that the primary somatosensory cortex, and parietal cortex more generally, play a causal role in localizing touch on the skin surface (Seyal, Siddiqui, & Hundal, 1997; Porro et al., 2007). Nevertheless, DS had no damage to parietal cortical areas or pathways from thalamus to S1, indicating additional neural correlates for tactile localization. First, the infarct caused lesion at superior and anterior corona radiata, which are most frequently associated with motor deficits (Cho et al., 2007; Jang, et al., 2006; Kwon et al., 2011; Shelton & Reding, 2001). Based on this, it is difficult to explain DS’s tactile localization deficits by his subcortical lesion. Second, from our tractography analyses (see Appendix A), DS’s subcortical lesion at superior and anterior corona radiata likely disrupted pathways from the thalamus to superior frontal gyrus, including pre-SMA. Several neuroimaging studies reported activation in general superior and middle frontal gyrus
during tactile spatial pattern discrimination or tactile localization (Li Hegner, Lee, Grodd, & Braun, 2010; Takahashi, Kansaku, Wada, Shibuya, & Kitazawa, 2012). However, with evidence that superior frontal gyrus is involved in cognitive control and executive function (Li et al., 2013), it is unclear if activation in superior frontal gyrus truly reflected somatosensory processing, or general task demand. With regards to pre-SMA, studies have found median nerve somatosensory-evoked potential (SEP) in humans (Barba, Frot, Guenot, Mauguiere, 2001; Barba, Valeriani, Colicchio, & Mauguiere, 2005), indicating that pre-SMA may process somatosensory information. In addition, SEP of middle latency (50-150ms) was uniquely found in pre-SMA (Barba et al., 2001; 2005), suggesting that the somatosensory processes likely occur in later stages. Given that DS’s tactile localization bias occurred in external reference frame, one possibility is that this area combines information from external space with the original somatotopic representation in localizing touch. We note that this account is speculative given limit evidence on the role of pre-SMA in somatosensory processes.

So far we have discussed two major findings from DS: A complete dissociation between tactile detection and localization, and localization errors in an external frame of reference specifically centered on the proximodistal axis of the hand. An unanswered question is why DS mislocalizes touch towards the left side of the hand, regardless of hand posture. Given limited evidence, we cannot make a strong claim. However, we suggest one possible interpretation given DS’s performance on the landmark localization task. As shown in Experiment 2.5, DS made substantial leftward and proximal errors on his contralesional left hand. Importantly, proprioceptive biases on the contralesional hand were in the same direction as his tactile localization biases. One possibility is that his tactile
localization biases stem from feedback processes from representations in external space to somatotopic representations. When the hand is touched, the brain not only represents its location on the skin surface, but also maps it to external space by integrating proprioceptive information. Given leftward and proximal biases in proprioception, after being mapped to external space, touch may be represented as to the left and proximal to the actual hand position. This biased external representation could then feed back to a somatotopic representation. Because of proprioceptive biases, where the touch is represented in external space is not occupied by the hand. However, there is a clear constraint that a touch must have occurred on the hand surface. During the feedback process the touch is projected to the leftmost and proximal part of the skin surface, leading to tactile localization biases. In normal cases, biases from feedback processes may be much less weighted by information from somatotopic space, making the effect of proprioceptive errors not noticeable. Nevertheless, DS’s lesion may have affected the relative weighting between somatotopic representation and effects of proprioceptive biases, leading to magnified localization errors.

On this explanation, one possible mechanism for proprioceptive information to influence tactile localization is by feedback processes from representations of tactile location in external space to somatotopic representation. We again note that this account is quite speculative. Future studies are needed to investigate the effect of proprioceptive biases on tactile localization on the body.

Finally, we report for the first time mislocalization of tactile stimuli across surfaces. Specifically, DS was substantially more likely to mislocalize tactile stimuli to dorsal side when stimulated on palmar side, compared to the opposite direction. Unfortunately, we do not have enough evidence from DS or prior literature to explain why such errors occurred.
Most previous tactile localization studies only present stimuli to one surface. Contextual constraints in past studies (e.g. top-down knowledge that tactile stimuli are only being presented to one surface) may either alter responses or perceptual processes to limit reported stimuli to one side. It is possible that such biases could also be observed in other individuals with brain damage, or in neurologically-intact individuals. We believe that it is valuable to examine both palm and dorsum surfaces to fully understand tactile localization processes for the entire hand.

Motivated by findings from DS, additional experiments were performed for evidence from neurologically intact individuals that tactile localization on the skin surface is influenced by external information. These experiments are presented in Chapter 3 and Chapter 4.
Chapter 3

THE EFFECTS OF VISUAL-PROPRIOCEPTIVE CONFLICT ON TACTILE LOCALIZATION: INVESTIGATING NEUROLOGICALLY INTACT INDIVIDUALS

Having found strong evidence from a brain-damaged individual that proprioceptive information influences tactile localization on the body surface, we next examined this question in neurologically intact individuals. In previous studies, the effects of proprioceptive information on tactile localization were examined by manipulating body posture relative to a reference point (e.g. gaze direction, Medina et al., 2018). The experiments in Chapter 3 adopt a different approach, assessing tactile localization on the hand when there is discrepancy across multiple sensory modalities regarding hand position in external space. To resolve spatial conflicts, the brain integrates information across sensory modalities based on their relative precision, leading to biases in felt hand position towards the more precise unimodal estimate (van Beers, Sittig, & van der Gon, 1999). If tactile localization on the body operates solely in somatotopic space, as stated in the serial model, biases in felt hand position in external space would not affect tactile localization judgments on the skin surface. Alternatively, if information regarding body position affects tactile localization, biases in hand position judgment would also cause biases in tactile localization on the skin surface.
One way to substantially bias felt hand position is by creating conflicts between proprioceptive and visual estimates. One example is the rubber hand illusion in which an individual views a life-sized rubber hand while the actual hand is placed a few inches away and hidden from view (Figure 12; Botvinick & Cohen, 1998). In this case, visual estimate of hand position (denoted as “V”), informed by the seen rubber hand, is spatially dissociated from proprioceptive estimate (denoted as “P”) from the actual hand. When the hidden hand and rubber hand receive synchronous brushstrokes, individuals felt the touch as originating from the brush touching the rubber hand, and perceived the hidden hand as shifting towards the visual estimate. In other words, both the spatial location of felt touch and hand position are “captured” by visual information (visual capture).

![Figure 12. Illustration of the rubber hand illusion. The participant views a rubber hand (V), with the actual hand (P) hidden from the view. When the rubber hand and actual hand are stroked in synchrony, the participant felt the touch as on the rubber hand, and felt hand hidden hand as shifting towards the rubber hand (Botvinick & Cohen, 1998).](image)

Interestingly, one study found that visual capture of touch and hand position led to delayed tactile detection (Folegatti et al., 2009). In the experiment, participants received
either synchronous or asynchronous visuotactile stimulation on the rubber hand and their own hand. To evaluate visual capture, participants rated the extent to which they felt touch as on the seen rubber hand, along with reporting the felt hidden hand position. Then, participants performed a speeded tactile detection task. As expected, after synchronous vs. asynchronous stimulation participants felt more strongly that the touch occurred on the rubber hand, and felt the hidden hand as closer to the visual estimate. Importantly, whereas detection accuracy was unaffected, participants were slower at detecting tactile stimuli after synchronous, but not asynchronous stimulation, compared with baseline performance before visuotactile stimulation. These findings provide initial evidence that spatial conflicts between visual and proprioceptive estimates regarding hand position lead to changes in tactile perception (i.e. detection speed) on the skin surface.

As discussed previously, a question regarding tactile localization is whether it is a strictly serial process, or if there are effects of external information on tactile localization on the skin surface. The single-case study reported in Chapter 2 provides strong evidence for a non-serial model. Given these findings, an important question is how information from external space influences tactile localization. Although Folegatti et al. (2009) suggested that conflicts between visual and proprioceptive estimates slowed down tactile detection, they did not address if these spatial conflicts influence perceived location of touch on the skin surface. If external information influences tactile localization on the skin surface, conflicts between visual and proprioceptive estimate in external space would bias tactile localization on the skin surface.

To address this question, we examined tactile localization in the mirror box illusion, which is more robust and powerful than the rubber hand illusion. In the mirror box illusion,
an individual places one hand on each side of a mirror that is aligned with the sagittal plane of the body, such that the hand reflection in the mirror (the “mirror hand”) looks like the hand hidden behind the mirror (Figure 13; Ramachandran & Rogers-Ramachandran, 1996). When the two hands are placed at different distances from the mirror, the hidden hand is at a different position from where it appears in the mirror, creating a mismatch between the proprioceptive estimate and visual estimate of the hidden hand position. When the individual moves both hands synchronously, such that the movements seen on the mirror hand are congruent with the movements performed by the hidden hand, the hidden hand is felt at where the individual sees it (i.e. at V), instead of where the hand was actually positioned (i.e. at P; Medina, Khurana, & Coslett, 2015).

After the mirror box illusion is established, participants localize tactile stimuli delivered to their hidden hand. When the illusion is successful (i.e. after visual capture), participants feel their hidden hand at the visually-defined location. As a result, tactile sensations on the hidden hand are externally localized at the location of the visual estimate. Meanwhile, although the consciously felt hand position is at the visual location, the unconscious, unimodal proprioceptive estimate of hand position may still influence tactile localization. This representation could inform the brain that the touch occurred where the hand is actually located, biasing tactile location estimate in external space away from the visually-defined location, towards the proprioceptively-defined location. Importantly, if information from external space feeds back to the skin surface, perceived tactile location on the skin surface would also shift towards the proprioceptive estimate. In this outline of the hypothesis, touch is anchored to the visual estimate of the hand (where the subject
perceives their hand to be) and is then biased towards the proprioceptive estimate. We refer to this hypothesis as the “anchoring hypothesis” throughout this chapter.

Figure 13. Illustration of the mirror box illusion. With the hands on each side of the mirror, visual estimate (V) and proprioceptive estimate (P) regarding the hidden hand position are dissociated.

We conducted three experiments to test the anchoring hypothesis, namely that tactile localization on the skin surface would be biased in the direction of the proprioceptive estimate relative to the visual estimate. Consistent with this prediction, by manipulating the relative position between proprioceptive and visual hand position in Experiment 3.1, tactile localization on the skin surface was biased towards the proprioceptive estimate. Then, Experiment 3.2 and 3.3 confirmed these findings and ruled out potential alternative accounts. With findings consistent with the anchoring hypothesis, we discuss potential mechanisms in the General Discussion section.

3.1. Experiment 3.1: Effects of visual-proprioceptive conflict on tactile localization

Methods

Design
A 2×2 design was used (Figure 14): Participants placed the right hand in front of the mirror, with the middle finger either 4” or 10” away from the mirror. The left hand was hidden behind the mirror, either 4” or 10” away. For easy references, each condition is named as P_xV_y, with P representing proprioceptive estimate and V visual estimate of hand position, and x and y denoting the distance to the mirror. These manipulations created two congruent conditions where both visual and proprioceptive estimates were at either 10” or 4” away from the mirror (Figure 14a and 14d). Two incongruent conditions were created with the proprioceptive estimate either 6” medial (i.e. away from the body midline; Figure 14b, P_4V_{10}) or lateral (Figure 14c, P_{10}V_4) to the visual estimate. Previous studies have shown that a mismatch of 6” between the proprioceptive and visual estimate in the mirror box reliably induced shifts in felt hand position (Medina et al., 2015; Liu & Medina, 2018). Across the hand position conditions, participants were stimulated on the dorsum of the hidden left hand and reported where on the skin surface they felt the stimulus (see Procedures below).
Figure 14. Manipulations in Experiment 3.1. Participants placed their right hand in front of the mirror, either 4” or 10” away from the mirror. The left hand was hidden behind the mirror, at either 4” or 10” from the mirror. The reflection of the right hand in the mirror (dashed outlines) looks like the hidden left hand. Dashed black lines indicate where the participants were viewing. A 9×9 dot grid (not seen by the participant) was drawn on the back of the hidden left hand (right panel). Of the 81 dots, only the nine dots in red were stimulated.

Participants

In a pilot experiment with two conditions (Figure 14c and 14d), we found significantly more localization biases towards the direction of proprioceptive hand position (i.e. towards the pinky of the hidden left hand) when the proprioceptive estimate was incongruent with visual estimate (P_{10}V_{10}) versus congruent (P_{4}V_{4}). The effect size was 1.37 and the power was 0.97 with 10 participants. Considering that the effect size could be inflated by a small sample size due to sampling biases, a smaller effect size was assumed in designing new experiments. With a moderate to high effect size of 0.8, 19 participants were needed to obtain a power of 0.9.

With the goal of 19 participants, 22 participants were scheduled (age: 24.6±5.1, 8 males), assuming attrition. One participant did not complete all the blocks and was
excluded from the analyses. In addition, given that tactile localization performance
decreases with tactile detection ability (Harris, Thein, & Clifford, 2004), participants were
excluded if the number of trials where tactile stimuli were not felt exceeded the criterion
(3 SDs of group mean; see Procedure below). One participant was excluded for this reason.
In total, data from 20 participants were analyzed.

Procedure

At the beginning of the experiment, the experimenter drew a 9×9 dot grid (0.75 cm
between adjacent dots; Figure 14, right panel) on the dorsum of the left hand. Then a picture
of the left hand was taken and printed out with the hand in real size. On the picture, the
dot-grid was labelled as A-I from the ulnar (pinky) to radial (thumb) side, and the rows as
1-9 from the knuckles to the wrist. Participants used this picture to make verbal localization
judgments by stating the grid coordinates (e.g. “B7”). Unknown to the participant, only
nine of the 81 dots were stimulated (marked red in Figure 14, right panel). After the hand
picture was taken, the nine target dots were redrawn with a different color for the
experimenter to locate.

Tactile stimuli were delivered using Semmes-Weinstein monofilaments (North
Coast Medical Inc., CA, USA). To induce tactile localization biases that could be
modulated by experimental conditions, tactile stimuli were slightly above threshold
(filament with a bending weight of 0.6g). To ensure that the participant could reliably
detect tactile stimuli of this intensity, the experimenter tapped random locations on the
dorsum of the left hand using the 0.6g filament before the experiment. If the participant
reported not feeling them in more than three consecutive trials, a filament of one scale
higher (1.0g) was used for that participant. Three out of 21 participants were tested with the 1.0g filament in this experiment.

At the beginning of each block, the experimenter placed the participant’s hands at the instructed locations. The left hand was placed with the participant’s eyes closed, hence its exact location was unknown to the participant. To facilitate visual-proprioceptive integration, participants first tapped the index finger of both hands synchronously for 20 seconds at a metronome set at 120 beats per minute, while focusing on the hand in the mirror. The tactile stimulation trials started immediately after tapping was completed. In each trial, the experimenter stimulated the instructed location on the participant’s left hand. Then, the participant referred to the hand picture to verbally report the coordinate of the dot on which they believed they felt the touch. The experimenter then typed the response to a computer for off-line coding. Trials in which the participant reported not feeling the stimulus were noted without being repeated.

Each of the four conditions were tested in two blocks. Each block contained 27 trials, with three trials per stimulus location. As a result, each of the nine tactile locations were tested in six trials in each condition. Block and trial orders were randomized for each individual. The entire experiment lasted for about one hour.

Data analyses and predictions

Tactile localization error was calculated as the distance in dot units between the responded dot and actual dot, with one unit being the distance between two adjacent dots (0.75 cm). Localization error was calculated on each trial in two dimensions, proximal-distal (i.e. wrist-finger) and medial-lateral (i.e. thumb-pinky).
To investigate the effects of visual-proprioceptive conflict on tactile localization, localization bias in each dimension was first analyzed with an omnibus repeated-measures ANOVA with Proprioceptive Position (10” and 4”) and Visual Position (10” and 4”) as independent variables. As discussed earlier, a serial model would predict no effect of the manipulations. Accordingly, any significant effects would indicate influences of external information on tactile localization. For this reason, results from the omnibus ANOVAs serve as overall indicators of whether external information influences tactile localization on the skin surface.

Whereas ANOVAs provide an overall impression of whether external information affects tactile localization, by considering proprioceptive and visual positions independently, they do not directly inform how tactile localization changes as a function of visual-proprioceptive conflict. Further paired t-tests were then performed to test the anchoring hypothesis. For medial-lateral bias, the hypothesis is that when touch is referred to the viewed hand, localization judgments would be biased towards the proprioceptive estimate. When the visual estimate was at 4” from the mirror, touch was anchored at 4”. If tactile localization is biased by proprioceptive estimate, there would be more lateral localization bias when proprioceptive estimate was lateral to the mirror hand (P10V4) vs. a matched congruent condition (P4V4; Figure 15). Along the same logic, when the visual estimate was at 10” from the mirror, there would be more medial localization bias when proprioceptive estimate was medial (P4V10) to the visual estimate vs. a matched congruent condition (P10V10). To test these predictions, paired t-tests were performed between different proprioceptive estimates at each visual estimate. No specific prior hypotheses were made on how visual-proprioceptive conflicts would affect proximal-distal bias.
Results

Overall participants reported not feeling touch on 3.8% trials, with no participants exceeding 13%. Trials in which participants did not detect the stimulus were excluded from the analyses of localization bias. For tactile localization bias for each target location in each condition, see Appendix B.

Medial-lateral localization bias

First, a repeated-measures ANOVA was performed on medial-lateral bias with Proprioceptive Position (10” and 4”) and Visual Position (10” and 4”) as independent variables (Figure 16a). There was a main effect Proprioceptive Position ($F(1,19) = 20.94, p < .001$), with more lateral biases when the hand was at a more lateral (10”: $M = -0.50$ units, $SD = 0.59$ units) versus medial position (4”: $M = -0.09$ units, $SD = 0.62$ units). There was also a main effect of Visual Position ($F(1,19) = 8.81, p = .008$), with more lateral biases when the viewed hand was at a more medial position (4”: $M = -0.42$ units, $SD = 0.55$ units) versus lateral (10”: $M = -0.16$ units, $SD = 0.65$ units). The interaction was not
significant \((F{(1,19)} = 0.57, \ p = 0.459)\). To summarize, tactile localization bias occurred towards the direction of proprioceptive position (i.e. more lateral biases when the actual hand was lateral at 10” vs. 4”), and away from the visual position (i.e. more lateral biases when the viewed hand was medial at 4” vs. 10”). These effects were further analyzed and interpreted below.

Figure 16. a. Medial-lateral localization bias in each condition in Experiment 3.1. Negative values denote lateral biases. Arrows denote the predicted direction of localization bias in visuo-proprioceptive mismatch conditions compared to the visuoproproprioceptively congruent conditions. b. Proximal-distal localization bias in each condition, with negative values denoting distal biases. Conditions are illustrated on the right side of each bar. Unless otherwise noted, bias bars indicate 95% within-subjects confidence intervals (Cousineau, 2005). *: \(p < .05\). **: \(p < .01\). ***: \(p < .001\).
To further test the anchoring hypothesis, paired \( t \)-tests were performed. Specifically, at each level of Visual Position, proprioceptive estimate was either congruent or incongruent with the visual estimate. If visual-proprioceptive conflict affects tactile localization, relative to the congruent conditions, tactile localization judgments would be biased towards the proprioceptive estimate in incongruent conditions. Consistent with this prediction, when the visual estimate was at 4” and the proprioceptive estimate at 10” (i.e. *lateral* to the visual estimate), biases were more *lateral* compared to when the visuoproprioceptive estimate was congruently at 4” (\( t (19) = 4.13, p < .001 \)). When the visual estimate was at 10” and the proprioceptive estimate at 4”, there were more *medial* biases than when visuoproprioceptive estimate was congruently at 10” (\( t (19) = 4.09, p < .001 \)). These findings are consistent with the anchoring hypothesis, providing evidence that external information influences tactile localization on the skin surface.

