



**HAL**  
open science

# Somatosensation and plasticity: perceptual, cognitive, and physiological effects

Malika Azaroual-Sentucq

► **To cite this version:**

Malika Azaroual-Sentucq. Somatosensation and plasticity: perceptual, cognitive, and physiological effects. Neuroscience. Université Claude Bernard Lyon 1, 2024. English. NNT : . tel-04929785

**HAL Id: tel-04929785**

**<https://hal.science/tel-04929785v1>**

Submitted on 4 Feb 2025

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

**THESE de DOCTORAT DE  
L'UNIVERSITE CLAUDE BERNARD LYON 1**

**Ecole Doctorale N° 476  
Neurosciences et Cognition**

**Discipline : Neurosciences**

Soutenue publiquement le 13/12/2024, par :  
**Malika Azaroual-Sentucq**

---

**Somatosensation and plasticity:  
perceptual, cognitive, and physiological  
effects**

---

Devant le jury composé de :

<b>Macaluso, Emiliano</b>	Pr. Université Lyon 1	Président
<b>Auvray, Malika</b>	Dr. Institut des Systèmes Intelligents et de Robotique (ISIR)	Rapporteure
<b>Heed, Tobias</b>	Pr. Paris Lodron University Salzburg	Rapporteur
<b>Kilteni, Konstantina</b>	Pr. Radboud University	Examinatrice
<b>Dijkerman, Chris</b>	Pr. Utrecht University	Examineur
<b>Farnè, Alessandro</b>	Dr. Centre de Recherche en Neurosciences de Lyon (CRNL), U1028	Directeur de thèse
<b>Muret, Dollyane</b>	Dr. Neurodiderot, UMR 1141	Co-directrice de thèse



“The seeker after the truth is not one who studies the writings of the ancients and, following his natural disposition, puts his trust in them, but rather the one who suspects his faith in them and questions what he gathers from them, the one who submits to argument and demonstration, and not to the sayings of a human being whose nature is fraught with all kinds of imperfection and deficiency.

The duty of the man who investigates the writings of scientists, if learning the truth is his goal, is to make himself an enemy of all that he reads, and, applying his mind to the core and margins of its content, attack it from every side. He should also suspect himself as he performs his critical examination of it, so that he may avoid falling into either prejudice or leniency.”

Hasan Ibn al-Haytham (a.k.a. Alhazen, the “Father of modern scientific method”), *Aporias against Ptolemy*, 11<sup>th</sup> century. [from Sabra A.I. (2003), Harvard magazine]



## REMERCIEMENTS - ACKNOWLEDGEMENTS

First and foremost, I would like to express my heartfelt gratitude to the jury members – Dr. Auvray, Prof. Heed, Prof. Kilteni, and Prof. Dijkerman – for kindly agreeing to evaluate my work and engage in interesting discussions with me. I truly appreciated and enjoyed our exchanges. Thank you all! I would also like to extend my thanks to the members of the PhD progress committee (“comité de suivi de thèse”), Dr. Reilly and Dr. Xerri, for their feedback and guidance throughout this journey.

Pour ces quatre années de travail, je tiens à débiter en adressant mes sincères et profonds remerciements à Alessandro et Dollyane. Un immense merci à vous, pour le temps et l'énergie que vous avez consacrés à encadrer mon travail, pour vos encouragements constants, et vos précieux feedbacks, exigeants, toujours très justes et constructifs, et qui m'ont tiré vers le haut. Je me suis vue progresser au fil de nos meetings, et je vous en suis infiniment reconnaissante. Merci d'avoir assuré mon encadrement avec autant de dévouement et de bienveillance tout au long de ces années. Merci de m'avoir guidée et d'avoir fait de moi la chercheuse que je suis aujourd'hui ! :)

Ensuite, je souhaite exprimer ma profonde gratitude à Silvia, qui m'a co-encadrée à mon arrivée au laboratoire en Master 2. Je n'oublie pas mes premiers pas au labo que tu as si gentiment accompagnés, et les premières manip où tu m'as rigoureusement formée aux tâches psychophysiques. Merci de m'avoir plongée dans le bain et de m'avoir transmis ton expertise, les bons réflexes et les bonnes pratiques en manip.

Je tiens également à remercier Luke Miller pour ses contributions aux études et pour m'avoir formée à l'analyse des données EEG, ainsi que Cécile Fabio pour m'avoir formée à l'acquisition des données EEG. Je vous suis profondément reconnaissante pour votre temps et votre dévouement.