Finally, the difference between the two congruent conditions, i.e. \( P_{4V} \) and \( P_{10V} \), did not reach significant level (\( t (19) = 1.60, p = .125 \)), although there was a trend towards more lateral biases in \( P_{10V} \) vs. \( P_{4V} \). This finding indicates that when visual and proprioceptive estimates were congruent, tactile localization was not strongly affected by the absolute hand position, further confirming that tactile localization was biased by *conflicts* between visual and proprioceptive estimates. These results also suggest that the main effects from the repeated-measures ANOVA were mainly driven by additional localization biases towards the actual hand position in the incongruent conditions (\( P_{4V} \) and \( P_{10V} \)) with respect to the congruent conditions (\( P_{4V} \) and \( P_{10V} \)), such that localization biases were towards the same direction with proprioceptive estimate, but
opposite with visual estimate. Overall, by demonstrating that visual-proprioceptive conflict in external space biased tactile localization, these findings provide additional evidence that tactile localization is not a strictly serial process. Importantly, these findings support the anchoring hypothesis that tactile localization on the skin surface is specifically biased towards the direction of proprioceptive estimate.

**Proximal-distal localization bias**

As revealed by a repeated-measures ANOVA (Figure 16b), there was a significant main effect of Proprioceptive Position ($F(1,19) = 10.84, p = .004$). Placing the actual hand at 4” induced less distal biases than when the actual hand was at 10” (4”: $M = -0.43$ units, $SD = 0.80$ units; 10”: $M = -0.61$ units, $SD = 0.79$ units). There was also a significant main effect of Visual Estimate ($F(1,19) = 7.24, p = .014$), with less distal biases when the viewed hand was at 10” ($M = -0.41$ units, $SD = 0.80$ units) than 4” ($M = -0.62$ units, $SD = 0.80$ units). Finally, there was a significant interaction ($F(1,19) = 4.54, p = 0.046$).

From Figure 16b, it is likely that the main effects and interaction effects reported above were driven by less distal bias in $P_4V_{10}$ compared with other conditions. To further test this, paired $t$-tests were compared between each pair of conditions. Indeed, there was a significantly less distal bias in $P_4V_{10}$ versus the other conditions ($ps < .001$), with no difference between the other three conditions ($ps > .45$). These findings will be discussed below.

**Discussion**

The aim of this experiment was to investigate the influence of visual-proprioceptive conflict on tactile localization. If tactile localization is a completely serial process, conflicts between visual and proprioceptive estimates of hand position in external space would not
affect where tactile stimuli are perceived on the hand surface. Alternatively, if external information influences tactile localization on the skin surface, conflicts between proprioceptive and visual estimate would also bias tactile localization. Specifically, on the anchoring hypothesis, with tactile sensation anchored to visual estimate, an incongruent proprioceptive estimate would bias tactile localization on the skin surface away from visual estimate, towards the proprioceptive estimate. Consistent with this prediction, compared with when both visual and proprioceptive estimate were at 4” (P4V4), a lateral proprioceptive estimate at 10” (P10V4) resulted in more lateral localization biases; compared with when both visual and proprioceptive estimate were at 10” (P10V10), a medial proprioceptive estimate at 4” (P4V10) reduced lateral localization biases. These findings will be further confirmed in later experiments, and are discussed in the General Discussion section. Finally, there was no significant difference between the two congruent conditions, i.e. P4V4 and P10V10, indicating that the absolute hand position did not strongly affect tactile localization when there were no visual-proprioceptive conflicts. This finding were also further investigated in later experiments.

Since visual-proprioceptive congruence was only manipulated in medial-lateral direction, no effects on proximal-distal localization biases were predicted. However, there was a significantly less distal bias in the P4V10 condition compared with other conditions (Figure 16b). Previous studies reported effects of gaze direction along the medial-lateral axis on distal localization biases (Medina et al., 2018). The study involved a similar setup, in which participants’ left hand was placed in the hidden side of a mirror box, and were asked to localize tactile stimuli on the hidden left hand in different conditions (Figure 4). Participants made more distal biases when directly viewing the right hand in front of the
mirror (i.e. gazing away from the hidden left hand), compared with when gazing towards the mirror hand, indicating that incongruent gaze direction led to more distal biases. The current study seems to be in contrast with previous findings, since the P4V10 condition, in which the least distal bias was found, actually involved incongruent gaze direction and hand position. Nevertheless, the two studies may not be directly comparable since the previous study did not manipulate visual-proprionceptive conflict. One possibility is that proximal-distal biases might be sensitive to overall manipulation of external information as opposed to be direction-specific. Finally, looking at Figure 16a and 16b, there were least medial-lateral biases and proximal-distal biases in the P4V10 condition compared with other conditions. Therefore, it is also likely that this condition resulted in overall more accurate localization judgments in both directions, although the underlying mechanism is unclear.

Overall in Experiment 3.1 visual-proprionceptive conflict induced tactile localization bias towards proprioceptive estimate, providing initial evidence for the anchoring hypotheses. We then conducted Experiment 3.2 to provide further evidence for the anchoring hypothesis, and to test potential alternative accounts.

3.2. Experiment 3.2: Controlling for the effects of hand position on tactile localization

In Experiment 3.1, tactile localization was biased towards proprioceptive hand position, away from visual position, consistent with the anchoring hypothesis. However, Experiment 3.1 also found an overall main effect of proprioceptive hand position, suggesting that simply placing the hand at different positions, regardless of visual hand position, biased tactile localization. With the proprioceptive hand position varying relative
to visual position, some of the tactile localization biases observed in Experiment 3.1 might have been caused by varying hand position alone, such that placing the hand laterally induced more lateral localization bias. Experiment 3.2 aimed to provide additional evidence for the anchoring hypothesis while controlling for the potential effects of proprioceptive hand position alone. For these purposes, a 2 (Vision) by 2 (Proprioceptive Position) design was used (Figure 17). The hidden left hand was placed at either 14” or 4” from the mirror. In the No-mirror condition (Figure 17a and 17b), the right hand was not placed in the mirror box, and participants closed their eyes during tactile stimulation. In the Mirror condition, participants viewed a mirror hand at 9” from the mirror. As a result, proprioceptive hand position was either 5” lateral (Figure 17c) or 5” medial (Figure 17d) to the visual hand position. This was designed for performing the comparison described below. In this experiment, the No-mirror conditions are denoted as P_xV_y, with V_y indicating no visual hand information.
Figure 17. Manipulations of hand positions in Experiment 3.2. Arrows in the Mirror conditions indicate predicted tactile localization bias directions. The null symbol in V∅ indicates no visual information.

With this design, first, the effects of proprioceptive hand position alone on tactile localization were examined by comparing P14V∅ (Figure 17a) and P4V∅ (Figure 17b). If hand position biases tactile localization in the consistent direction, there would be more lateral localization bias when the hand was placed laterally (P14V∅) vs. medially (P4V∅).

Importantly, the unique effects of visual-proprioceptive conflict, controlling for the effects of hand position, were examined by comparing the effects of proprioceptive hand position between the two Vision conditions (i.e. P14V∅ - P4V∅ vs. P14V9-P4V9). In the No-mirror condition, difference in medial-lateral localization bias between P14V∅ and P4V∅ was solely caused by difference in proprioceptive hand position. In the Mirror condition, in addition to the absolute hand position, the two proprioceptive positions were on the opposite side relative to the visual estimate. In this condition, the anchoring hypothesis would predict tactile localization be “pulled” towards each proprioceptive estimate, i.e. towards the
opposite directions (Figure 17c and 17d, arrows). These effects would add to the effects caused by hand position alone, magnifying the difference between the two proprioceptive hand positions. As a result, difference between П_14V_9 and П_3V_9 would be larger than difference between П_14V_0 and П_3V_0. This finding would provide additional evidence for the anchoring hypothesis by demonstrating the pure effects of visual-proprioceptive conflict on tactile localization, controlling for the effects of hand position alone.

Methods

Participants

Twenty-one participants (Age: 18.6±1.0, one male) were tested in the experiment. One participant was excluded because the experiment was not completed. As a result, 20 participants were included in the final analyses.

Design

As discussed above, a 2 (Proprioceptive Position: 14” and 4”) × 2 (Vision: Mirror and No-mirror) design was used (Figure 17). Since the limb was placed either lateral or medial to the same visual estimate, and constrained by the width of the mirror box, spatial mismatch between visual and proprioceptive estimate was reduced to 5” (as opposed to the 6” in Experiment 3.1).

Procedure

The procedure for the Mirror condition was the same as in Experiment 3.1. For the No-mirror condition, only the left hand was placed in the mirror box. At the beginning of No-mirror blocks, participants tapped the left index finger for 20 seconds with eyes closed. Then, in each trial, participants closed their eyes as the experimenter applied touch, then
they opened the eyes and verbally reported the coordinates of the perceived stimulus location.

As with Experiment 3.1, each condition was tested in two blocks. Within each block, 27 tactile stimulation trials were tested.

Data analyses and predictions

As with Experiment 3.1, omnibus repeated-measures ANOVAs were performed on medial-lateral and proximal-distal localization bias separately, with Proprioceptive Position (14” and 4”) and Vision (Mirror and No-mirror) as independent variables. Paired t-tests were performed to test specific hypotheses. First, to examine if hand position alone biases tactile location, medial-lateral bias was compared between P14V∅ and P4V∅ (Figure 17a vs. Figure 17b). There would be more lateral localization bias in P14V∅ vs. P4V∅ if tactile localization is biased towards the direction of hand position. Importantly, to examine the pure effects of visual-proprioceptive conflict, controlling for the effects of hand position alone, differences between the two proprioceptive positions were compared across the Vision conditions (P14V9-P4V9 vs. P14V∅-P4V∅). In the Mirror condition, visual-proprioceptive conflicts would bias tactile localization towards the opposite directions (i.e. towards each proprioceptive hand position), leading to a larger difference of P14V9-P4V9 vs. P14V∅-P4V∅.

Results

Overall participants reported not feeling the stimulus on 2.7% trials, with no participant exceeding 10%. Statistical analyses of medial-lateral and proximal-distal biases are presented below. For tactile localization bias for each target location in each condition, see Appendix B.
**Medial-lateral localization bias**

First, a repeated-measures ANOVA was performed on medial-lateral bias (Figure 18a). As with Experiment 3.1, there was a main effect of Proprioceptive Position ($F(1,19) = 24.20, p < .001$). Placing the left hand at a lateral position (14”: $M = -0.34$ units, $SD = 0.52$ units) induced more lateral localization biases than when the left hand was at 4” ($M = 0.07$ units, $SD = 0.45$ units). There was no main effect of Vision ($F(1,19) = 0.62, p = .442$; Mirror: $M = -0.105$ units, $SD = 0.51$ units; No-mirror: $M = -0.17$ units, $SD = 0.45$ units). Importantly, there was a significant interaction between Proprioceptive Estimate and Vision ($F(1,19) = 4.56, p = .046$), indicating that the effect of proprioceptive information differed whether the visual estimate was available or not.

To investigate the interaction effect, the effect of Proprioceptive Position was examined at each level of Vision condition and compared across Vision conditions. Two important findings were found. First, for both the Mirror and No-mirror conditions, there were significantly more lateral biases when the left hand was at 14” vs. 4” ($ps < .007$). These findings indicate that proprioceptive hand alone biased tactile localization towards the hand position, with more lateral bias in $P_{14}V_{\emptyset}$ vs. $P_{4}V_{\emptyset}$, when visual information was not presented. Importantly, the effect was larger in the Mirror ($D = 0.55$ units) versus the No-mirror ($D = 0.27$ units) condition. This finding indicates that in addition to different tactile localization biases caused by hand position alone (i.e. in No-mirror condition), visual-proprioceptive conflicts biased tactile localization further towards each proprioceptive estimate, leading to larger difference in the Mirror condition between the two proprioceptive hand positions. The finding thus provides further evidence for the anchoring hypothesis.
Figure 18. a. Medial-lateral localization bias in each condition in Experiment 3.1. Negative values denote lateral biases. Arrows with different lengths indicate that the difference between $P_{14}V_9$ and $P_4V_9$ was predicted to be larger than difference between $P_{14}V_6$ and $P_4V_6$. b. Proximal-distal localization bias in each condition, with negative values denoting distal biases. Conditions are illustrated on the right side of each bar.

**Proximal-distal localization bias**

For proximal-distal localization bias (Figure 18b), there was a main effect of Proprioceptive Position ($F(1,19) = 14.32$, $p = .001$). Placing the left hand at 14” ($M = -0.36$ units, $SD = 0.89$ units) induced more distal biases than when the left hand was at 4” ($M = -0.16$ units, $SD = 0.90$ units). The effect of Vision did not reach significance ($F(1,19)$)
= 3.77, p = 0.067; Mirror: \( M = -0.33 \) units, \( SD = 0.93 \) units; No-mirror: \( M = -0.19 \) units, \( SD = 0.88 \) units). There were no significant interaction effects (\( F(1,19) = 2.17, p =0.157 \)).

**Discussion**

This experiment was designed to test the anchoring hypothesis with a new design that controls for the effect of proprioceptive position on tactile localization. First, without any viewed hand, simply placing the hidden hand at a lateral position (P1 vs. V0) led to more lateral tactile localization bias than when the hand was at a medial position (P4 vs. V0). This finding indicates that proprioceptive hand position alone biases tactile localization to the direction of hand position. Importantly, the difference in medial-lateral bias between proprioceptive positions was larger in the Mirror vs. No-mirror conditions, indicating that beyond the effects of hand position alone, visual-proprioceptive conflicts introduced additional bias to tactile localization towards each proprioceptive estimate. This finding provides additional and confirmatory evidence for the anchoring hypothesis that tactile localization is biased towards proprioceptive estimate relative to visual estimate. Furthermore, it provides further evidence that tactile localization is not a strictly serial process, but involves feedback from external to somatotopic representations.

The finding that tactile localization was biased towards the hand position in the No-mirror condition also provides evidence that external information influences tactile localization, supporting a non-serial model. Because participants closed their eyes in the No-mirror condition, the effects of hand position are unlikely explained by relative position between hand and gaze direction, as previously reported (Medina et al., 2018; Harrar & Harris, 2009). Alternatively, tactile localization on the skin surface might be biased towards hand position encoded in a trunk-centered or head-centered frame of reference, with more
lateral bias as the hand was placed lateral to the body or the head. Such finding falls along the line with past studies that tactile localization on the skin surface can be influenced by body position coded in multiple reference frames (Medina et al., 2018; Harrar & Harris, 2009; Ho & Spence, 2007). Whereas past literature interpreted these findings as tactile stimuli being encoded in multiple reference frames, the mechanism of how tactile location information in external reference frames feeds back to the skin surface remains to be investigated.

In Experiment 3.1, no statistical differences were found between the two congruent conditions -- P_{4V4} and P_{10V10}, although there was a trend towards more lateral localization bias when the hand was placed laterally (i.e. in P_{10V10} vs. P_{4V4}). This finding indicates that when visual and proprioceptive estimates were congruent, the absolute hand position did not substantially bias tactile localization. In contrast, Experiment 3.2 demonstrated that proprioceptive position alone, without visual information, biased tactile localization towards the direction of hand position. One possibility is that hand position does bias tactile localization, but since in Experiment 3.1 the hand position only differed by 6” (as opposed to 10” in Experiment 3.2), differences in medial-lateral localization bias caused by hand position alone were not as large to be observed with the given sample size.

To summarize so far, Experiment 3.1 showed that under visual-proprioceptive conflict, tactile localization on the hand was biased towards the proprioceptive estimate. Experiment 3.2 further confirmed this finding by controlling for the effects of hand position alone in the analyses. Taken together, these findings are consistent with the anchoring hypothesis that when visual and proprioceptive estimates regarding hand position are spatially incongruent, tactile localization on the skin surface is biased towards
proprioeptive estimate. The details of the anchoring hypothesis will be further discussed in the General Discussion section. Before fully accepting the anchoring hypothesis, there is one additional alternative account, addressed in Experiment 3.3.

3.3. Experiment 3.3. Controlling for the effects of gaze-proprioceptive spatial mismatch on tactile localization

Experiments 3.1 and 3.2 demonstrated that under visual-proprioceptive conflict, tactile localization was biased towards proprioceptive estimate, consistent with the anchoring hypothesis. While manipulating visual and proprioceptive hand positions, relative position between proprioceptive hand position and gaze direction was also manipulated. Previous literature reported effects of gaze-proprioceptive spatial mismatch on tactile localization on the skin surface (Medina et al., 2018). It is thus possible that tactile localization bias found in the previous experiments was caused by hand position encoded relative to gaze direction. To test this alternative account, in this experiment, participants viewed an object in the mirror instead of a mirror hand. The position of the object and hidden hand were manipulated across conditions, shown in Figure 19. The left hand was positioned at either 10” or 4” from the mirror, and the mirror reflection of the object appeared at either 10” or 4” from the mirror. Conditions in this experiment will be denoted as P_xO_y, with O standing for “object”.

84
Figure 19. Conditions in Experiment 3.3. The left hand was positioned at either 10” or 4” behind the mirror. An object (illustrated by the red rectangle) was positioned at either 4” or 10” in front the mirror, with its mirror reflection at either congruent or incongruent position with the hidden hand.

In this design, the relative position between proprioceptive hand position and gaze direction was manipulated in the same way as in Experiment 3.1. Therefore, the only difference between Experiment 3.1 and 3.3 is visual content, with gaze direction controlled. In Experiment 3.1, in addition to gazing at instructed locations, participants were viewing a mirror hand, providing a visual estimate of hand position. If visual-proprioceptive conflict biases tactile localization towards proprioceptive estimate, as predicted from the anchoring hypothesis, viewing a mirror hand would lead to more localization bias towards proprioceptive estimate than viewing an object. A direct comparison between Experiment 3.1 and 3.3 was performed to examine the effect of visual content on tactile localization bias, focusing on conditions with visual-proprioceptive and gaze-proprioceptive mismatch. Details of the analysis are presented in the Data analyses section below.
**Methods**

**Participants**

As with Experiment 3.1, the aimed sample size was 19. Twenty-one participants were scheduled (age: 23.6±4.4, 9 males), assuming attrition. One participant was excluded because only six out of eight blocks were completed. Overall 20 participants were included in the analyses.

**Design**

As presented before (Figure 19), a 2 (Proprioceptive Position) by 2 (Object Position) design was used. The object was a cylinder placed aligned with the tip of the middle finger along the transverse axis. The object hence served as a “fixation point”.

**Procedure**

The procedure is the same as in Experiment 3.1, except for the following. At the beginning of each block, the experimenter placed the cylinder in front of the mirror, and the participant’s left hand behind the mirror, at the instructed locations. Then the participant tapped the left index finger for 20 seconds while looking at the mirror reflection of the cylinder. After tapping, the experimenter started the trials in which the nine tactile stimulus locations on the left hand were stimulated in random orders, while the participants kept focusing on the cylinder object.

**Data analyses**

As discussed earlier, the main purpose of this experiment was examining whether visual-proprioceptive conflict biases tactile localization while controlling for gaze direction. For this reason, the critical comparison was the visual-proprioceptive/gaze-proprioceptive mismatch conditions across Experiment 3.1 and Experiment 3.3, with
medial-lateral localization bias as dependent variable. As shown in Figure 20, an ANOVA was performed with Proprioceptive Position (4” and 10”) as a within-subjects factor, and Visual Content (hand or object) as a between-subjects factor. Note that here proprioceptive position also determines gaze direction, as when proprioceptive position was at 4”, gaze was at 10”, and vice versa. If visual-proprioceptive conflict caused additional tactile localization bias beyond the effects of gaze-proprioceptive mismatch, an interaction would be expected. Specifically, when participants were viewing at 10” (with P at 4”), both visual content conditions (P4O10 and P4V10) involved the same amount of gaze-proprioceptive mismatch. With gaze-proprioceptive mismatch controlled, if viewing a mirror hand caused additional tactile localization bias, there would be more medial bias in the viewing hand condition (Figure 20, the top red arrow). Similarly, when participants were viewing at 4”, there would be more lateral bias in P10V4 vs. P10O4 condition (Figure 20, the lower red arrow). With the difference between visual contents occurring in the opposite directions in these two situations, an interaction effect would be expected.
Figure 20. Conditions in Experiment 3.1 and Experiment 3.3 that were analyzed. Numbers on the top denote distance from the mirror. P, O, and V stand for proprioceptive hand position, object position, and visual hand position, respectively. Red labels highlight conditions from Experiment 3.1. Red arrows indicate predicted directional tactile localization bias induced specifically by visual-proprioceptive conflict relative to gaze-proprioceptive conflict.

In conditions in Figure 20, viewing a hand introduced two differences from viewing an object. First, participants were viewing a hand stimulus vs. a non-hand stimulus. Second, viewing a hand led to a visually-defined spatial representation of hand position, causing visual-proprioceptive conflict in hand position estimate. Whereas the expected direction-specific tactile location bias described in the previous paragraph is unlikely caused by viewing a hand stimulus per se, we performed an additional analysis to confirm this. Previous studies found no differences in tactile localization whether the stimulated body part was visible or invisible (Harrar & Harris, 2009), and whether participants were viewing the body or object (Medina et al., 2018), when gaze was directed towards the stimulated body part. These past findings indicate that without spatial mismatch between hand position and gaze direction, visual content does not influence tactile localization. To test this, an additional ANOVA was performed across Experiment 3.1 and 3.3, on conditions with no mismatch between proprioceptive position and visual hand position.
(P_{4}V_{4} and P_{10}V_{10} in Experiment 3.1) or object position (P_{4}O_{4} and P_{10}O_{10} in Experiment 3.3). Based on previous findings, at each proprioceptive position we predicted that medial-lateral localization bias would not differ whether participants were viewing a hand or object. Such findings would provide a control result that simply presenting a visual hand stimulus is not sufficient for biasing tactile localization compared with viewing an object. Although the expected directional tactile localization bias described in the previous paragraph is unlikely attributed to general effects of viewing a hand stimulus, these control findings would directly rule out this possibility, providing further evidence for the anchoring hypothesis.

The same analyses were performed on proximal-distal bias. See the Appendix B for the results.

**Results**

First, an ANOVA was performed across Experiment 3.1 and Experiment 3.3, focusing on the incongruent conditions (Figure 21a). There was a main effect of Proprioceptive Position ($F(1,38) = 18.86, p < .001$). As previously found, there was more lateral bias when proprioceptive position was lateral (10": $M = -0.54$ units, $SD = 0.60$ units) vs. medial (4": $M = -0.15$ units, $SD = 0.63$ units). The main effect of Visual Content was not significant ($F(1,38) = 0.78, p = .384$; View hand: $M = -0.27$ units, $SD = 0.59$ units; View object: $M = -0.42$ units, $SD = 0.47$ units). Importantly, there was a significant interaction ($F(1,38) = 9.41, p = .004$), consistent with the anchoring hypothesis. As shown in Figure 21, when the hand was at 4”, medial to the gaze direction (10”), viewing a hand caused more medial tactile localization bias ($t(38) = -2.21, p = .034$). When the hand was lateral to the viewing position, there was a trend that viewing a hand caused more lateral
localization bias, although it was not significant ($t(38) = 0.66, p = .515$). These findings indicate that tactile localization bias under visual-proprioceptive conflict cannot be fully accounted by gaze-proprioceptive mismatch. With gaze direction controlled, tactile localization was biased towards proprioceptive estimate of hand position when participants were viewing a hand, providing further evidence for the anchoring hypothesis.

Figure 21. a. Medial-lateral localization bias in the incongruent conditions in Experiment 3.1 and 3.3. Arrows indicate the direction of tactile localization bias when participants viewed a hand (Experiment 3.1) vs. object (Experiment 3.3). b. Medial-lateral localization bias in the congruent conditions in Experiment 3.1 and 3.3. Error bars are 95% CI calculated from the raw data.

An additional ANOVA was performed across Experiment 3.1 and Experiment 3.3, focusing on the congruent conditions (Figure 21b). Consistent with previous findings, there
was a main effect of Proprioceptive Position ($F(1,39) = 16.33$, $p < .001$), with more lateral bias when the hand was at a lateral position (10”, $M = -0.47$ units, $SD = 0.56$ units) vs. medial (4”, $M = -0.24$ units, $SD = 0.53$ units). The main effect of Visual Content was not significant ($F(1,39) = 0.34$, $p = .560$; View hand: $M = -0.31$ units, $SD = 0.57$ units; View object: $M = -0.40$ units, $SD = 0.44$ units), nor the interaction ($F(1,39) = 1.81$, $p = .186$). Consistent with past literature, when gaze direction and hand position were spatially congruent, tactile localization bias did not differ between viewing the hand and object at either hand position (paired $t$-tests, $ps > .3$), indicating that simply viewing a hand stimulus was not sufficient for biasing tactile localization. These findings further confirmed that when there was spatial mismatch between gaze direction and hand position, the additional tactile localization bias associated with viewing a hand was specifically caused by visual-proproprioceptive conflict in hand position estimate, as opposed to general effects of viewing a hand stimulus per se.

**Discussion**

The aim of this experiment was to further test the anchoring hypothesis while controlling for the potential effects of gaze-proproprioceptive mismatch on tactile localization. With gaze direction and proprioceptive hand position controlled, viewing a mirror hand induced additional tactile localization bias towards proprioceptive estimate compared with simply fixating at an object. These findings indicate that beyond any effects of gaze-proproprioceptive mismatch, visual-proproprioceptive conflict additionally biases tactile localization towards proprioceptive estimate, providing further evidence for the anchoring hypothesis.
While the anchoring hypothesis was supported by an interaction between proprioceptive hand position and visual content, the effect seemed to be primarily driven in one direction. When participants gazed at 10” with the hand at 4” (i.e. medial to gaze), viewing a hand induced more medial localization than fixating at an object, supporting the anchoring hypothesis. When participants gazed at 4” with the hand at 10” (i.e. lateral to gaze), the anchoring hypothesis predicts more lateral localization bias for viewing a hand vs. an object. Despite such a trend, no statistical differences were found between viewing a hand vs. an object. These findings might suggest that visual-proprioceptive conflict biases tactile localization only when proprioceptive estimate is medial to visual estimate. However, we note that this finding is worth further examination with a larger sample size or within-subjects design. Given the noise in tactile localization judgments, and given that the comparisons were between independent groups, it is possible that our sample size was not large enough to observe the effects in both directions.

Whereas we found more localization bias towards proprioceptive estimate when participants were viewing a mirror hand vs. an object in the mismatch conditions, no effects of visual content were found in the congruent conditions (Figure 21b). This is consistent with previous studies showing no differences in tactile localization whether the stimulated body part was visible or invisible (Harrar & Harris, 2009), or whether participants were viewing the body or an object (Medina et al., 2018). Taken together, these findings highlight two points. First, simply presenting a visual hand may not be sufficient for biasing tactile localization relative to viewing an object. Second, along with the directional tactile localization biases towards proprioceptive estimate, these findings further support that the additional tactile localization bias induced by viewing a hand relative to viewing an object
are specifically driven by spatial mismatch between visual and proprioceptive estimates, as opposed to general effects of presenting a visual hand stimulus. Taken together, these findings provide further evidence for the anchoring hypothesis.

3.4. General discussion

The aim of this study was to further examine if tactile localization is not a strictly serial process in neurologically intact individuals. Using the mirror box illusion, we examined tactile localization bias when the felt hand position was captured by visual information, away from proprioceptive estimate. Across multiple experiments, we demonstrated that when there was spatial mismatch between visual and proprioceptive estimate regarding hand position, tactile localization on the skin surface was biased towards the direction of proprioceptive estimate relative to the visual estimate. These effects could not be fully accounted for by hand position alone (Experiment 3.2), or gaze-proprioceptive mismatch (Experiment 3.3), as the bias preserved when these factors were controlled. Taken together, these findings support the anchoring hypothesis outlined at the beginning of this chapter, that tactile location estimate was anchored to the visual estimate of hand position and biased by proprioceptive information. We discuss possible mechanisms underlying the anchoring hypothesis below, focusing on how touch is anchored to visual position, and how it is biased by proprioceptive estimate.

One possible mechanism of the anchoring effects is visual capture of hand position as a result of multisensory integration (Figure 22). To form a coherent percept, information from multiple sensory modalities are integrated by weighting each sensory information in proportion to their relative precision (Ernst & Banks, 2002; Ernst & Bulthoff, 2004; van...
Beers et al., 1999). In the mirror box illusion, spatial mismatch is created between a visual estimate and proprioceptive estimate regarding the hidden hand position. When participants make synchronous hand movements, the movements seen on the mirror hand match the movements made on the actual hand, providing congruent visual-motor information and facilitating integration between visual and proprioceptive estimates. Because visual information is typically more precise than proprioceptive information, the visual estimate is more strongly weighted, biasing felt hand position towards the visual estimate. When the distance between proprioceptive and visual estimates is not too large, the hidden hand is felt at where the visual estimate is located, as measured by multiple approaches (Figure 22, ①; Holmes & Spence, 2005; Medina et al., 2015). When the felt hand position coincides with viewed hand position, participants perceive tactile sensation on the viewed hand, and localize touch in external space to the visual hand position (Figure 22, Touch(V)).
Figure 22. One possible mechanism of the anchoring hypothesis. First, felt hand position (Fvp) is shifted onto the visual estimate (V) as a result of multisensory integration (1). Consequently, touch on the actual hand (X on the P hand) is felt as on the mirror hand (X on the V hand), and externally localized at the visual position/felt hand position (2, Touch(V)/Touch(Fvp)). Meanwhile, there is still a proprioceptive estimate of hand position (P), providing information that touch occurred further away from the visual estimate in external space (2, Touch(P)). Given two conflicting tactile location estimates, one anchored on visually-defined location and one at proprioceptively-defined location, tactile location estimate was biased away from the anchoring point, towards proprioceptive estimate (3). Finally, the external bias fed back to the skin surface, biasing tactile localization on the skin surface towards proprioceptive estimate (4).

On the anchoring hypothesis, touch is not just localized to the visual estimate, but anchored to the viewed position. By anchoring, visually-defined tactile location estimate dominates over other possible tactile location estimates, e.g. one defined by proprioceptive estimate, discussed below. One possible reason for touch being predominantly localized to the visual location is because visual information is more precise than other modalities, which then leads to more precise estimates of tactile location in external space. Without visual information, localizing touch in external space is fairly noisy (Medina & Duckett, 2017), because tactile information on the skin surface is combined with typically noisy proprioceptive information (van Beers et al., 1999). Nevertheless, accurately and precisely localizing touch in external space is essential for directing movements towards tactile stimuli, which is typically achieved by using visual information in daily life. For this reason,
when the felt hand position is generally congruent with visual information, the brain anchors touch to the visually-defined location to minimize variance in tactile localization in external space.

While I hypothesized that tactile stimuli are anchored to the visual hand position, there is an alternative account. It is possible that the tactile location estimate is anchored to the conscious felt hand position, instead of on the visual hand per se (Figure 22, Touch(Fvp)). In experiments with full visual capture, these two estimates are not separable. First, the conscious felt hand is perceived as the participants’ own hand to which any tactile sensations are referred. Second, with the clear knowledge that the hidden hand would be stimulated, the brain has prior estimates that the touch would occur at where the hand was located in external space. The benefit of anchoring touch to the expected location might be to constrain tactile location estimates within a reasonable spatial range occupied by the hand so as to prevent substantial localization biases. On this possibility, touch is primarily anchored to the felt hand position, but not necessarily the visually-defined location.

Whether touch is anchored to the viewed hand or the felt hand position, the actual proprioceptive hand position is away from the anchoring point. How does proprioceptive estimate bias tactile localization? For this effect to occur, several representations need to be maintained/generated. First, the brain needs to still maintain a unimodal proprioceptive estimate of hand position, even though the conscious felt hand position is biased by visual estimate. Second, and importantly, this proprioceptive estimate must be referenced when tactile stimuli are localized to external space. As a result, in addition to the visually-defined location, tactile stimuli on the hidden hand are also localized in external space at proprioceptively-defined location. Given two conflicting tactile location estimates in
external space, one anchored to the visually-defined location, or felt hand location, and one at the proprioceptive-defined location, tactile location estimate is biased away from the anchoring point and towards proprioceptive estimate (Figure 22, ③). As discussed earlier, touch is primarily anchored to the visually-defined location because visual information is more precise than proprioceptive information. For this reason, proprioceptively-defined tactile location estimate is much less weighted than the visually-defined tactile location estimate, leading to only small amount of bias in external tactile location estimate towards proprioceptive hand position. On the skin surface, first, there is a tactile location representation solely based on somatotopic information (Figure 22, X on the V hand). Importantly, biases in external space project back to the skin surface, informing the brain that the touch occurs on the part of skin surface that is more towards the proprioceptive estimate than X, pulling tactile localization judgments away from X, towards the proprioceptive estimate (Figure 22, ④). Because tactile location estimates in external space are fairly noisy (Medina & Duckett, 2017), feedback information from external space should be less weighted than the original somatotopic tactile location estimate (Figure 22, X), leading to only a small amount of bias. This is demonstrated by overall robust yet small tactile localization bias induced by visual-proprioceptive conflict across the experiments in this Chapter. In addition, although tactile location estimate is biased away from the visual position, there is a constraint that touch must occur on the body surface, i.e. within the border of the seen hand surface. Therefore, when integrating feedback external information with somatotopic representation, the brain ensures that tactile localization bias on the skin surface will not beyond the boundary of the seen hand.
A potential alternative, but not exclusive, mechanism of anchoring regards shifts in a peri-hand space representation from being centered on the actual hand to the visual hand. In the following paragraphs, I will first explain the peri-hand space representation using findings from monkey and human studies, then discuss how it could be a mechanism of the anchoring hypothesis. With peri-hand space specific to the hands, the concept was broadly referred to as peripersonal and came from single-cell recording studies on monkeys. From these studies, bimodal neurons were identified in ventral premotor cortex that responded to tactile stimuli and visual stimuli near the body (e.g. hand, face, etc.; Fogassi, et al., 1996; Rizzolatti et al., 1998). Importantly, their tactile and visual receptive fields are spatially aligned, such that the visual receptive fields are in space that immediately extends outward of the tactile receptive fields. Accordingly, the visual receptive fields were always centered on the body, regardless of gaze direction or body position in space (Graziano, Yap, & Gross, 1994). These findings have led to a proposal that these neurons represent space centered on and close to the body, i.e. peripersonal space, in which visual and tactile information are integrated.

One important feature of the bimodal neurons is that their visual receptive fields are predominantly anchored to visually-defined body parts as opposed to proprioceptively-defined (Graziano, 1999). First, compared with when the hand and arm were visible, the firing rate of bimodal neurons in response to near-hand visual stimuli decreased when the hand and arm were occluded, indicating the importance of visual information in defining peri-hand space. Second, when the monkey viewed a fake arm with its own arm occluded, bimodal neurons responded to visual stimuli presented close to the fake arm. Importantly, visual receptive fields were always centered on the fake arm when the fake arm was moved,
even though the fake arm was displaced from the actual arm. These findings provide evidence for visual dominance over proprioception in constructing peripersonal space representation, a point that will be important in explaining tactile localization bias in the current study.

In humans, studies of visuotactile extinction have provided evidence for visuotactile peri-hand space representations (di Pellegrino, Ladavas, & Farne, 1997). Brain-damaged individuals with visuotactile extinction were able to detect unilateral tactile stimuli, but failed to detect a contralesional tactile stimulus when a visual stimulus was presented near the ipsilesional hand simultaneously. The extent of visuotactile extinction was comparable to the unisensory tactile extinction, where an ipsilesional tactile stimulus extinguished a contralesional tactile stimulus (Ladavas, di Pellegrino, Farne, & Zeloni, 1998; Farne, Pavani, Meneghello, & Ladavas, 2000), indicating shared functions of visual and tactile stimuli in this context. Several characteristics of visuotactile extinction mirror the bimodal neurons. First, visuotactile extinction occurred only when the visual stimulus was presented near the contralesional hand, but not far, similar to the near-hand visual receptive fields of bimodal neurons. Second, visuotactile extinction operates in a body-centered reference frame, as opposed to external space. For example, visual stimuli on the ipsilesional hand still extinguished contralesional tactile stimuli when the hands were crossed (di Pellegrino et al., 1997). Given these characteristics, one account for visuotactile extinction regards the functional role of bimodal neurons, such that a visual stimulus near the ipsilesional hand activated these neurons, which in turn activated somatosensory representation on the ipsilesional hand. The somatosensory representation then acted as in unisensory tactile extinction, winning more attentional resource over the contralesional
tactile stimulus, extinguishing the detection of the contralesional stimulus. These studies provide evidence for representation of peri-hand space where visual and tactile information are integrated.

As discussed earlier, visual information regarding the body is critical in defining visual receptive fields of bimodal neurons. Similarly, visual information of the ipsilesional hand is important for visuotactile extinction to occur. For example, tactile stimuli were not extinguished by ipsilesional near-hand visual stimuli when the ipsilesional hand was occluded (di Pellegrino et al., 1997). Interestingly, one study demonstrated visuotactile extinction when visual stimuli were presented to a seen rubber hand, with the patients’ actual hands occluded, indicating that visuotactile peripersonal space was biased to be centered on the seen rubber hand (Farne et al., 2000). In their rubber hand condition, participants’ ipsilesional hand was placed behind the back, while they saw a rubber hand placed on the table along with the contralesional hand. When the contralesional hand was touched along with a visual stimulus near the rubber hand, participants failed to report the tactile stimulus, demonstrating visuotactile extinction. Three important findings are worth highlighting. First, the tactile detection rate was comparably low whether participants were viewing their own ipsilesional hand or a rubber hand, indicating visual dominance over proprioception. Second, the effects occurred without having to induce the rubber hand illusion by synchronous visuotactile stimulation, indicating that visual information of a hand was sufficient for biasing peri-hand space representation. Finally, the rubber hand induced larger visuotactile extinction when it was in a plausible orientation (i.e. fingers pointing forward with the stump of the rubber hand covered) vs. not plausible (i.e. rotated 90° and with the stump visible). These findings indicate that visuotactile peripersonal space
was predominantly constructed around the visual hand, provide that it is in an anatomically plausible posture.

To summarize so far, both monkey and human studies provide evidence that there is a spatial representation centered on and close to the hand, where tactile and visual information are integrated. In addition, the spatial representation is predominantly centered on the visually-specified body part, but not proprioceptively-defined, provide that the viewed body is in a plausible posture. How can this peripersonal spatial representation explain the tactile localization bias observed in the current study? In the mirror box illusion, participants view a mirror hand that is in a congruent orientation (i.e. fingers pointing forward) with their hidden left hand. Given the vivid visual hand stimulus and congruent orientation, visual information of the hand dominates proprioceptive information, causing the representation of visuotactile peripersonal space shift and center on the viewed mirror hand. This visually-defined peri-hand space representation informs the brain that touch occurs around the viewed hand, causing tactile information to be anchored to the mirror hand (Figure 23, ①).
Figure 23. An alternative mechanism for the anchoring hypothesis. First, provided with a vivid visual hand (V) in a congruent orientation with the actual hand, representation of the peri-hand space shifts and centers on the viewed hand (1). As a result, touch is referred to the viewed hand (X on the V hand) and externally localized at the visual estimate of hand position (2, Touch(V)). Although touch is referred to the visual hand, given the spatial mismatch between visual and proprioceptive hand position estimates, the shift might not be complete and there might still be residual tactile information on the actual hand. This leads to an additional tactile location estimate defined by proprioceptive hand (2, Touch(P)). This proprioceptively-defined tactile representation biases tactile localization estimate away from the anchoring point (3), which then feed back to the skin surface, leading to tactile localization bias on the skin surface towards the proprioceptive estimate (4).