Mes remerciements vont ensuite aux étudiantes qui ont travaillé avec moi et ont consacré beaucoup de leur temps et énergie pour que les manip tournent en toutes circonstances : Maria, Précillia, Oumnia, Valentina et Fatma, avec une mention spéciale à Oumnia, qui s'est dévouée outre-mesure et m'a beaucoup soulagée dans mes périodes plus chargées. Dans ce travail, un remerciement tout particulier va à mon informaticien préféré, mon frère Ayoub, qui m'a patiemment aidée à créer et débiter tous mes scripts Matlab. Merci d'avoir répondu présent à toutes mes sollicitations, même les plus « last-minute » et d'avoir pris de ton précieux temps pour me soulager.

Je remercie aussi Fred pour la construction et l'adaptation du matériel de manip. Merci d'avoir toujours apporté une solution à nos besoins spécifiques, et merci de ta persévérance pour que tout soit optimisé ! Et un tout aussi grand merci à Roméo et Éric pour leur aide précieuse sur les setups. Merci à vous deux d'avoir toujours apporté une réponse à mes demandes, vous m'avez été d'une grande aide ! Sans oublier Sonia, Jean-Louis et Cécile T., merci à vous trois d'avoir été si disponibles et d'avoir facilité grandement mes démarches administratives.

Un grand merci aussi à Ali, qui s'est montré toujours disponible pour participer à mes manip, le « pilote 001 » de toutes mes expériences. Merci d'avoir toujours pris de ton temps pour ça

malgré ton emploi du temps chargé ! Et merci à Tristan pour le soutien moral. C'est toujours un plaisir d'échanger sur les difficultés de recrutements et autres joies de l'expérimentation !

À Clara et Marion, un immense merci pour votre présence, votre soutien émotionnel et pour tous les services rendus. Vous avoir à mes côtés depuis le début de cette aventure, et savoir que je pouvais toujours compter sur vous, c'était très rassurant, je vous en remercie infiniment !

Plus généralement, je tiens à exprimer ma gratitude envers chaque membre de l'équipe Impact qui rendent l'environnement de travail très agréable. Travailler dans ce cadre sain, nourri d'empathie et de bienveillance, a été une véritable source d'épanouissement pour moi et m'a aidée à grandir en tant que chercheuse. Je tiens à remercier spécifiquement Denis, David, Fadila, Marine et Gérard pour leurs conseils, toujours donnés avec gentillesse. Plus largement encore, je remercie le personnel de l'école doctorale, et notamment Geoffrey Maillard, pour sa disponibilité et réactivité.

Au-delà du laboratoire, je remercie toutes celles et ceux qui m'ont permis de garder un équilibre sain et ont contribué d'une façon ou d'une autre à faciliter mon quotidien. Merci à mes amies de toujours, Sarah et Diana. Merci à vous deux pour votre présence et votre soutien dans cette grande aventure, merci pour vos encouragements et votre positivité constante ! J'adresse un grand merci à ma famille et ma belle-famille, à toutes celles et ceux qui m'ont fait ressentir leur soutien et leur fierté, qui m'ont donné encore plus d'énergie pour aller jusqu'au bout. Petite mention spéciale à Dr. Ammy, pour son soutien et ses encouragements. Merci d'avoir partagé ton expérience de thèse avec moi, et de m'avoir toujours comprise et conseillée !

Un immense merci à mes sœurs et mon frère, Radia, Elhame, Shehrazade et Ayoub, pour m'avoir aidée à relativiser dans les moments les plus difficiles de cette thèse. Merci pour votre soutien, votre amour, vos prières, et de m'avoir cru capable d'y arriver (j'y suis arrivée ! on y est arrivés tous ensemble ! :D). Merci aussi à Saad et Amina d'avoir été là et de m'avoir témoigné votre soutien !

Merci du fond du cœur à Hakim, mon mari, pour son soutien indéfectible et pour avoir vécu cette aventure de thèse si intensément à mes côtés, d'avoir été là pour fêter les petites victoires et consoler les petites déceptions. Et surtout, merci à toi d'avoir enduré ces derniers mois au plus près de moi !