Although touch is referred to the visual hand, given the spatial mismatch between visual and proprioceptive hand position estimates, the shift might not be complete and there might still be residual tactile information on the actual hand. When the residual tactile information is remapped to external space by referencing the proprioceptive estimate, this proprioceptively-defined tactile location estimate (Figure 23, Touch(P)) in external space would not match the visually-defined tactile location (Figure 23, Touch(V)), biasing tactile location estimate away from the anchored point and towards proprioceptive estimate (Figure 23, 3). Finally, same as in the mechanism outlined above, biases in external space then feed back to the skin surface, leading to biased tactile localization on the skin surface towards proprioceptive hand position (Figure 22 and Figure 23, 4).
To summarize, two potential mechanisms of the anchoring hypothesis were discussed, primarily differing on how touch is anchored to the visual hand position. In the first mechanism, anchoring requires the hand to be felt at the visual hand estimate. Touch is then anchored to the visual location by referencing the felt hand position. A potential alternative hypothesis was also discussed under this first mechanism, that touch is anchored to the felt hand position, but not the visual hand per se. In the second mechanism, anchoring was primarily driven by visual information of the hand, i.e. presenting a visual hand stimulus was enough to bias the peri-hand space representation to be centered on the viewed hand. This mechanism does not necessarily rely on visual capture of felt hand position. These mechanisms are not mutually exclusive, and may function together to cause tactile localization bias.

Despite differing in how anchoring occurred, both mechanisms involve similar processes for how tactile localization on the skin surface is biased. First, both mechanisms propose that two tactile location estimates in external space are formed, one anchored at the visually-defined location, and one at the proprioceptively-defined location. In resolving the conflicts, in external space, tactile location estimate was biased away from the anchoring point towards the proprioceptive estimate. Importantly, such external biases feed back to the skin surface, leading to tactile localization on the skin surface shift towards the proprioceptive estimate. Other than providing strong evidence that tactile localization is not a strictly serial process, findings from the current study provide a potential mechanism that external information influences tactile localization on the skin surface via feedback processes.
Chapter 4

EFFECTS OF FINGER POSTURE ON TACTILE LOCALIZATION

Experiments in the previous two chapters provide evidence that information regarding hand position affects tactile localization on the hand surface. In these experiments, external position of the entire hand was manipulated without varying the relative distance between stimulus locations. For example, in Chapter 3, the relative position between stimuli on the hand dorsum was constant regardless of where the left hand was positioned. In daily life, tactile stimuli are not only localized on a continuous skin surface, but also integrated across body parts. The problem of localizing touch among body parts is even more complex because the relative position between body parts constantly changes. In studying the functional organization of tactile processes, it is necessary to investigate tactile localization among body parts. In terms of testing the serial model, one approach is examining tactile localization across body parts while manipulating the relative position (e.g. distance) between body parts. If localizing touch on the body solely operates in a somatotopic space, relative position between body parts should not affect tactile localization performance. Alternatively, if proprioceptive information is considered during tactile, there would be mislocalization across body parts as a function of body part positions in external space.

There are multiple approaches of manipulating the relative position of different body parts. For example, studies have manipulated body position relative to the canonical
position by having participants cross the hands or fingers (e.g. Benedetti, 1985; Badde, Roder, & Heed, 2019; Haggard et al., 2006). In addition, studies have manipulated relative distance between body parts (Coslett, 1998; Overvliet et al., 2011). This chapter focuses on a paradigm of this kind, in which participants judge which finger is touched with the distance between fingers manipulated. This paradigm is chosen for three reasons. First, it is easy to manipulate distance between fingers, and to quantify response errors both in terms of somatotopic distance (i.e. how many fingers away) and external distance (e.g. X cm away). Second, there have been inconsistent findings regarding if tactile localization among fingers is affected by finger distance. Finally, it has been a question of whether tactile stimuli on fingers are represented differently from other body parts in terms of spatial frame of reference. These points are discussed below.

Regarding whether tactile localization among fingers is affected by finger posture, there have been inconsistent findings. First, it is unclear whether finger distance affects overall tactile localization accuracy. Whereas Overvliet et al. (2011) found overall increased localization accuracy when the fingers were separate versus close together, no influence of finger distance was found in healthy participants in another study (Coslett, 1998). Apart from accuracy, it is also unclear how finger distance might affect the spatial distribution of tactile localization errors. In Overvliet et al.’s study (2011), placing the fingers close equally increased mislocalization to all fingers, whereas in one brain-damaged individual, placing the fingers closer specifically increased mislocalization to the spatially adjacent finger (Coslett, 1998). The first purpose of Experiment 4 is to address these questions (Conditions 1 and 2 below).
In addition to within-hand, the question of whether finger position affects tactile localization has also been tested across hands. One study directly compared if tactile localization on the fingers and hands operate in different frames of reference (Haggard, et al., 2006). In the experiment, participants placed their two hands either vertically aligned, or palm facing each other with the fingers interwoven. In each trial a tactile stimulus was presented to one of the eight fingers (thumbs excluded), and participants were asked to report either which hand, or which finger regardless of hand, was stimulated. They found that interweaving fingers decreased hand identification accuracy but did not affect finger identification, concluding that localizing touch to a finger operates solely in somatotopic space. However, conflicting findings were shown in another study using a modified paradigm, suggesting that finger identification was also affected by hand posture. The experiments in Chapter 2 and Chapter 3 have shown that tactile localization on the hand is affected by hand position. By testing tactile localization among fingers in Experiment 4, additional evidence can be provided regarding whether the fingers and hand are represented differently in terms of spatial reference frame. If, as shown by Haggard et al. (2006), fingers are represented in somatotopic space, tactile localization should not be affected by finger distance. Alternatively, if finger position is considered during tactile localization, there would be more mislocalization when the fingers are spatially close to each other.

In addition to testing a serial model, Experiment 4 uses a novel design to investigate anatomical constraints in the effects of finger distance on tactile localization. In previous studies, the effect of relative finger distance on tactile localization were found between anatomically adjacent fingers (e.g. the middle and ring finger, Coslett, 1998). However, for anatomically more distant body parts (e.g. hand and foot), spatial proximity did not affect
tactile perception (Badde et al., 2019). These findings indicate that the effect of spatial proximity might depend on the anatomical distance between body parts, such that spatial proximity only affects tactile localization among anatomically adjacent, but not anatomically distant, body parts. To address this question, Experiment 4 investigates the effect of spatial proximity on tactile localization between the index and ring fingers, which are anatomically non-adjacent, by placing the index and ring finger on a different plane (Condition 3 and 4 below).

4.1. Experiment 4

Design

Participants were presented with a vibrotactile stimulus (see Procedure below) on one of the four fingers (thumb excluded) on the left hand, and reported on which finger they felt the stimulus. The thumb was excluded because based on previous studies (Manser-Smith et al., 2018) and past testing experience, mislocalization between the thumb and other fingers is typically very low (<5%), hence does not contribute to the analyses of mislocalization. Four conditions with different finger postures were included:

Condition 1 – All Fingers Far: Fingers were separated 5 cm apart from each other (Figure 24a).

Condition 2 – All Fingers Close: Fingers were placed close to each other, 5 mm apart (Figure 24b).

Condition 3 – Index and Ring Far: Placing the ring finger and index finger 5 cm apart (Figure 24c). The position of the thumb and pinky remained the same as in Condition 2. In this condition, anatomically nonadjacent fingers (i.e. the ring finger and index finger) were externally far.
Condition 4 – Index and Ring Close: Placing the ring finger and index finger 5 mm apart (Figure 24d). In this condition, anatomically nonadjacent fingers (i.e. the ring finger and index finger) were externally close.

Figure 24. Illustration of the four conditions in Experiment 4. a. Condition 1: The hand was placed on the table with the fingers separated by 5 cm. b. Condition 2: The hand was placed on the table with the fingers separated by 5 mm. c. Condition 3: The hand was lifted, with only the index and ring finger placed to a lower plane, separated by 5 cm. d. Condition 4: The hand was lifted, with only the index and ring finger placed to a lower plane, separated by 5 mm.

In previous studies, the number of trials for each stimulus location and each condition ranged from five (Overvliet et al, 2011) to 50 (Manser-Smith et al., 2018). Within a one-hour session, four blocks with 128 trials each were included. Each finger posture condition was tested in one block, within which each finger was stimulated in 32 trials. The order of the blocks and trials were randomized for each individual. Participants were allowed to move and relax the hand in between the blocks.
Participants

Participants were college students recruited from the General Psychology course. Two factors were considered in determining the sample size. First, the number of participants needed for observing any spatial patterns in localization errors. One previous study (Manser-Smith et al., 2018) found directional localization biases such that stimuli on the index finger tended to be localized towards the pinky (d=1.82), and stimuli on the ring finger tended to be localized towards the thumb (d=1.63). With the smaller effect size among the two (1.63) and a sample size of 20, a power above 0.99 was acquired. Second, the number of participants needed for observing an effect of finger position on tactile localization. Overvliet et al. (2011) found more accurate tactile localization overall when the fingers were separate versus close (N=10). With an effect size of 1.53 and sample size of 10, a power of 0.99 was acquired. The current study assumed a smaller effect size than these studies for two reasons. First, this experiment investigates modulation of localization errors by finger posture, which might be a smaller effect than the spatial distribution of localization errors itself found in Manser-Smith et al.’s study (2018). In addition, in Overvliet et al.’s study the results were collapsed across all the fingers, whereas in the current experiment the effects of spatial position would be analyzed for each individual finger (see Data Analyses below), which would show smaller effects. For these reasons, a moderate to high effect size of 0.6 was assumed, for which 32 participants were needed to obtain a power of 0.9.

Forty-one participants were scheduled and tested (age: 19.3±1.3, 6 males), assuming attrition. One participant was excluded because the experiment was not completed. One participant was excluded because the number of trials in which no
responses were made was above three group standard deviations, which could reflect either not being attentive or adopting different strategies. Seven participants were excluded because for at least one finger, tactile localization accuracy was below chance level (25%) in the staircase procedure (see Procedure below) even for the strongest tactile stimuli. In total, 32 participants were included in the analyses.

Procedure

Participants placed their left hand on the table, palm facing down and aligned with body midline. Throughout the experiment the left hand was occluded under a box. Tactile stimuli were delivered from vibrotactile stimulators (Ortofon Inc.) strapped on the dorsum of the first segment of digit 2 (index finger) to digit 5 (pinky). Stimuli consisted of a “signal” sine wave at 120 Hz, imposed at a background sine wave at 100 Hz (noise vibration). From past testing experience, these intensities could effectively elicit tactile localization errors across the fingers.

Before the main experiment, a pre-test was performed to find the intensity of the tactile signal that yielded about 50% localization accuracy for each finger. If no stimulus intensity resulted in exact 50% accuracy, the intensity level with the closest above 50% accuracy was chosen. During the staircase procedure, the fingers were naturally stretched out, separating by about 2.5 cm. From previous studies in our lab, stimulus intensities yielded from such staircase procedures could elicit tactile localization errors that could be modulated by different experimental conditions.

Each trial began with the background sine wave on all fingers. Then 250 ms later one of the fingers received a signal vibration for 150 ms. Participants fixated at a cross at the center of the screen during tactile stimulation. Each tactile stimulation lasted for
1000ms. After the tactile stimulation, the screen displayed “please respond”, upon which participants verbally named the finger on which they believe they felt a signal. An experimenter then entered the response to the computer by pressing the key corresponding to the reported finger.

The main experiment then started with tactile stimuli selected from the pre-test. At the beginning of each block, the experimenter placed the fingers to the instructed positions with the participants’ eyes closed. The procedure of each trial was the same as in the pre-test.

**Data analyses and predictions**

With two fingers placed on a different plane, Conditions 3 and 4 involved atypical finger postures that might introduce systematic differences from Conditions 1 and 2. For this reason, Conditions 1 and 2 were analyzed separately from Conditions 3 and 4. Analyses were performed to investigate the effect of relative finger distance on two aspects of tactile localization: accuracy and distribution of mislocalization. For null results, additional Bayesian statistical tests were performed to evaluate the relative likelihood between the null hypothesis and alternative hypotheses.

**Condition 1 and 2, accuracy**

To investigate the effect of finger distance on localization accuracy in Conditions 1 and 2, a repeated-measures ANOVA was performed with Finger and Distance (All Fingers Far and All Fingers Close) as independent variables. Dependent variable was localization accuracy. If tactile localization is affected by finger position, there would be more mislocalization when the fingers are close vs. far, challenging the serial model (Overvliet et al., 2011). Alternatively, if localizing touch on the fingers only utilizes
somatotopic information, no effects of Distance would be expected. Finally, post-hoc analyses were performed in case of an interaction between Finger and Distance to test the effect of Distance for individual stimulated fingers.

**Conditions 1 and 2, mislocalization pattern**

An additional analysis was performed to compare the distribution of mislocalization between All Fingers Far and All Fingers Close. If mislocalization changes as a function of spatial distance, there would be a stronger tendency of mislocalizing on the adjacent fingers in the All Fingers Close condition vs. in the All Fingers Far condition, as the fingers were less distinguishable in external space when placed close together. To test this, a mean localization bias was calculated for each finger in each condition as the average signed distance in the number of fingers between the stimulated and responded finger across all the *incorrect* trials. Then a 4 (Finger) by 2 (Distance) repeated-measures ANOVA was performed on mean localization bias.

**Conditions 3 and 4**

To investigate the effects of spatial proximity on anatomically non-adjacent fingers, tactile localization accuracy and error distributions were compared between Conditions 3 and 4. Since Conditions 3 and 4 specifically manipulated spatial proximity between the index and ring finger, the main analysis focused on these two fingers. First, localization accuracy was analyzed with a 2 (Finger: index and ring) by 2 (Distance: Index-Ring Close and Index-Ring Far) repeated-measures ANOVA. If spatial distance also affected anatomically non-adjacent fingers, there would be higher localization accuracy in the far (Condition 4) versus close (Condition 3) condition. As with the previous analyses, Bayesian statistical tests were performed in cases of important null results.
Analyses of mislocalization focused on errors made between the index and ring finger. For each finger, the percentage error made on the other finger (i.e. mislocalization of the index-finger stimuli to the ring finger, and vice versa) was calculated. The percentage error was then analyzed with a repeated-measures ANOVA analysis with Finger (index and ring finger) and Distance (Index-Ring Close and Index-Ring Far) as independent variables. If spatial proximity also affects mislocalization on anatomically non-adjacent fingers, there would be a main effect of spatial distance, with more errors for Index-Ring Close vs. Index-Ring Far. Alternatively, if spatial proximity does not affect anatomically non-adjacent fingers, no effects of Distance would be observed. Bayesian analyses were performed in cases of important null results.

**Results**

First, to make sure that tactile intensities chosen from the staircase procedure did yield relatively matched baseline localization performance across fingers, localization accuracies during the staircase procedure at the chosen intensities were compared across fingers (Figure 25). A one-way repeated-measures ANOVA was performed across fingers, from which no significant differences were found ($F (3,93) = 2.15, p = .099$). Therefore, tactile intensities later used in the main experiment had comparable baseline localization performance across fingers.
Figure 25. Tactile localization accuracy for each finger during the staircase procedure, at intensities later used in the main experiment.

For the main localization task, overall participants failed to make responses in 1.7% trials. The no-response rate did not differ significantly across fingers ($F(3,72) = 2.15, p = .101$; index: 1.8%; middle: 1.6%; ring: 1.3%; pinky: 2.0%). Analyses on localization accuracy and spatial distribution of errors are presented below.

**Condition 1 and Condition 2 (all fingers far vs. all fingers close)**

First, a repeated-measures ANOVA was performed on localization accuracy with Finger (index to pinky) and Distance (All Fingers Far vs. All Fingers Close; Figure 26). The main effect of Distance was not significant ($F(1,31) = 0.77, p = .386$), nor was the interaction between Finger and Distance significant ($F(3,93) = 0.15, p = .929$). These findings indicate that finger posture did not influence tactile localization. There was a main effect of Finger ($F(3,93) = 8.83, p < .001$). Post-hoc tests found significantly higher localization accuracy on the middle ($M = 68.2\%, SD = 18.4\%$) and ring finger ($M = 69.2\%, SD = 14.3\%$) compared with the index ($M = 52.6\%, SD = 23.9\%$) and pinky ($M = 54.7\%, SD = 21.4\%;$ Bonferroni-corrected $p < .02$), with no difference between middle and ring
(Bonferroni-corrected $p > .99$) or between index and pinky fingers (Bonferroni-corrected $p > .99$). The null results regarding the effects of Distance was further confirmed by a Bayesian Repeated-measures ANOVA, from which the only alternative model that was more likely than a null model involved only the main effects of Finger (posterior probability of the model given data relative to the null model: BF10 > 9e5), but not the main effect of Distance or interaction (BF10 < 1). Therefore, no evidence was found for the effects of finger distance on tactile localization among fingers.

Figure 26. Response rate for each stimulated finger, collapsed across participants, for a. the All Fingers Close condition, b. the All Fingers Close condition and c., the difference between All Fingers Far and All Fingers Close condition. In a. and b., darker colors indicate higher response rate. Numbers in bold (i.e. along the diagonal) are correct responses for the stimulated finger, i.e. accuracy. In c., darker yellow denotes more positive values, i.e. more responses in the All Fingers Far vs. All Fingers Close condition. Darker blue denotes more negative values, i.e. more responses in the All Fingers Close vs. All Fingers Far.

Although no differences in overall localization accuracy were found between the two Distance conditions, it is still likely that the distribution of mislocalizations differ across postures. To test this, a mean localization bias was calculated for each finger in each
condition as the average signed distance between the stimulated finger and responded finger across all the incorrect trials. Positive values denote ulnar biases (i.e. towards pinky). Then a 4 (Finger) by 2 (Distance) repeated-measures ANOVA was performed on mean localization bias (Figure 27). There was no main effect of Distance ($F(1,27) = 2.06, p = .163$) nor interaction between Finger and Distance ($F(3,81) = 0.68, p = .233$), indicating that finger distance did not affect overall distribution of mislocalization. There was a main effect of Finger ($F(3,93) = 393.0, p < .001$). Post-hoc tests revealed significant differences between all pairs of fingers (Bonferroni-corrected $p < .001$). This main effect of finger is expected because the possible incorrect responses differ across fingers. For the index and middle finger, the majority of alternative responses are in ulnar direction (towards larger finger numbers), hence positive biases. For the ring and pinky finger, the majority of alternative responses are in radial direction (towards smaller finger numbers), hence negative biases. In addition, for the index and pinky finger, all alternative responses are distributed towards one side of the correct finger, whereas for the middle and ring finger, alternative responses could be made on either side. Therefore, the absolute mean bias was larger for the index and pinky vs. middle and ring finger.
Figure 27. Average localization errors for each finger in each condition, calculated as the number of fingers. Positive values denote biases towards the pinky, negative values denote biases towards the index finger.

**Condition 3 and Condition 4 (Index-Ring Far vs. Index-Ring Close)**

Since the distance between the index and ring finger was manipulated, dependent variables are “cross-finger errors”: i.e. mislocalizations of index stimuli to the ring finger, and vice versa. A 2 (Finger: index and ring) by 2 (Distance: Index-Ring Far and Index-Ring Close) repeated-measures ANOVA was performed (Figure 28). First, there was a main effect of finger \( (F(1,31) = 33.24, p < .001) \), such that participants made more cross-finger errors for stimuli delivered to index finger \( (M = 0.21, SD = 0.15) \) vs. to ring finger \( (M = 0.05, SD = 0.07) \). The main effect of Distance was not significant \( (F(1,31) = 3.17, p = .085) \); fingers close: \( M = 0.14, SD = 0.15 \); fingers far: \( M = 0.12, SD = 0.14 \). Importantly, there was a significant interaction effect \( (F(1,31) = 4.60, p = .040) \). Specifically, for stimuli delivered to index finger, participants made significantly more mislocalizations to the ring
finger when the fingers were close ($M = 0.23, SD = 0.15$) vs. far ($M = 0.18, SD = 0.15$; paired $t$-test: $t(31) = 2.09, p = .045$). However, cross-finger errors for stimuli delivered to the ring finger did not differ across Distance conditions ($t(31) = 0.53, p = .60$; close: $M = 0.046, SD = 0.073$; far: $M = 0.050, SD = 0.067$).

Figure 28. Response rate for each stimulated finger, collapsed across participants, for the a. Index-Ring Far condition, b. Index-Ring Close condition, and c., the Difference between the Index-Ring Far and Index-Ring Close conditions. In a. and b., darker colors indicate higher response rate. Numbers in bold (i.e. along the diagonal) are response rate on the stimulated finger, i.e. accuracy. In c., darker yellow denotes more positive values, i.e. more responses of each type in Index-Ring Far vs. Index-Ring Close. Darker blue denotes more negative values, i.e. less responses of each type in Index-Ring Far vs. Index-Ring Close. The red asterisk indicates that for stimuli on the index finger, more responses were made on the ring finger when the fingers were close vs. far, with $p < .05$.

An additional omnibus analysis was performed to investigate the effect of manipulating distance between index and ring finger on localization performance on all fingers. For this purpose, a 4 (Finger: all four fingers) by 2 (Distance: Index-Ring Far and Index-Ring Close) repeated-measures ANOVA was performed on localization accuracy. There was no main effect of Distance ($F(1,31) = 0.86, p = .360$) nor an interaction effect ($F(3,93) = 1.07, P =0.365$). The main effect of Finger was significant ($F(3,93) = 25.86, p$
such that localization accuracy was highest for the middle finger, then ring finger, and finally index and pinky (Bonferroni-corrected $ps < .02$ except for comparison between index and pinky (Bonferroni-corrected $p > .99$)).

**Exploratory analyses**

**The effects of plane on tactile localization**

Although not originally planned to be analyzed, it is possible that placing fingers on different planes affected tactile localization. To explore this, a repeated-measures ANOVA was performed on tactile localization accuracy with Plane (Same plane: collapsing across All Fingers Far and All Fingers Close; Different plane: collapsing across Index-Ring Far and Index-Ring Close) and Finger as dependent variables (Figure 29).

There was a main effect of plane ($F (1,31) = 7.67$, $p = .009$). Placing the index and ring finger on a different plane decreased overall localization accuracy compared with when all fingers were in the same plane (different plane: $M = 0.57$, $SD = 0.23$; same plane: $M = 0.61$, $SD = 0.21$). There was also a main effect of finger ($F (3,93) = 21.54$, $p < .001$). As with results from previous analyses, overall participants were more accurate on the middle and ring fingers than index and pinky (pair-wise post-hoc: $ps < .001$). Interestingly, there was also a significant interaction effect ($F (3,93) = 5.76$, $p = .001$). To understand the interaction effects, paired $t$-tests were performed between the same- and different-plane condition for each finger. It turned out that for the index, ring, and pinky finger, placing the index and middle finger on a different plane decreased localization accuracy, although the difference was not significant for the ring finger (index: $t (31) = 2.43$, $p = .021$; ring: $t (31) = 1.48$, $p$
= .149; pinky: $t(31) = 2.93, p = .006$). In contrast, for the middle finger, placing the index and ring finger on a different plane increased accuracy ($t(31) = 2.83, p = .008$).

Figure 29. Response rate for each stimulated finger, collapsed across participants, for a. conditions with all fingers in the same plane (All Fingers Far and All Fingers Close) and b. with the index and ring finger on a different plane from the rest of the hand (Index-Ring Far and Index-Ring Close conditions), and c. the difference between the same plane vs. different plane conditions. In a. and b., darker colors indicate higher response rate. Numbers in bold (i.e. along the diagonal) are response rate on the stimulated finger, i.e. accuracy. In c., darker yellow denotes more positive values, i.e. more responses of each type in different plane vs. Same plane. Darker blue denotes more negative values, i.e. less responses of each type in Different plane vs. Same plane. Bold numbers along the diagonal indicate changes in localization accuracy. The red asterisks indicate that across all stimulated fingers, more responses were made on the middle finger in the Different plane vs. Same plane conditions, $p < .001$.

As shown in Figure 29c, there was an overall increase in the percentage of responses made on the middle finger in the different- vs. same-plane condition across all stimulated fingers. This indicates that the increased localization accuracy for the middle finger described in the previous paragraph might reflect an overall stronger tendency to responding on the middle finger when the fingers were not on the same plane. To test this, the percentage of responses made on the middle finger was analyzed using a repeated-
measures ANOVA with Stimulated Finger and Plane as independent variables. There was indeed a main effect of Plane ($F(1,31) = 24.15, p < .001$), with no interaction with Stimulated Finger ($F(3,93) = 0.513, p = .674$). These findings confirmed that across all stimulated fingers, there was an overall higher rate of middle finger responses when the index and ring finger were placed on a different plane vs. when all the fingers were on the same plane. Finally, as expected, there was a main effect of Finger ($F(3,93) = 164.02, p < .001$), with the highest response rate on the middle finger when the middle finger was stimulated, the lowest when the pinky was stimulated, and no differences between when the index and ring finger were stimulated ($p = .579$; all other $ps < .001$).

Asymmetrical error rates on first-neighbor fingers on each side

Previous studies showed that mislocalization is more likely to occur on fingers that are anatomically closer to the stimulated finger vs. farther (Schweizer et al., 2001; Manser-Smith et al., 2018). If mislocalization is only determined by distance, participants should make similar amounts of errors on the first-neighbor fingers on both the ulnar and radial side. To statistically test this, a “first-neighbor bias” was calculated as the average signed bias (in the number of fingers) across errors made on first-neighbor fingers. If equal errors were made on both first-neighbor fingers, the “first-neighbor bias” would be zero. One-sample $t$-tests were then performed to compare the first-neighbor indices with zero. For stimuli on the middle finger, there were significantly more errors on the ring vs. index finger ($t (31) = 5.40, p < .001, M = 0.40, SD = 0.42$). For stimuli on the ring finger, there were significantly more errors on the middle vs. pinky finger ($t (31)= -7.86, p < .001, M = -0.47, SD = 0.34$).
One interpretation of these findings is that individuals respond towards the center of the response space under conditions of uncertainty. This central tendency has been reported previously when participants localized touch among all five fingers, where radial biases were found for pinky and ulnar biases for the index finger (Manser-Smith et al., 2018). Moreover, in Manser-Smith et al. (2018), no directional biases were found on the middle finger, from which the authors concluded that the biases were towards the hand midline coded in higher-order hand representations. If the central tendency is based on the hand midline, there would be no directional biases on the middle finger in the current study either. However, there was a clear ulnar bias on the middle finger in the current study. An alternative interpretation is that the central tendency was towards the midline of the response space. By excluding the thumb in the current study, the center of the response space was no longer on the middle finger, but shifted towards the ulnar direction. As a result, more responses were made on the ring finger vs. index finger for stimuli delivered to the middle finger.

Another interpretation is that individuals respond towards the side with more response options. With uncertainty in tactile information, the brain makes the best guess regarding its location. Given knowledge of the response options, a touch is more likely to occur on the side with more response options, leading to directional biases. It is not possible to disentangle these two interpretations of the directional bias with the current design. Future studies can tease apart these possibilities by manipulating the probability at which each finger is stimulated, such that fingers towards the center of the response space is less frequently stimulated than fingers on the border of the response space.
4.2. General discussion

The major question of this experiment is whether tactile localization among fingers is affected by finger posture. First, the prediction was that if tactile localization is affected by distance, there would be overall more mislocalization, and in particular more errors on neighboring fingers, when the fingers are close in space vs. far apart. However, no differences in localization accuracy or error distribution were found between All Fingers Far and All Fingers Close, providing no evidence for proprioceptive information influencing tactile localization among fingers. Second, in Index-Ring Far and Index-Ring Close, distance between the index and ring finger was selectively manipulated to investigate the effects of distance between anatomically non-adjacent fingers on tactile localization. Given that no effects of finger distance were found from All Fingers Far and All Fingers Close, it would not be predicted that distance between anatomically non-adjacent fingers would affect tactile localization. Nevertheless, for stimuli delivered to the index finger, participants made more responses on the ring finger when the two fingers were close vs. far, indicating effects of finger distance on tactile localization for the index finger. No effects were found for stimuli delivered to the ring finger. Finally, we did an exploratory analysis testing if tactile localization differed when all the fingers were on a same plane vs. different planes. Compared with when all the fingers were on the same plane, participants were more likely to feel touch middle finger when the index and ring finger were placed on a lower plane, regardless of which finger was stimulated. We will first discuss this unexpected finding, and then the null effects of finger distance on tactile localization.
First, placing the index and ring finger on a lower plane led to a higher tendency of responding the middle finger, regardless of which finger was stimulated. To our knowledge, this is the first study demonstrating effects of finger plane on tactile localization on the fingers. It is difficult to infer the mechanism based on the current dataset, but we discuss a potential possibility relating to past findings on preferred position of each finger during tactile processing (Romano et al., 2019). In the study, participants placed one hand on top of the other hand, with the palms facing each other. In each trial, participants received a tactile stimulus on either the index finger or the thumb on either hand. Given the relative position of the hand, the tactile stimulus occurred on a relative “top” position (if it was on the top hand) or a “bottom” position (if it was on the bottom hand). Participants were asked to report whether the touch occurred on the top or bottom, regardless of which finger. The critical finding was that participants were faster and more accurate responding to thumb stimuli if the thumb was at a bottom position, and on index-finger stimuli if the index finger was at a top position. The finding on accuracy indicates a tendency of mapping touch to a lower location in external space when it occurred on the thumb, and a higher location when it occurred on the index finger.

In addition to the thumb and index finger, follow-up experiments using the same paradigm demonstrated a preference for a higher position for the index, middle, ring, and pinky finger, with stronger preference for the index and middle finger than ring and pinky (Romano et al., 2019). How can these findings potentially explain our results? First, with the middle finger being the first neighbor of index finger, and towards the side of more response options for the ring finger, there was a general bias of mislocalization on the middle finger when the index and ring fingers were stimulated. Then, in the Index-Ring
Far and Index-Ring Close condition, the index and ring finger were placed on a lower plane, with the middle finger and pinky staying on an upper plane. As discussed earlier, there was a tendency to localize touch at the preferred finger position in external space. It is thus likely that when the index and ring finger were on a lower plane, there was a bias of localizing touch at a preferred upper position. Given that the pinky and middle fingers were on the upper plane, the brain might assign touch to either the pinky or middle finger. However, given the general bias of mislocalizing on the middle finger, the brain would be more likely to assign touch to the middle finger vs. pinky, leading to more responses on the middle finger. Previous studies have also shown that touch was assigned to the body part that is currently occupying the space where the touch is preferably mapped to (Badde et al., 2019). For example, when the right hand was touched with the hands crossed, there was an initial tendency of mapping the touch to the anatomical right side of the body. Accordingly, participants were more likely to mislocalize touch to the body part, either hand or foot, that was currently on the right side of the body. These findings also demonstrate that information regarding tactile location in external space feeds back to the skin surface, supporting a non-serial model of tactile localization. Future studies can test this account by systematically varying the plane where each finger is placed based on each finger’s preferred location.

Although the hypothesis above can account for the index and ring finger, it does not explain a stronger bias of responding the middle finger when the middle finger itself or the pinky was touched, given that both of these fingers were on an upper plane. An additional possibility might be that by placing the flanker index and ring fingers on a lower plane, the middle finger became more salient as the center of the hand. As discussed earlier
in the results section, there was either a response bias towards the center of the hand (i.e. middle finger; Manser-Smith et al., 2018), or center of the response space (i.e. between the middle finger and ring finger). When two of the four fingers were placed on a different plane, finger positions differed in both medial-lateral and vertical dimension, making it harder to compute the center of the response space. In this situation, the brain might rely more on the anatomical center of the hand. Meanwhile, the hand configuration highlighted the center position of the middle finger, leading to stronger bias of responding the middle finger.

Other than the effects of finger plane, we did not find influences of finger distance within a plane on tactile localization. Previous findings provide mixed evidence on whether distance between fingers affects tactile localization. The study with the most similar paradigm as the current experiment was from Coslett (1998), in which placing the fingers together increased mislocalization of suprathreshold stimuli to the spatially closer fingers. However, such effects were found only on the contralesional hand in a patient with left neglect along with visual, tactile, and auditory extinction, but not on the ipsilesional hand of the same patient or healthy controls. It is likely that in the study, localization performance on the ipsilesional hand and in healthy controls were too accurate (accuracy > 98%) to be modulated by proprioceptive information. However, even in the current study where localization accuracy was reduced to about 60%, effects of finger posture were still not observed. One possibility is that in normal cases, effects of finger distance on this task is so minimal that could not be easily observed at behavioral level. An alternative possibility is that the effects found in the neglect patient were not on tactile perception per se, but on other aspects of the task. For example, it is possible that the patient could
accurately localize touch, but had difficulty selecting the correct finger during the response stage. When the fingers were close together, hence less distinguishable from each other in external space, he may have had more difficulty isolating the correct finger, leading to more confusion between spatially closer vs. more distant fingers. In a different task where the individual had to judge if a hand shown in a random posture was a left or right hand, he was less accurate judging left (contralesional)- vs. right-hand stimuli, indicating impairments in some representations of the left hand. Accordingly, impaired tactile localization when the fingers were close might also reflect general deficits in hand representations, such that the patient could not select the correct finger to respond.

In contrast to Coslett (1998) and the current study, another study found overall higher localization accuracy when the fingers were separate vs. close together (Overvliet et al., 2011). A major methodological difference in Overvliet et al.’s study (2011) was that there were three stimulus locations on each fingertip, and participants had to localize touch to a specific stimulus location, as opposed to just a finger. The task hence required two levels of localization, one by which the brain narrows response options to a specific fingertip, the other by which the brain localize touch within that fingertip. Because correctly localizing touch to a fingertip is prerequisite for accurately identifying which specific location within that fingertip is touched, the brain might rely on additional information to first minimize cross-finger errors. One strategy is to “group” stimulus locations based on whether they belong to the same fingertip or different fingertips, so as to constrain localization errors within fingertips. In addition to somatotopic information, such “grouping” can also be informed by external information: whereas relative positions between stimulation sites within a fingertip do not change with finger posture, relative
positions between stimulation sites across fingertips do vary with finger distance. The brain might therefore use both somatotopic and proprioceptive information to differentiate fingertips, and then primarily uses somatotopic information to localize touch within that fingertip, resulting in effects of finger position on tactile localization. In the current study where participants were only identifying which finger was stimulated, only one level of differentiation was needed, i.e. across fingers. Because there is no need to “group” locations within fingertips, the brain might only use somatotopic information to differentiate between fingers. On this explanation, the effects of finger distance on tactile localization may depend on the specific tasks. This account is based on findings from these studies, future investigations are needed to particularly manipulate task demands and observe the effects of finger distance.

Other studies also demonstrated task-dependent effects of finger posture on tactile localization. In line with the current experiment, one study found no effects of finger/hand posture when participants were asked to identify which finger is touched (Haggard et al., 2006). In the experiment, participants placed their two hands either vertically aligned, or palm facing each other with fingers interwoven. In each trial a tactile stimulus was presented to one of the eight fingers (thumbs excluded), and participants were asked to report either which hand, or which finger regardless of hand, was stimulated. They found that interweaving fingers decreased hand identification accuracy but did not affect finger identification, concluding that assigning stimuli to a finger does not take proprioceptive information into account. Opposing results were presented in another study in which participants judged whether two stimuli, delivered on either the index or middle finger on either hand, occurred on the same type of finger. When the stimuli occurred on different
types of fingers across hands (left index and right middle, or vice versa), participants were faster when the fingers were interwoven, for which the two stimulated fingers were adjacent in external space (Riemer, Trojan, Kleinbohl, & Holzl, 2010). Across these studies, influences of finger position also varied with task: There were no effects of finger position when the task involved identifying a single finger (Haggard et al., 2006), whereas the effects were observed when the task involved making judgments based on multiple tactile locations (Riemer et al., 2010). In both cases discussed in this and the previous paragraph, effects of finger posture on tactile perception was observed when the task was harder than simply identifying a finger.

To summarize so far, no strong evidence was found on effects of distance between fingers on tactile localization. Such findings are in line with previous studies showing that finger posture did not affect performance when participants had to report which single finger was touched (Haggard et al., 2006; Coslett, 1998). On the other hand, in studies involving more complex tasks (Overvliet et al., 2011; Riemer et al., 2010; Tame et al., 2007), tactile perception was influenced by finger posture. Taken together, whether proprioceptive information of the fingers affects tactile perception might be task-dependent. Specifically, when the task only involves localizing a single touch to a specific finger, proprioceptive information does not affect performance. In contrast, when the task involves integrating multiple tactile representations, for example, which two fingers were touched, additional effects of proprioceptive information were observed. The underlying mechanism for these task-dependent effects is unclear, but future studies on this topic should account for task differences across studies.
So far findings were discussed in conditions where all the fingers are in the same plane (Figure 24a and 24b, Condition 1 and 2). A novel manipulation in Experiment 4 was selectively varying distance between the index and ring finger by placing these fingers on different planes (Condition 3 – Index-Ring Far, and Condition 4 – Index-Ring Close). The purpose was to test if placing anatomically non-adjacent fingers closer in space would induce more mislocalizations on these fingers, despite being anatomically non-adjacent. It is surprising that although no effects were found when the distance between adjacent fingers was manipulated (All Fingers Far, All Fingers Close), selectively placing the index and ring finger close induced more mislocalization to the ring finger for stimuli delivered to the index finger. No effects were found on localizing stimuli delivered to the ring finger. Taken together with findings from the All Fingers Close and All Fingers Far condition, it is likely that finger distance affects tactile localization only when anatomically non-adjacent fingers are placed together. The fact that the effects of distance were found only on the index finger but not ring finger might be due to overall lower localization accuracy on the index finger. It is possible that when somatotopic representations are less precise, external representations are more strongly weighted, leading to stronger effects of finger distance on tactile localization. Nevertheless, more evidence will be needed to support this account. Moreover, in this study, only the index and ring finger were manipulated. Future studies can replicate this finding by generalize to other anatomically non-adjacent fingers.