Enfin, pour clôturer ces remerciements comme il se doit, j'adresse ma plus profonde gratitude et reconnaissance à mes parents bien-aimés, pour leur accompagnement dans cette thèse et dans la vie, et pour leur soutien sans faille depuis toujours. Sans leur amour, leurs conseils, leurs prières et leur immense soutien, je n'aurais jamais pu accomplir ce travail. Je suis honorée de rejoindre aujourd'hui la team des Dr. Azaroual, et de marcher (au moins un petit peu) dans les pas de baba. Mama, baba, les mots ne sont pas assez lourds pour refléter ma gratitude, mais je vous le dis comme je le peux, et comprenez-le au-delà des mots : merci infiniment, pour votre contribution à cette thèse, et pour absolument tout.







## ABSTRACT

Somatosensation is an essential function for human perception, action and cognition, being crucial for fine motor skills and self bodily awareness. My PhD work is interested in somatosensation and its plasticity at cognitive, perceptual and physiological levels.

While it is widely accepted that somatosensation contributes to building multiple mental body representations (MBRs), its contribution to each MBR remains unclear. A first aim of my work was to answer this question by leveraging repetitive somatosensory stimulation (RSS), known to temporarily improve tactile acuity (TA) by inducing plastic changes in the primary (SI) and secondary (SII) somatosensory cortex. This randomized sham-controlled double-blind study conducted on 33 adults investigated the effects of RSS on three MBRs of the stimulated right index finger (rD2): the body image (BI), the body model, and the superficial schema. The results revealed that the BI is selectively affected by RSS, as the stimulated rD2 was perceived significantly smaller after RSS, while the other MBRs were left unaffected. This suggests that somatosensory processes contribute differently to the BI than to the other two MBRs.

Somatosensation can be assessed by measuring TA. Accurately measuring this feature of touch is essential as it is used in clinical practice and research attempting to restore tactile perception. A widely used -but criticized- task is the two-point discrimination task (2PDT), while the grating orientation (GOT) and two-point orientation (2POT) tasks are suggested to be more reliable alternatives. Critically, whether these tasks measure similar aspects of TA has yet to be determined. The second aim of my thesis was to answer this question by comparing the performance in these tasks and linking them to anatomical measures at the fingertips, and by leveraging RSS. In this study, RSS was applied on the rD2 of 29 adults and its impact on the tasks was assessed at the rD2 as well as at the ID2 (control) and ID3 which has been recently found to display TA improvement following RSS. At baseline, 2POT and GOT correlated to the fingertip area. Following RSS, 2PDT and GOT were both improved at the rD2, 2PDT and 2POT also at ID3. Overall, the results suggest that the three tasks capture both similar and different aspects of TA.

Because RSS is used to induce plasticity in the somatosensory system, understanding its mechanisms of action is important. While cortical changes in the SI and SII representations of the stimulated finger have been associated to the local effect of RSS, the physiological mechanisms responsible for local and remote effects (on the unstimulated hand) have not been explored yet. My third aim was to investigate them through EEG, testing the hypothesis of a modulation of cortical inhibition between the fingers' representations of both hands. This study is made of two randomized sham-controlled double-blind experiments, each conducted on 41 adults, undergoing EEG and 2PDT. Because we identified a methodological bias in our first design, we conducted a second experiment aimed at obviating it. We found that after both sham and RSS, the intra- and inter-hemispheric inhibition significantly increased, potentially driven by the inhibition increase between ID2 and ID3 and between ID3 and rD3 which appear (non-significantly) larger than in other pairs, as well as larger after RSS than sham. Because of potential issues also in the second experiment, these results are preliminary, and another

experiment is planned to solve them. The final experiment would hopefully clarify if RSS affects inhibition.

Overall, studying somatosensation at multiple levels, my work shows that somatosensation contributes differently to the BI than to the other MBRs, which allows to refine current MBR models, and multiple tasks should be used to comprehensively assess TA, while it does not allow to conclude on the neural mechanisms underlying the effects of RSS.

## RÉSUMÉ

La somatosensation est essentielle pour la perception, l'action et la cognition, déterminante pour la motricité fine et la conscience de soi. Mon doctorat s'intéresse à la somatosensation et à sa plasticité aux niveaux cognitif, perceptif et physiologique.

S'il est admis que la somatosensation contribue à la construction de multiples représentations mentales du corps (MBRs), sa contribution à chaque MBR reste floue. Le premier objectif de mon travail était de répondre à cette question en exploitant la stimulation somatosensorielle répétée (RSS), connue pour améliorer temporairement l'acuité tactile (AT) via des changements plastiques dans le cortex somatosensoriel primaire (SI) et secondaire (SII). Cette étude randomisée en double aveugle contre sham, menée sur 33 adultes, a étudié les effets de la RSS sur trois MBR de l'index droit stimulé (rD2) : l'image corporelle (BI), le modèle corporel et le schéma superficiel. Les résultats révèlent que la BI est sélectivement affectée par la RSS, le rD2 étant perçu plus petit après la RSS, tandis que les autres MBRs n'ont pas été affectées. Cela suggère que la somatosensation contribue différemment à la BI qu'aux autres MBRs.