Interestingly, previous studies also demonstrated differential effects of finger distance on anatomically adjacent vs. non-adjacent fingers. In the study, participants were asked to identify which two of the four fingers (thumb excluded) on the left hand were touched (Tame, Dransfield, Quettier, & Longo, 2017). The four fingers were either
touching each other, or slightly separated, or fully splayed. For a specific purpose, results were presented in terms of the number of fingers between the two reported fingers, instead of explicit localization errors. Interestingly, despite an overall underestimation, the number of in-between fingers increased with distance between the fingers, indicating effects of finger distance on localizing two simultaneous tactile stimuli. Such effects occurred, however, only when non-adjacent fingers were stimulated, but not adjacent fingers. The authors concluded that adjacent fingers are represented in somatotopic space, whereas non-adjacent fingers are represented in both somatotopic and external space. Other studies also tested tactile perception with adjacent fingers either crossed or uncrossed. In one study, blindfolded participants touched a ball with the middle finger and a point with the ring finger, and judged the relative position between the ball and point (Benedetti, 1985). The critical finding was that when the fingers were crossed, relative position between the ball and point was biased towards the anatomical positions of the two fingers, as if the brain mapped tactile information to the canonical finger positions. This finding also indicates that the brain may only considers the canonical position, but not online proprioceptive information from adjacent fingers during tactile processing, consistent with findings from the current study that distance between adjacent fingers did not affect tactile localization.

In summary, Experiment 4 did not provide strong evidence that distance between fingers affects tactile localization, at least in a task where participants localized a single touch to a specific finger. However, taken together with previous studies, these findings might reflect task-dependent effects of finger position on tactile localization. In addition, there is a potential differentiation between adjacent vs. non-adjacent fingers in terms of
whether proprioceptive information is considered during tactile processing. Finally, tactile localization might be affected by whether fingers are in the same plane or different planes.
Chapter 5

NEURAL CORRELATES OF TACTILE LOCATION REPRESENTATIONS IN SOMATOTOPIC AND EXTERNAL SPACE

In the previous chapters, behavioral investigations were presented to investigate the effects of external information on tactile localization on the body. This chapter presents a neuroimaging study investigating the neural correlates of tactile location representations in different reference frames. As discussed before, tactile locations are represented in both somatotopic and external reference frames. In addition, both the single-case study (Chapter 2) and experiments using the mirror box illusion (Chapter 3) provide evidence that information from external space influences tactile localization on the skin surface, indicating feedback processes from external to somatotopic tactile location representations. Given the behavioral findings, the first purpose of this experiment is to identify brain areas that represent touch in somatotopic space and external space, respectively. In addition, if perceived tactile location on the skin surface is influenced by body posture, there would be brain areas in which the representation of somatotopic location is affected by body posture. The second purpose of this experiment was to identify these brain areas.

One way to investigate if a given brain area “represents” certain information is by applying multi-voxel pattern analysis (MVPA) methods on functional neuroimaging data. Unlike the traditional general linear model that compares the overall amount of activation
between conditions, MVPA investigates the information content in the brain by analyzing the activation pattern across voxels (Norman et al., 2006). For example, in Figure 30 below, although the overall activation across the voxels does not differ between two conditions, the specific pattern across the voxels differs, indicating different representations for the two conditions. Therefore, MVPA decodes experimental conditions from multi-voxel patterns. Previous studies have used multi-voxel pattern analysis (MVPA) to investigate brain areas that encode tactile locations on the skin surface (Beauchamp et al., 2009; Kim et al., 2015). For example, multi-voxel patterns in the primary and secondary somatosensory cortices were found to differ between tactile stimuli on the thumb, middle, and pinky fingers (Beauchamp et al., 2009). However, in previous studies, the relative location between different stimuli in somatotopic and external frames of reference were always aligned, making it not possible to dissociate representations in these reference frames. To dissociate somatotopic and external reference frame, this experiment examined brain activity elicited by tactile stimuli while manipulating hand posture (Figure 31, see Methods below). By decoding multi-voxel patterns elicited by stimuli at the same location in external space but different locations in somatotopic space, brain areas that represent tactile locations in somatotopic space can be identified. On the same logic, by decoding multi-voxel patterns elicited by stimuli at the same somatotopic location but differing in external location, brain areas that represent tactile locations in external space will be identified.
Figure 30. Illustration of multi-voxel patterns associated with two experimental conditions. Each cell represents a voxel, with darker colors indicating higher amount of activation.

In addition to decoding somatotopic and external tactile representations, this study investigated in which brain area the representation of somatotopic location is influenced by hand posture. As discussed in the previous chapters, one possible mechanism for external information influencing tactile localization on the skin surface is by feedback processes from external to somatotopic representations. Therefore, brain areas where the representation of somatotopic locations vary with hand posture are potential neural correlates where somatotopic information and information fed back from external representations are integrated. For this purpose, we trained the classifier to decode index- and ring-finger stimuli with one hand posture, and tested the classifier with data collected either under the same posture (e.g. trained with palm up, tested with palm up) or the other posture (e.g. trained with palm up, tested with palm down). If hand posture does not influence somatotopic representation, a classifier trained with one hand posture should transfer well to the other posture. On the other hand, if hand posture influences somatotopic representation, patterns tested with one posture would not match patterns tested with the other posture, leading to lower decoding accuracy when the classifier is trained and tested across postures vs. within the same posture.
Previous studies found that S1, secondary somatosensory cortex (S2), posterior parietal cortex (PPC) and the medial superior temporal (MST) area of the visual cortex could reliably decode tactile stimuli on different fingers (Beauchamp et al., 2009; Kim et al., 2015). Among these areas, since S1 is somatotopically organized, we predict that S1 will reliably decode stimulus location on the skin surface (i.e. between the index finger and ring finger).

Past literature provides evidence that structures in the frontal and parietal lobe respond to hand posture change during tactile stimulation (Lloyd, Shore, Spence, & Calvert, 2003; Takahashi et al., 2012; Miyazaki et al., 2016). For example, when the right hand was stimulated, more activation was found in right ventral intraparietal sulcus when the hand was crossed over the body midline vs. in the anatomical right side (Lloyd et al., 2003). In addition, there is evidence that temporarily disrupting PPC by TMS affected tactile localization in external space, but not on the skin surface, indicating that PPC is important for remapping stimulus location from the skin surface to external space (Azañón, Longo, Soto-Faraco, & Haggard, 2010). Therefore, we predict that posterior parietal cortex will represent tactile location in external space.

5.1. Experiment 5

Methods

Participants

Previous studies on decoding tactile information had sample sizes ranging from seven to ten participants (Kim et al., 2015; Beauchamp et al., 2009). Given that it is common for MVPA studies to have less than ten participants, eight participants (Age: 27.4±8.4, 4 males) were tested.
Design and procedure

A 2 (stimulus location) by 2 (hand posture) design was used (Figure 31). In each trial, participants received a tactile stimulus on the tip (glabrous surface) of either the right index finger or ring finger, with the right hand placed either palm facing up or facing down. This manipulation dissociated stimulus location in somatotopic reference frame (i.e. fingertips) and an external reference frame. Specifically, Figure 31a and 31c are conditions in which tactile stimuli are at the same location in somatotopic space (i.e. index fingertip), but different locations in external space, so are Figure 31b and 31d. On the other hand, Figure 31a and 31d are conditions in which tactile stimuli are at the same location in external space, but differ in somatotopic space (i.e. index vs. ring finger), so are Figure 31b and 31c.

Figure 31. Manipulations of Experiment 5. Participants receive tactile stimulation on the tip of either the right index finger or ring finger, with the hand either palm facing up or facing down. Cells with the same background color contain conditions with the same external location (a. and d.: left; b. and c.: right).
Participants laid supine in the scanner with their right hand placed on their right lap. In each trial, participants received a 4-second vibrotactile stimulus on either the right index or ring finger, while fixating at a black square at the center of the screen projected to a mirror mounted in the head coil. After the 4-second stimulation, the center square turned white and lasted for eight seconds before the next trial began. There were two types of trials, test trial and catch trial. In test trials, the 4-second stimulus contained eight 400ms vibrotactile pulses (30 Hz suprathreshold sine waves) separated by 100ms to prevent adaptation (Sanchez-Panchuelo, 2012). To ensure that participants focused on the tactile stimuli, an orthogonal task was included by adding catch trials. In catch trials, there was a 1-second no-vibration period with a random onset during the 4-second tactile stimuli. When participants detected the catch trials, they were asked to press a button with the left hand after the 4-second tactile stimulus ended, i.e. during the inter-trial interval. This was done to prevent overlap between button presses and tactile stimulation, making the events easier to model (see Data analyses below).

Since the tactile stimulators used to deliver vibrotactile stimuli contained delicate wire connections, hand posture was carefully turned by the experimenter instead of the participants themselves. Meanwhile, entering the scanning room during a run might introduce noise to the signal, which would then affect modeling of hemodynamic responses. We therefore manipulated hand posture across functional runs, and the experimenter entered the scanning room between runs to change the hand posture. In MVPA studies, each functional run typically contains all experimental conditions so that the classifier is not accidentally decoding systematic differences across runs. We note that manipulating hand posture across runs would not cause such problems because we would not decode
palm-up vs. palm-down trials. In addition, conditions that were entered into MVPA (Figure 31, a. to d.) were mixed within each functional run. Therefore, differences in multi-voxel patterns between conditions would not be confounded by systematic differences between functional runs.

There were eight blocks in total – four blocks with the palm facing up, and four blocks with the palm facing down. The order of the hand posture was manipulated in an ABBAABBA manner, with the first posture counterbalanced across participants. Whenever the hand posture needed to be changed, the experimenter entered the scanning room and carefully turned the hand over, while ensuring that the position of the tactile stimulators in external space remained the same. Each block contained 18 test trials, nine trials on each finger. In addition, each block contained four catch trials, two on each finger. Trial order was randomized for each functional run and each participant.

Materials

Vibrotactile stimuli were presented using MRI-compatible piezoelectric devices (PTS-C2, Dancer Design, St. Helens, UK) attached to each fingertip. The stimulators were mounted on a foam block with the distance between the stimulators match the typical distance between the index finger and ring finger. During the experiment, participants’ right hand rested on the foam block, with the fingertips strapped to the stimulators using MR-compatible medical tapes.

Imaging parameters

Structural and functional neuroimaging were conducted on a 3.0T Siemens Magnetom Prisma scanner with a 64-channel head coil. A T1-weighted structural image was acquired using an MPRAGE sequence (TR = 2080.0 ms, TE = 4.64 ms, flip angle =
7°, voxel size = 0.7 × 0.7 × 0.7 mm, 208 sagittal slices). Functional images were collected using a T2*-weighted EPI pulse sequence (TR = 1000 ms, TE = 32.0 ms, flip angle = 61°, voxel size = 2 × 2 × 2 mm).

Data analyses

Preprocessing

Standard preprocessing steps were performed in the FSL toolbox (FSL 6.0, FMRIB’s Software Library, www.fmrib.ox.ac.uk/fsl), including: Brain-extraction of the structural image using the BET tool, motion correction of the functional images using the MCFLIRT tool, and temporal filtering with a default high-pass filter of 100s. To reduce spatial noise while preserving the high spatial resolution for MVPA, functional images were spatially smoothed with a 2 mm full-width-half-maximum Gaussian kernel. Functional images were co-registered to the high-resolution T1 images and then to a standard MNI image (1 × 1 × 1 mm resolution) using linear transformation for group-level analyses.

Univariate general linear model (GLM) analysis

To confirm that the current paradigm was effective in eliciting somatosensory activation, a standard univariate GLM analysis was performed to examine what brain areas were activated by tactile stimulation. GLM analyses were performed at three levels. For the first-level GLM, each functional run from each participant was analyzed separately. Each functional run was modeled with 11 regressors: test trials on the index finger, test trials on the ring finger, catch trials on the index finger, catch trials on the ring finger, button presses, and the six parameters output by the motion correction process. Button press events were modelled within 1-second time windows starting from the time when the
buttons were pressed. Each regressor was created by convolving the box-car function of the periods of the stimulus condition with a double-gamma function. Because the primary goal of GLM was observing which brain areas were activated by tactile stimuli regardless of hand posture, the contrast of interest was comparison between tactile stimulation vs. baseline. An F-test was performed to combine the effect of tactile stimuli on the index and ring finger, to investigate overall activation caused by test trials against baseline. At second-level GLM, all functional runs from each participant were combined using a fixed-effect analysis. Finally, at third-level GLM, second-level results were combined across participants. Given the relatively small sample size, and given that primary purpose of this analysis is to confirm the validity of the paradigm within this group, a fixed-effects analysis was used at the third-level. Result maps were thresholded at FWE corrected $p < .001$.

*Whole-brain searchlight MVPA*

With the goal of identifying brain areas that represent somatotopic and external tactile locations, to perform thorough search with spatial specificity, whole-brain searchlight MVPA were performed (Kriegeskorte, Goebel, & Bandettini, 2006). In searchlight MVPA, a “searchlight” containing a group of voxels travels throughout the brain, centering on each voxel in turn. A decoding analysis is performed on all voxels within the searchlight, and decoding accuracy is assigned to the center voxel. As a result, searchlight MVPA yields a whole-brain map of decoding accuracy. Two decoding analyses were performed for each participant: Somatotopic decoding and external decoding. In somatotopic decoding, trials were labelled by which finger (i.e. somatotopic location) was stimulated, and the classifier was trained and tested in differentiating multi-voxel patterns.
associated with each finger. In external decoding, trials were labelled by external locations of tactile stimuli. Then decoding accuracy maps were analyzed at group-level (see below).

For each participant, only test trials were included in the searchlight analyses. For each functional run, the preprocessed (i.e. after motion correction, spatial smoothing, and temporal filtering) time series of each voxel was normalized relative to the mean and standard deviation of their own time series along the temporal dimension. Each trial was treated as an exemplar for the advantage of a large volume of training and testing data, as well as modeling online neural signal (Beauchamp et al., 2009). For each trial, the normalized time series was averaged across the eight volumes (i.e. 8 seconds given TR of 1 second) during the following inter-trial interval as the decoding sample. Given temporal delay in hemodynamic responses, eight volumes after each tactile stimulus (eight seconds) were assumed to capture a relatively full profile of the neural signal (Harrison & Tong, 2009).

Searchlight MVPA was performed using linear discriminant analysis (LDA) classifier implemented in the CoSMoMVPA toolbox (Oosterhof, Connolly, & Haxby, 2016; Vannuscorps et al., 2018), with each spherical searchlight containing 100 voxels. Typically, decoding analyses are performed using leave-one-run-out cross-validation methods: In each iteration, the classifier is trained on data from all but one run, and tested on data from the left-out run. However, given that in the current study hand posture was manipulated across functional runs, using leave-one-run-out methods could be problematic. Table 3 demonstrates the problem using a simplified design with two trials per run and four runs. Assuming in an iteration of leave-one-run-out procedure of somatotopic decoding, Run 1 was extracted as the testing data. During training, the classifier was “taught” that
sample 3, 5, and 7 corresponded to Category A (i.e. index finger), and sample 4, 6, and 8 corresponded to Category B (i.e. ring finger). Importantly, external locations were not balanced. Among sample 3, 5, and 7, two corresponded to the category of “left”, and 1 “right”. If a brain area happens to represent external locations, it would consider sample 3, 5, and 7 as more likely to be “left” than “right”. Then, during testing, because sample 2 is a “left” trial, this brain area would classify sample 2 as in the same category as sample 3, 5, and 7, which were in the same spatial side category but wrong finger category. Since the decoding accuracy was evaluated based on somatotopic location, this brain area would be considered as systematically misclassifying samples, demonstrating below-chance accuracy and causing difficulty in interpreting data. To solve this problem, a leave-two-run-out method was used in the current study: In each iteration, a pair of palm-up and palm-down runs were left out, making somatotopic and external location categories balanced in both training and testing dataset. As a result, 16 iterations were carried out in each MVPA, with all combinations of palm-up and palm-down runs left out in turn. After this level of analysis, each participant had two accuracy maps, one on decoding somatotopic locations (i.e. index finger and ring finger), one on external locations (i.e. left and right relative to the hand midline).
Table 3. Examples demonstrating the problem of leave-one-run-out in the current design

<table>
<thead>
<tr>
<th>Run</th>
<th>Sample (Trial)</th>
<th>Hand posture</th>
<th>Finger</th>
<th>Spatial side from the participant</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>Palm up</td>
<td>Index</td>
<td>Right</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>Palm up</td>
<td>Ring</td>
<td>Left</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>Palm down</td>
<td>Index</td>
<td>Left</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>Palm down</td>
<td>Ring</td>
<td>Right</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>Palm down</td>
<td>Index</td>
<td>Left</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>Palm down</td>
<td>Ring</td>
<td>Right</td>
</tr>
<tr>
<td>4</td>
<td>7</td>
<td>Palm up</td>
<td>Index</td>
<td>Right</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
<td>Palm up</td>
<td>Ring</td>
<td>Left</td>
</tr>
</tbody>
</table>

In addition to the decoding maps, 100 null maps were created from each participant to be used in the group-level analyses. For each participant, finger labels within each run were randomly shuffled 100 times. For each random set of labels, searchlight MVPA was performed to generate a decoding accuracy map. This was performed to simulate decoding accuracies under the null hypothesis. Because finger labels and external location labels were coupled within each posture, shuffling finger labels had the same randomization effects as shuffling external location labels. Therefore, the same null maps were used for group-level analysis of both somatotopic and external decoding. For group-level analysis of each type of decoding (somatotopic and external), for each voxel, a one-sample t-test was performed on decoding accuracy across participants, with 0.5 (chance decoding accuracy given two categories) as the null. This map was thresholded at $p < .005$ and then corrected for multiple comparison using a cluster-based Monte Carlo simulation (cosmo_montecarlo_cluster_stat; Oosterhof et al., 2016; Vannuscorps et al., 2018). In each iteration of Monte Carlo simulation, one of the 100 null maps from each participant was randomly drawn. Then, one-sample t-tests were performed on each voxel across the randomly drawn maps, resulting in a new map of $p$-values. This map was thresholded at...
the same criteria as the original map \((p < .005)\). The same steps were repeated 1000 times, resulting in 1000 maps under the null hypothesis. The largest cluster size from each null map was calculated, forming a distribution of maximum cluster size under the null hypothesis. Finally, the original thresholded map was compared against this cluster distribution, with cluster sizes ranked the top 5% considered as significant (Oosterhof et al., 2010; Kim et al., 2015). The cluster connectivity scheme was the same as previously used: Two voxels were considered as connected if they share a face, but not just an edge or vertex (Stelzer, Chen, & Turner, 2013).

**ROI MVPA -- Decoding somatotopic locations across hand postures**

In addition to identifying brain areas that represent somatotopic and external locations, the second aim of this study was investigating in which brain areas are representations of somatotopic location influenced by hand posture. To address this question, clusters found in the searchlight analyses that could decode somatotopic locations were chosen as ROIs and transformed back to each participant’s functional space. In each participant, within each ROI, two ROI MVPAs were performed. In the first analysis (same-posture decoding), somatotopic decoding was performed on functional runs with the same posture (e.g. trained on index vs. ring for palm facing down, tested also on palm facing down). In the second analysis (across-posture decoding), somatotopic decoding was performed across different postures (e.g. trained on index vs. ring for palm facing down, tested on palm facing up). The logic is that, if changing hand posture does not change representation of somatotopic location, a classifier trained on one posture should generalize to the other posture. On the other hand, if changing hand posture modulates somatotopic representations, difference between the index and ring finger learnt during training would
not generalize to the other posture, leading to decreased decoding accuracy when tested with the other posture.

With four functional runs for each hand posture, in same-posture decoding, there was one testing run and three available training runs. In contrast, in across-posture decoding, all the four functional runs with the other posture were available. To ensure that differences between same- and across-posture decoding accuracy were not a result of unmatched number of training samples, in across-posture decoding, three functional runs were randomly chosen as training data in each iteration.

**Results**

**Univariate GLM analyses**

The purpose of the GLM was to confirm that our paradigm did elicit somatosensory activation by testing the contrast of test trials vs. inter-trial interval baseline. As shown in Figure 32, tactile stimulation activated a large set of regions. Consistent with previous literature, tactile stimuli activated bilateral S1 and S2, as well as supplementary motor area (Beauchamp, Yasar, Kishan, & Ro, 2007; Beauchamp et al., 2009). In addition, significant activity was also found in parietal and frontal areas, including contralateral premotor cortex; bilateral inferior parietal lobule/parietal-occipital region (IPL/PO); bilateral superior frontal gyrus (SFG); paracingulate gyrus; precuneus cortex; bilateral cerebellum (lobule VI). Having confirmed that the paradigm was effective in eliciting somatosensory activation, we then present results from MVPA.
Figure 32. Brain areas activated by tactile stimuli in test trials compared to baseline. Statistical maps are thresholded at FWE corrected $p < .001$. S1: Primary somatosensory cortex. SMA: Supplementary motor area. SPL: Superior parietal lobe. IFG: Inferior frontal gyrus. Pre-SMA: Pre-supplementary motor area. PMC: Premotor cortex. SFG: Superior frontal gyrus. IPL/PO: inferior parietal lobule/parietal-occipital region. S2: Secondary somatosensory cortex.

**Whole-brain searchlight MVPA**

**Somatotopic decoding**

From the searchlight analysis decoding tactile stimuli on the index finger vs. ring finger, one cluster was found in contralateral (left) S1, extending to M1 (Figure 33; 6412 voxels, peak mean accuracy across participants = 0.73, cluster-corrected $z = 3.09, p = .001$). An additional, marginally significantly cluster was found in contralateral premotor cortex (BA6; 492 voxels, peak accuracy = 0.56, cluster-corrected $z = 1.635, p = .051$; Figure 33).

Prior studies divided the premotor cortex into dorsal and ventral subregions, with the boundary at around $z = 48$mm (Tomassini et al., 2007; Mayka, Corcos, Leurgans, & Vaillancourt, 2006). Our cluster lays well above the boundary, hence more likely locates in dorsal premotor cortex. Whereas previous studies found contralateral S2 and PPC to decode tactile stimuli on different fingers (Beauchamp et al., 2009; Kim et al., 2015), no significant clusters were found in these areas in this study.
Figure 33. Clusters in contralateral primary somatosensory and premotor cortex that decoded tactile location in somatotopic space. Slices are shown in MNI coordinates.

*External decoding*

The searchlight MVPA identified two clusters that carried information regarding whether a touch occurred in external space. One cluster located at contralateral (left) anterior cingulate cortex (Figure 34, top; BA24, Walton et al., 2007; 575 voxels, peak accuracy = 0.55, cluster-corrected $z = 2.03$, one-tail $p = .021$); the other at contralateral middle occipital gyrus (Figure 34, bottom; 491 voxels, peak accuracy = 0.54, cluster-corrected $z = 1.75$, $p = .040$). The exact visual area of the occipital cluster could not be determined without performing retinotopic mapping. After being overlaid to a Brodmann’s area template, the occipital cluster is located in BA18, and is likely the dorsal portion of visual area V2 (Stilla & Sathian, 2008; Wohlschlager et al., 2005).
ROI MVPA -- *In which brain areas are somatotopic representations modulated by hand posture* 

Given that contralateral (left) S1 and possibly dorsal premotor cortex decoded tactile locations on the skin surface, the next question is whether the representations are modulated by hand posture. If these areas are neural correlates of tactile localization being affected by external information, representations of tactile stimuli on each finger would vary with hand posture. To test this, contralateral premotor cortex and S1 were transformed back to each participant’s functional space and serve as ROIs for an MVPA. For each participant, two somatotopic decoding analyses were performed in each ROI. In the same-posture analysis, a classifier was trained and tested on index- and ring-finger trials on functional runs of the same hand posture. In the across-posture analysis, a classifier trained
on index- and ring-finger trials using functional runs of one hand posture, and tested on a functional run of the other hand posture. If hand posture influences somatotopic representation, a classifier trained on one posture would not show lower accuracy when it is tested on the other posture vs. the same posture. To test this, a paired $t$-test was performed across participants for each ROI between the accuracy from the same-posture and across-posture decoding. Nevertheless, no significant differences were found in either S1 ($t (7) = -.28, p = .785$) or premotor cortex ($t (7) = 1.03, p = .335$), providing no evidence that somatotopic representations in these areas are modulated by hand posture.

5.2. General Discussion

By dissociating somatotopic and external reference frames, this experiment aimed to identify brain regions that represent touch in somatotopic and external reference frames respectively. In addition, this study examined in which brain areas somatotopic representations are influenced by hand posture. First, searchlight MVPA found contralateral (left) anterior cingulate cortex and occipital lobe represented tactile location in external space, providing the first piece of evidence in the literature regarding the neural correlates of external tactile location representation. Second, this study examined brain areas that represent touch in somatotopic space. As expected, searchlight MVPA associated somatotopic decoding with activity patterns in S1, but also found tentative evidence for somatotopic encoding in premotor cortex as well. Third, no evidence was found that somatotopic representations in S1 or dorsal premotor cortex were modulated by hand posture. Finally, to ensure that the paradigm was effective and valid, univariate GLM was performed to examine which brain areas were activated by touch compared to baseline. As
expected, activation was found in contralateral S1 and S2, along with a broad set of frontal and parietal regions. We discuss the major findings below.

First, we identified a cluster in the contralateral occipital lobe, located in BA18, that represented tactile location in external space. The exact visual area could not be precisely determined without performing retinotopic mapping. From past studies, this cluster likely corresponds to the dorsal part of visual area V2 (Stilla & Sathian, 2008; Wohlschlager et al., 2005). This finding contrasts with previous findings that lateral occipital-temporal cortex responded to tactile object and/or visual hand information, as those areas are along the ventral visual pathway (Bracci et al., 2011; Amedi et al., 2010). Previous studies on both primates and humans found that V2 has topographical organization of the contralateral visual field, and neurons in V2 responded to simple visual orientations (e.g. single bar orientations) as well as complex contours and shapes (e.g. angles and curves; Anzai, Peng, & Essen, 2007; Hegde & van Essen, 2000). These findings indicate its major function in visual perception. Interestingly, neuroimaging studies on humans found shared activation in V2 for both visual perception and imagery of spatial locations (Cichy, Heinzle, & Haynes, 2011). In the study, participants were either presented with pictures of objects on the screen, on either side of the center fixation (perception condition), or asked to imagine an object picture on either side of the screen (imagery condition). MVPA was performed to test whether brain areas could decode spatial location of object pictures, whether visually perceived or imagined. Interestingly, above-chance decoding accuracy was achieved in low-level visual areas including V1, V2, and V3, indicating that these areas represent both perceived and imagined spatial location. Another study found shared function in this occipital area in processing visual and tactile
information (Stilla & Sathian, 2008). In the study, participants were asked to compare the roughness of two consecutively presented tactile surfaces, or two visually presented surfaces. Both modalities activated dorsal portion of middle occipital gyrus, at around the same coordinates as our occipital cluster. Given that this occipital area represents imagined visual location, and may have shared functions across visual and tactile modalities, it is possible that the above-chance external decoding found in the current study was driven by imagery of tactile locations. Specifically, participants might be imagining the external location of tactile stimuli during the experiment. The reason why only contralateral, but not bilateral occipital lobe, might decode spatial location is that the area only represents tactile stimuli on the contralateral hand or contralateral side of space. This account is speculative, as participants were not cued to process tactile spatial information, and there is no evidence that participants were imaging the spatial side of tactile stimuli.

We also found above-chance decoding of external tactile localizations in contralateral anterior cingulate cortex. This finding is surprising because anterior cingulate cortex has been associated with high-level cognitive functions such as response selection and conflict monitoring (Walton et al., 2007; MacDonald et al., 2000; Botvinick, Cohen, & Carter, 2004; Turken & Swick, 1999). For example, in a color-word Stroop task, anterior cingulate cortex was activated when participants were naming the color vs. word in incongruent trials, with the amount of activation correlated with response time, reflecting the process of resolving response conflicts (MacDonald et al., 2000). One study tested a brain-damaged individual with anterior cingulate cortex lesion to establish causal relationship between this brain area and response selection (Turken & Swick, 1999). Whereas the performance on a Stroop task was within the normal range when using verbal
response, the individual’s performance dropped substantially with manual responses, highlighting the role of anterior cingulate cortex in selecting manual motor responses. Other studies also demonstrated the role of anterior cingulate cortex in reward-driven action selection. In one study, monkeys were trained to associate one action with rewards. After the association had been established, the experimenter switched the association and the monkeys had to perform another action to gain the reward. For monkeys with anterior cingulate cortex lesioned after training, although they could switch to the other action upon feedback, they were less likely to sustain the new action compared with normal monkeys, indicating the role of anterior cingulate in selecting optimal action based on reward history (Kennerley et al., 2006). All these findings highlight the role of anterior cingulate cortex in selecting responses based on environmental cues such as task demands or rewards.

Nevertheless, it is difficult to explain why anterior cingulate cortex decoded tactile location in external space using past evidence. Although our study involved a task in which participants judged whether there was a 1-second gap in each tactile stimulus, the spatial location of tactile stimuli was irrelevant to the task. Therefore, our results are unlikely explained by the response selection function of anterior cingulate cortex. In monkeys, neurons from a subregion of BA24 (BA24c, rostral cingulate motor area) responded to passive joint movements, suggesting that this area might process somatosensory (i.e. proprioceptive) information (Akazawa et al., 2000). In humans, one study found activation of anterior cingulate cortex when participants judged the distance between two tactile stimuli (Spitoni et al., 2010). In each trial, participants were touched at two points on the forearm, and then 1 second later on the thigh. Participants either judged which pair of stimulus had longer distance, or was more intense. Both tasks hence involved stimulus
comparison and response selection. Interestingly, anterior cingulate cortex, among other parietal and frontal areas, was more activated when participants judged tactile distance vs. intensity, suggesting its role in processing spatial tactile information. However, note that this past study found activation in *ipsilateral* anterior cingulate cortex, whereas we found *contralateral* anterior cingulate cortex to decode external tactile location. It is therefore hard to infer the role of anterior cingulate cortex in these tasks. Further studies are needed to confirm and specify the role of anterior cingulate cortex in processing sensory information.

With regards to tactile locations on the skin surface, contralateral S1 was found to decode tactile stimuli on different fingers at above-chance level. This finding was expected given that S1 has a somatotopic organization (Penfield & Boldrey, 1937) and was found in previous studies to decode fingers at above-chance accuracy (Beauchamp et al., 2009; Kim et al., 2015). An additional cluster, although with marginal statistical significance, was found in dorsal premotor cortex. In monkeys, dorsal premotor cortex has been associated with planning reaching movements towards visual targets, with the firing rate tuned to properties (e.g. direction) of the planned movements closely before movement onset (Crammond & Kalaska, 1996; Churchland, Santhanam, & Shenoy, 2006). In both monkeys and humans, dorsal premotor cortex was activated during selection of movements based on arbitrary stimulus-movement mappings (e.g. opening the hand when seeing a triangle; Toni, Rushworth, & Passingham, 2001; Halsband & Passingham, 1985). These findings emphasize the role of dorsal premotor cortex in processing motor information based on sensory cues. Interestingly, one study found neurons in monkey dorsal premotor cortex (area F2) responded to tactile stimuli, with tactile receptive fields having similar
somatotopic organization as mapped by limb movements, although the function of somatosensory activity was unknown (Raos, Franchi, Gallese, & Fogassi, 2002). In a more recent study, neural activity was recorded when monkeys reached to a visual target among distractors (Song & McPeek, 2010). Importantly, a subset of neurons fired when the target appeared in their preferred direction, with firing time-locked to the onset of the visual target array, regardless of movement onset, indicating their specialized role in target selection as opposed to movement planning. This finding indicates that dorsal premotor cortex also processes sensory information. Nevertheless, little evidence was reported from past studies that premotor cortex encodes tactile locations on the skin surface. With the marginal significance level and lack of prior evidence, this finding requires further investigations and confirmation.

Having found that contralateral S1 and tentatively dorsal premotor cortex encoded tactile locations in a somatotopic reference frame, further analyses were performed examining whether somatotopic representations in these areas were modulated by hand posture. In both areas, accuracy of decoding which finger was stimulated did not differ whether the classifier was trained and tested within the same posture, or across hand postures, providing no evidence that hand posture affected somatotopic representations in these areas. The finding on S1 is consistent with the finding that neurons in S1 have receptive fields on the skin surface, regardless of body position in external space (Penfield & Boldrey, 1937). Meanwhile, it is worth noting that it has not been thoroughly examined whether body position affects the firing profile of neurons in S1. The finding of significant somatotopic decoding in premotor cortex may also suggest that representations in this area are strictly somatotopic and are not influenced by hand posture. However, we note that
more evidence is needed to first confirm that premotor cortex does encode somatotopic locations before further accounting for hand posture. Finally, whereas we did not find differences between same-posture and across-posture decoding, the results do not necessarily mean that somatotopic representations in these areas are not influenced by hand posture. One possibility could be that in normal individuals, effects of body posture on the representations of fingers were too small to be observed. This could be particularly possible given that the vibrotactile stimuli were moderately intense, possibly resulting in unambiguous somatotopic representations. In addition, the spatial resolution of the functional images might not be high enough to capture subtle changes in brain activation patterns.

Finally, previous studies found higher-level areas including contralateral S2 (Beauchamp et al., 2009), PPC and SMG (Kim et al., 2015) to also decode tactile stimuli on different fingers. However, the current study only identified S1 as significantly decoding between different fingers. The reason for why the studies differ is not completely clear, but two differences in experimental design are worth considering. First, previous studies involved a larger number of trials or longer stimulation durations. In Beauchamp et al. (2009), each body site was stimulated in total of 150 trials of two seconds each. In Kim et al. (2015), each finger was stimulated in nine trials of 30 seconds each. Both studies collected more time points for each finger than the current study (144 seconds in each condition), which potentially led to more robust signals and boosted decoding accuracy in higher-level brain areas. Second, with fixed hand posture in past studies, somatotopic and external reference frames were always aligned. Therefore, tactile stimuli across fingers differed in both somatotopic and external space. It is possible that areas such as S2, PPC
and SMG represent both somatotopic and external locations, and the alignment of external
and somatotopic reference frames made patterns associated with each stimulus location
more distinct to decode. In contrast, in the current study, half of the index-finger trials share
the same external location with half of the ring-finger trials, eliminating different patterns
associated with external locations. As a result, multi-voxel patterns across stimulus
locations were less distinct than in past studies, and no higher-level areas were identified
from searchlight MVPA.

To summarize, we examined the neural correlates of tactile location representation
in somatotopic and external reference frames. We found contralateral anterior cingulate
cortex and middle occipital gyrus (putatively V2) to encode stimulus locations in external
space. To our knowledge, this is the first study using MVPA to examine tactile location
representation in external space. In addition, we found contralateral primary somatosensory
cortex and tentatively contralateral dorsal premotor cortex to represent tactile location in
somatotopic space (i.e. fingers), with somatotopic representations unaffected by hand
posture. Whereas the findings regarding anterior cingulate cortex, middle occipital gyrus,
and premotor cortex are novel, we note that more studies are needed to confirm these
findings and to investigate the functional role of tactile spatial representations in these areas.
Chapter 6

SUMMARY AND CONCLUSIONS

6.1. Summary of the findings

In testing the serial model of tactile localization, three behavioral investigations were performed to examine whether tactile localization on the skin surface is influenced by information from external space. In Chapter 2, patient DS made substantial errors in localizing touch on both the palm and dorsum of the contralesional hand, always localizing touch towards the left side in space relative to the hand long axis, whether the hand was palm facing down, palm facing up, or rotated 90°. Importantly, perceived tactile locations on the skin surface were strongly affected by hand posture, clustering around the pinky when the hand was palm facing down, and around the thumb and index finger when the hand was palm facing up. The localization biases were unlikely to be response errors, as DS performed well in general pointing tasks, and demonstrated similar tactile localization bias when responded verbally. In addition, given normal tactile detection on the contralateral hand, DS’s deficits were specific to tactile localization processes, but not due to general degraded sensory information. These findings provide strong evidence that tactile localization on the skin surface is influenced by hand posture, indicating that tactile localization is not a strict serial process. In addition, the data provide evidence that tactile localization on the skin surface was specifically biased in an external reference frame centered on the hand long axis.
Given evidence from the single case study in Chapter 2, Chapter 3 presented experiments on neurologically intact populations to further address if external information influences tactile localization on the body surface. Using the mirror box illusion, a spatial mismatch between the visual and proprioceptive estimate of hand position was created. During this mismatch, tactile localization on the hand dorsum was biased in the direction of the proprioceptive estimate relative to the visual estimate. These effects were robust after controlling for the effects of hand position alone (Experiment 3.2) and gaze-propiroception mismatch (Experiment 3.3). The data support the anchoring hypothesis that tactile location estimates in external space are anchored to the visually-defined location, and then biased towards the proprioceptively-defined location. These biases in external space then feed back to the skin surface, leading to tactile localization biases on the skin surface towards the proprioceptive estimate. Multiple mechanisms underlying the anchoring effects were discussed. Importantly, all mechanisms imply that external information affects tactile localization on the skin surface via feedback processes – information regarding tactile location in external space feeds back to the skin surface, biasing tactile localization. These findings thus provide strong evidence against the serial model in tactile localization, which predicts no influences of external information on tactile localization on the body surface. In addition, the data indicate a potential non-serial model which involves feedback processes from external tactile representation to somatotopic tactile representation.

The experiment in Chapter 4 investigated if tactile localization across the fingers is affected by relative finger position. One novel finding was that compared with when all the fingers were on the same plane, participants were more likely to respond middle finger
when the index and ring finger were placed on a lower plane, regardless of which finger was stimulated. This finding also provides evidence that external information, i.e. finger plane, influences tactile localization among the fingers. However, no effects of relative finger distance on tactile localization were found. Considering this study and previous studies, whether relative finger distance affects tactile localization may depend on task demands.

Finally, the neuroimaging study in Chapter 5 investigated brain areas that represent tactile location in external and somatotopic reference frames, respectively. For somatotopic representation, MVPA identified the contralateral primary somatosensory cortex, consistent with the widely confirmed somatotopic organization in primary somatosensory cortex. In addition, contralateral dorsal premotor cortex decoded different fingers at marginally above-chance accuracy. For external representation, contralateral middle occipital gyrus (putatively V2) and anterior cingulate cortex (BA24) decoded tactile locations in external space at above-chance accuracy, providing novel evidence that these areas encode tactile location in external space. Finally, in both contralateral primary somatosensory cortex and dorsal premotor cortex, accuracy in decoding different fingers did not change whether the classifier was trained and tested within a hand posture, or across hand postures. These findings suggest that somatotopic representations in these brain areas may not be influenced by hand posture.
6.2. Mechanisms of how external information influences tactile localization on the body surface

With evidence that tactile localization on the body surface is influenced by external information, one question is how to modify the serial model to account for these findings. Both Chapter 2 and Chapter 3 discussed mechanisms that information regarding tactile location in external space maps back to somatotopic space, being integrated with the original somatotopic representation. Integration of external information and somatotopic representation follows several rules. First, because the tactile location estimate in external space is calculated by combining somatotopic tactile location with proprioceptive information, the external tactile location estimate is noisier than the somatotopic tactile location estimate. Therefore, in normal systems information from external space is less weighted than the somatotopic representation to prevent adding substantial noise to the tactile location estimate on the skin surface. This principle is demonstrated by findings from Chapter 3 that visual-proprioceptive conflict caused a robust yet small tactile localization bias. In the case of DS reported in Chapter 2, given consistent directional biases in proprioceptive judgments of hand position and tactile localization, it is possible that the tactile localization bias was caused by biases in external tactile localization following proprioceptive biases. One possibility is that the lesion affected the integration of external information and somatotopic representation, magnifying the weights assigned to feedback external information. A second constraint is that touch is localized within the boundary of the skin surface. In DS, tactile localization judgments clustered around the border of the hand surface, suggesting extreme tactile localization biases yet constrained by the hand border.
It is worth noting that across the experiments, participants made explicit judgments of perceived tactile locations. This brings up the potential possibility that hand posture influences the conscious response stage, but not perception per se. For example, one possibility is that without having to make conscious judgments, the perceived tactile location on the skin surface remained invariant to different hand postures. Dissociations between explicit responses and unconscious information processing has been reported in research on visual system. For example, when a tilted Gabor patch was presented in the peripheral visual field, acuity in orientation discrimination decreased when the Gabor patch was flankered by other Gabor patches (“crowding”; Rajimehr, Montaser-Kouhsari, & Afraz, 2003; also see Bi, Cai, Zhou, & Fang, 2009). In one study, a target orientation stimulus along with flankers was presented for four seconds for adaptation, followed by a test stimulus in either the same or orthogonal orientation with the target (Rajimehr et al., 2003). Although participants were at chance level reporting the target orientation during adaptation, they were more accurate reporting the test orientation when it was orthogonal to the target orientation versus same, demonstrating adaptation effects. These findings indicate that although the information regarding the target orientation could not be consciously accessed, the information was still perceived to an extent that it influenced behavior. Neuroimaging studies found that orientation-selective neural responses were preserved despite crowding (Bi et al., 2009), suggesting the crowding effects occurred at later stages than the initial sensory processing.

Given evidence from the visual domain, it is likely that tactile localization also involves multiple stages. First, there is an initial processing stage by which information regarding tactile location is processed. Such information may or may not be available for
conscious report. Then, there is a later stage where the tactile location information enters consciousness and can be explicitly reported. Importantly, information explicitly reported may not completely preserve the output from the initial processing stage, combining information from additional sources to make a conscious responses. On this assumption, the initial processing stage of tactile localization can still be serial, such that the represented tactile location on the skin surface is not influenced by external information, and information from external space only influences the later, conscious report stage. Given that we always had participants provide explicit responses, it is difficult to dissociate the sensory versus response stages. Future studies can develop implicit tactile localization tasks to investigate whether there are also multiple stages in tactile perception, and at which stage external information influences tactile location representation on the skin surface.

6.3. Neural correlates of integration of external information and somatotopic representation

With behavioral evidence that external information does influence tactile localization on the skin surface, the next question is what brain areas integrate information from external space with somatotopic representation. In patient DS reported in Chapter 2, tactile localization on the skin surface was strongly influenced by hand posture. From the DTI analyses, DS’s subcortical lesion at anterior and superior corona radiata primarily disrupted fiber tracts connecting the thalamus and superior frontal gyrus including pre-SMA. The role of pre-SMA in processing somatosensory information has not been widely tested. Previous studies found somatosensory-evoked potentials in pre-SMA with middle
latency (50-150ms; Barba et al., 2001; 2005), suggesting that pre-SMA processes somatosensory information at later stages. A speculative account is that the later stage processes involves feedback from external to somatotopic representations. Future studies are needed to examine the function of pre-SMA in somatosensory processing.

6.4. Conclusion

In summary, this dissertation provided strong evidence, from both brain-damaged and neurologically intact individuals, that information from external space influences tactile localization on the skin surface. The findings indicate that tactile localization is not a strict serial process by which information flows from somatotopic space to external space in one direction. Instead, there are feedback processes by which information from external space influences somatotopic representation, forming interactive loop between representations in multiple reference frames. The exact neural mechanism of how information from external and somatotopic space is integrated remains to be investigated. One potential possibility is that such integration process is carried by brain areas that computes motor information based on sensory cues.
REFERENCES


with pure sensory stroke. *Archives of Physical Medicine and Rehabilitation, 84*(11), 1692-1702.


APPENDIX A
DIFFUSION-WEIGHTED IMAGING ANALYSIS ON DS

Given that DS had white matter damage in his T1-weighted scan, we performed diffusion-tenser imaging (DTI) to investigate integrity of fiber tracts in the right hemisphere. A DTI image was acquired using a 3.0T Siemens Magnetom Prisma scanner using an echo planar sequence (TE = 106.0 ms, TR = 5300 ms, voxel size = 1.4 \times 1.4 \times 4 \text{ mm}, 35 sagittal slices) with 64 diffusion-directions with a diffusion weighting of $b = 1000$ and $b = 0$. A T1-weighted structural image was acquired using an MPRAGE sequence (TR = 2080.0 ms, TE = 4.64 ms, flip angle = 7°, voxel size = 0.7 \times 0.7 \times 0.7 \text{ mm}, 208 sagittal slices).

Images were processed and analyzed using the FSL package (FMRIB Software Library v5.0, Oxford, UK). For preprocessing, the diffusion-weighted image was first corrected for eddy currents and susceptibility. Next, the 3D image with no diffusion weighting ($b=0$) was brain-extracted using the BET tool, and then co-registered to the T1-weighted structural image.

Tractography analyses were performed using the FDT diffusion toolbox in FSL. First, diffusion parameters were estimated using the BEDPOSTX tool. Next, tractography was done using the ProbtrackX tool (number of samples = 5000, curvature threshold = 0.2). In addition, a whole-brain map of fractional anisotropy (FA) values was obtained using the DTIFIT toolbox in FSL.
Given our interest in DS’s somatosensory perception, we first investigated the integrity of fiber tracts connecting the thalamus and S1 in both hemispheres. To do this, we created masks on the entire thalamus and one axial slices on the S1 hand area in each hemisphere in the extracted T1-weighted image. For the thalamus, we first created masks in the standard MNI (Montreal Neurological Institute) brain template based on the Harvard-Oxford Subcortical Structural Atlas, and then transformed the masks to DS’s T1-weighted space. For each hemisphere, we ran two tractographic analyses, one with the thalamus mask as seed space and SI hand area mask as a waypoints mask, the other in the opposite direction. From each tractography analysis, a map was generated where the value of each voxel represents the number of samples that went through that voxel from the seed space. This map was then thresholded such that only voxels that contained at least 10% of the maximal number of samples were kept (Azadbakht et al., 2015; Rafal et al., 2015). These maps were used to render 3D views of the fiber tracts.

To quantify the strength of connectivity, we calculated mean FA values across voxels that contained fiber tracts. To do this, we first created a binary fiber tracts mask with 1’s in voxels that survived thresholding in both tractography directions and 0’s elsewhere. Then, we transformed the FA-value map from the diffusion space to the T1-weighted structural space. This new FA-value map was then masked by the fiber tracts mask for calculating the mean FA values across voxels containing the fiber tracts.

Figure A1 displays the fibers tracts between the thalamus and S1 hand area in both hemispheres. Fiber pathways between the thalamus and S1 are intact in the ipsilesional (right) hemisphere. We also found similar connectivity strength between thalamus and SI hand area in both hemispheres: Mean FA value of 0.40 in the contralesional (left)
hemisphere, and 0.46 in the ipsilesional (right) hemisphere. These findings indicate that pathways from the thalamus to S1 were not affected by the lesion, and are consistent with the intact tactile detection on DS’s contralateral hand.

![Probabilistic tractography between the thalamus and S1 hand area in each hemisphere. M1 hand knob refers to the hand area in primary motor cortex as a landmark for visualization.](image)

Figure A 1. Probabilistic tractography between the thalamus and S1 hand area in each hemisphere. M1 hand knob refers to the hand area in primary motor cortex as a landmark for visualization.

We also examined the connection between the primary and secondary somatosensory cortex (S2). Using neuroanatomical tracers, previous studies demonstrated connection between primary and secondary somatosensory cortex in monkeys (Disbrow, et al., 2003). In humans, secondary somatosensory cortex was more activated during manipulation of complex vs. simple objects (Binkofski et al., 1999, also see Reed, Shoham, & Halgren, 2004), indicating its role in higher-level tactile perception. We therefore investigated whether DS’s impairment in tactile localization could have been caused by disruption of connection between S1 and S2. To do this, we manually created masks in DS’s T1-weighted structural space at estimated S2 area in parietal operculum. In each hemisphere, two tractography analyses were performed, one with the S1 hand mask as the seed, and the S2 mask as waypoints and termination, the other in the opposite direction. As
shown in Figure A2, connection between S1 hand area and S2 was not disrupted by the lesion. The strength of connectivity was comparable between the two hemispheres, with a mean of 0.32 in the ipsilesional (right) hemisphere, and 0.37 in the contralesional hemisphere.

Figure A 2. Probabilistic tractography between the S1 hand area and S2 in each hemisphere. M1 hand knob refers to the hand area in primary motor cortex as a landmark for visualization.

We then investigated which fiber tracts were likely disrupted by the lesion. This cannot be directly studied in the lesioned hemisphere because the target fiber tracts were already disrupted. Instead, we examined which fiber tracts travel through the superior and anterior corona radiata in the contralesional, left hemisphere. To do this, we first manually masked the lesion in the ipsilesional (right hemisphere). Then we flipped the lesion to the contralesional hemisphere to obtain a “mirrored lesion” mask. Next, we ran tractography analyses with the contralesional thalamus mask as the seed and the mirrored lesion area as the waypoints mask. The idea is to examine what fiber tracts would have existed had there not been a lesion. Of interest was which cortical area the fiber tracts terminate at.
Figure A3 displays a 3D view of the fiber pathways from the contralesional thalamus through the mirrored lesion mask. There are two major pathways, one terminating at dorsal premotor cortex, the other at superior frontal gyrus, including pre-supplementary motor area (pre-SMA). Figure A4 displays selected slices showing the starting and terminating points, as well as where the fiber tracts when through the mirrored lesion area.

Figure A3. 3D view of probabilistic tractography from contralesional thalamus through the mirror lesion area. The thalamus is displayed in sagittal view for visualizing where the fiber tracts meet the thalamus in anterior-posterior dimension. CS: central sulcus.
As can be seen in Figure A4, the fiber tracts terminating at dorsal premotor cortex went through the posterior border of the mirrored-lesion mask. To ensure that the fiber tracts were not accidentally revealed due to potential biases in creating the mask, we ran additional analyses to confirm this finding. First, we created masks in premotor cortex in the ipsilesional (right) hemisphere based on the landmarks from past literature (Ahdab et al., 2014). Next, a tractography analysis was performed with the thalamus mask as seed and premotor mask as termination as well as waypoints. If the connection between the thalamus and premotor cortex was indeed disrupted by the lesion, no fiber tracts would be
detected. Nevertheless, the analysis revealed fiber pathways from the thalamus to the premotor cortex that went through the border of the actual lesion (Figure A5), suggesting that although the area was affected by the infarct, the fiber pathways were intact.

![Figure A 5. Multi-slice view of the fiber tracts between the thalamus and the premotor cortex in ipsilesional (right) hemisphere, shown in FA values.](image)

We then did a further analysis to compare the fiber pathways connecting the thalamus and premotor cortex between the two hemispheres, to confirm that the fiber pathways in the ipsilesional (right) hemisphere were indeed intact. To do this, in each hemisphere, we created an axial “wirepoints” mask in the premotor cortex along the fiber tracts found from the previous analyses. Next, we masked the thalamic area in each hemisphere that is connected with premotor cortex based on the Oxford Thalamic Connectivity Probability Atlas. If the fiber tracts found in the previous analyses were anatomically valid, there would be fiber tracts between the premotor wirepoints masks and the atlas-based thalamus masks. In each hemisphere, we ran two tractography analyses, one with the premotor wirepoints mask as seed and atlas-based thalamus mask as termination, and the other in the opposite direction. We then calculated mean FA across voxels shared by fiber tracts in both directions in each hemisphere.
As displayed in Figure A6, connection between the premotor wirepoints mask and atlas-based thalamus mask was found in both hemispheres. In addition, the mean FA values were comparable between the two hemispheres, with 0.38 in the left (contralesional) hemisphere and 0.41 in the right (ipsilesional) hemisphere. These findings indicate that fiber tracts between the thalamus and premotor cortex were intact in the ipsilesional hemisphere, and the lesion primarily disrupted fiber tracts connecting the thalamus and superior frontal gyrus.

Figure A 6. Multi-slice view of the fiber tracts between the premotor wirepoints mask and atlas-based thalamus mask in both hemispheres, shown in FA values.
APPENDIX B

ADDITIONAL FIGURES AND ANALYSES ON EXPERIMENT 3.1 TO 3.3

Experiment 3.1: Effects of visual-proprioceptive conflict on tactile localization

Figure B1 displays average judgments for each target location in each condition.

Figure B 1. Average judgments for each target location in each condition in Experiment 3.1. Unless otherwise noted, bias bars indicate 95% within-subjects confidence intervals (Cousineau, 2005). The black dots represent actual stimulus locations.
Experiment 3.2: Controlling for the effects of hand position on tactile localization

Figure B2 displays average judgments for each target location in each condition.

Figure B 2. Average judgments for each target location in each condition in Experiment 3.2. The black dots represent actual stimulus locations.
Experiment 3.3. Controlling for the effects of gaze-proprioceptive spatial mismatch on tactile localization

Figure B3 displays average judgments for each target location in each condition.

Figure B 3. Average judgments for each target location in each condition in Experiment 3.3. The black dots represent actual stimulus locations.

Proximal-distal localization bias

First, an ANOVA was performed on the incongruent conditions across Experiment 3.1 and 3.3 (Figure B4a). There was a main effect of Proprioceptive Position (F (1,39) = 14.48, p < .001), with more distal biases when the hand was at a lateral position (10°: M = -0.49 units, SD = 0.75 units) vs. medial (4°: M = -0.23 units, SD = 0.75 units). The main effect of Visual Content was not significant (F (1,39) = 0.41, p = .527; View hand: M = -
0.45 units, $SD = 0.83$ units; View object: $M = -0.26$ units, $SD = 0.57$ units.). The interaction was not significant ($F (1,39) = 3.57, p = .066$).

Next, an ANOVA was performed on the congruent conditions across Experiment 3.1 and 3.3 (Figure B4b). No main effects or interaction were significant (Proprioceptive Position: $F (1,39) = 1.51, p = .226$; Visual Content: $F (1,39) = 2.32, p = .136$; interaction: $F (1,39) = 1.75, p = .193$). These findings are consistent with previous studies that when gaze direction was congruent with hand posture, tactile localization did not differ whether individuals were viewing a hand or object (Medina et al., 2018).
Figure B 4. a. Proximal-distal localization bias in the incongruent conditions in Experiment 3.1 and 3.3. b. Proximal-distal localization bias in the congruent conditions in Experiment 3.1 and 3.3. Error bars are 95% CI calculated from the raw data.
APPENDIX C

IRB APPROVAL
DATE: March 21, 2019

TO: Jared Medina, Ph.D.
FROM: University of Delaware IRB


SUBMISSION TYPE: Continuing Review/Progress Report

ACTION: APPROVED
APPROVAL DATE: March 21, 2019
EXPIRATION DATE: April 2, 2020
REVIEW TYPE: Expedited Review

REVIEW CATEGORY: Expedited review category # (4,7)

Thank you for your submission of Continuing Review/Progress Report materials for this research study. The University of Delaware IRB has APPROVED your submission. This approval is based on an appropriate risk/benefit ratio and a study design wherein the risks have been minimized. All research must be conducted in accordance with this approved submission.

This submission has received Expedited Review based on the applicable federal regulation. Please remember that informed consent is a process beginning with a description of the study and insurance of participant understanding followed by a signed consent form. Informed consent must continue throughout the study via a dialogue between the researcher and research participant. Federal regulations require each participant receive a copy of the signed consent document.

Please note that any revision to previously approved materials must be approved by this office prior to initiation. Please use the appropriate revision forms for this procedure.

All SERIOUS and UNEXPECTED adverse events must be reported to this office. Please use the appropriate adverse event forms for this procedure. All sponsor reporting requirements should also be followed.

Please report all NON-COMPLIANCE issues or COMPLAINTS regarding this study to this office. Please note that all research records must be retained for a minimum of
three years.

Based on the risks, this project requires Continuing Review by this office on an annual basis. Please use the appropriate renewal forms for this procedure.

If you have any questions, please contact Renee Stewart at (302) 831-2137 or stewartr@udel.edu. Please include your study title and reference number in all correspondence with this office.
DATE: February 14, 2019

TO: Jared Medina
FROM: University of Delaware IRB

STUDY TITLE: [1025292-4] Examining Somatosensory Plasticity After Stroke

SUBMISSION TYPE: Continuing Review/Progress Report

ACTION: APPROVED
APPROVAL DATE: February 14, 2019
EXPIRATION DATE: March 14, 2020
REVIEW TYPE: Expedited Review

REVIEW CATEGORY: Expedited review category # (9)

Thank you for your submission of Continuing Review/Progress Report materials for this research study. The University of Delaware IRB has APPROVED your submission. This approval is based on an appropriate risk/benefit ratio and a study design wherein the risks have been minimized. All research must be conducted in accordance with this approved submission.

This submission has received Expedited Review based on the applicable federal regulation. Please remember that informed consent is a process beginning with a description of the study and insurance of participant understanding followed by a signed consent form. Informed consent must continue throughout the study via a dialogue between the researcher and research participant. Federal regulations require each participant receive a copy of the signed consent document.

Please note that any revision to previously approved materials must be approved by this office prior to initiation. Please use the appropriate revision forms for this procedure.

All SERIOUS and UNEXPECTED adverse events must be reported to this office. Please use the appropriate adverse event forms for this procedure. All sponsor reporting requirements should also be followed.

Please report all NON-COMPLIANCE issues or COMPLAINTS regarding this study...
to this office. Please note that all research records must be retained for a minimum of three years.

Based on the risks, this project requires Continuing Review by this office on an annual basis. Please use the appropriate renewal forms for this procedure.

If you have any questions, please contact Renee Stewart at (302) 831-2137 or stewartr@udel.edu. Please include your study title and reference number in all correspondence with this office.
DATE: July 11, 2019

TO: Timothy Vickery, PhD
FROM: University of Delaware IRB

STUDY TITLE: [932881-5] Neural networks underlying the integration of knowledge and perception: MRI studies
SUBMISSION TYPE: Continuing Review/Progress Report

ACTION: APPROVED
APPROVAL DATE: July 11, 2019
EXPIRATION DATE: July 21, 2020
REVIEW TYPE: Expedited Review
REVIEW CATEGORY: Expedited review category # (4, 7)

Thank you for your Continuing Review/Progress Report submission to the University of Delaware Institutional Review Board (UD IRB). The UD IRB has reviewed and APPROVED the proposed research and submitted documents via Expedited Review in compliance with the pertinent federal regulations.

As the Principal Investigator for this study, you are responsible for and agree that:

• All research must be conducted in accordance with the protocol and all other study forms as approved in this submission. Any revisions to the approved study procedures or documents must be reviewed and approved by the IRB prior to their implementation. Please use the UD amendment form to request the review of any changes to approved study procedures or documents.
• Informed consent is a process that must allow prospective participants sufficient opportunity to discuss and consider whether to participate. IRB-approved and stamped consent documents must be used when enrolling participants and a written copy shall be given to the person signing the informed consent form.
• Unanticipated problems, serious adverse events involving risk to participants, and all non-compliance issues must be reported to this office in a timely fashion according with the UD requirements for reportable events. All sponsor reporting requirements must also be followed.

Oversight of this study by the UD IRB REQUIRES the submission of a CONTINUING REVIEW seeking the renewal of this IRB approval, which will expire on July 21, 2020. A continuing review/progress report form and up-to-date copies of the protocol form and all other approved study materials must be submitted to the UD IRB at least 45 days prior to the expiration date to allow for the required IRB review of that report.

If you have any questions, please contact the UD IRB Office at (302) 831-2137 or via email at hsrb-research@udel.edu. Please include the study title and reference number in all
correspondence with this office.