La somatosensation peut être évaluée par la mesure de l'AT, mesure essentielle en clinique et dans la recherche sur la restauration tactile. Une tâche courante mais critiquée est le test de discrimination de deux points (2PDT), tandis que les tâches d'orientation de grille (GOT) et d'orientation de deux points (2POT) sont considérées plus fiables. Il reste à déterminer si elles mesurent des aspects similaires de l'AT. Le deuxième objectif de ma thèse était de répondre à cette question en comparant les performances dans ces tâches, les reliant à des mesures anatomiques des doigts, et en utilisant la RSS. Dans cette étude, la RSS a été appliquée au rD2 de 29 adultes et son impact sur les tâches a été évalué au rD2, ID2 (contrôle) et ID3, sur lequel on a récemment montré une amélioration de l'AT après la RSS. Le 2POT et le GOT étaient corrélés à la surface du bout des doigts. Après la RSS, le 2PDT et le GOT se sont améliorés au rD2, et le 2PDT et le 2POT également au ID3. Les résultats suggèrent que les trois tâches mesurent à la fois des aspects similaires et distincts de l'AT.

La RSS étant utilisée pour induire une plasticité dans le système somatosensoriel, il est important de comprendre ses mécanismes d'action. Alors que les changements corticaux dans les représentations SI et SII du doigt stimulé ont été associés à l'effet local de la RSS, les mécanismes responsables des effets locaux et distants restent inexplorés. Mon troisième objectif était d'étudier ces mécanismes via l'EEG, en testant l'hypothèse d'une modulation de l'inhibition corticale (IC) entre les représentations des doigts des deux mains. Cette étude comporte deux expériences randomisées en double aveugle contre sham, chacune menée sur 41 adultes, soumis à un EEG et un 2PDT. Un biais méthodologique ayant été identifié dans notre premier protocole,

une seconde expérience a été réalisée pour y remédier. Nous avons constaté qu'après sham et RSS, l'IC intra- et inter-hémisphérique augmentait significativement, possiblement grâce à l'augmentation de l'IC entre ID2 et ID3 et entre ID3 et rD3, (non significativement) plus élevée que dans les autres paires et plus élevée après RSS que sham. En raison de problèmes potentiels dans la deuxième expérience également, ces résultats sont préliminaires et une nouvelle expérience est prévue pour les clarifier. La dernière expérience devrait permettre de déterminer si la RSS affecte l'inhibition.

En somme, en explorant la somatosensation à différents niveaux, mon travail montre qu'elle contribue différemment à la BI qu'aux autres MBRs, permettant ainsi d'affiner les modèles actuels. Il montre aussi que plusieurs tâches devraient être utilisées pour évaluer pleinement l'AT. En revanche, il ne permet pas de conclure sur les mécanismes neuronaux qui sous-tendent les effets de la RSS.



## LIST OF ABBREVIATIONS

CNS	Central nervous system
CN	Cuneate nucleus
DH	Dorsal horn
DCN	Dorsal column nuclei
PSDC	Postsynaptic dorsal column
VPL	Ventroposterior lateral nucleus
IPS	Intraparietal sulcus
IPL	Inferior parietal lobule
LOC	Lateral occipital complex
EBA	Extrastriate body area
TPJ	Temporoparietal junction
SI/SII	Primary/secondary somatosensory cortex
MI	Primary motor cortex
BA 1, 2, 3a, 3b	Brodmann areas 1, 2, 3a, 3b
PPC	Posterior parietal cortex
IPS	Intraparietal sulcus
LTMR/HTMR	Low/High threshold mechanoreceptor
SAI/II & FAI/II	Slowly/rapidly adapting afferents fibers of type I or II
RF	Receptive field
NMDA	N-methyl-D-aspartate
GABA	Gamma-aminobutyric acid
STDP	Spike-timing-dependent plasticity
LTP/LTD	Long-term potentiation/depression
ICMS	Intracortical microstimulation
MBR	Mental body representation
2PDT	Two-point discrimination task
2POT	Two-point orientation task
GOT	Grating orientation task
3DT	Three-dot task
D1-5	Digits 1 to 5
rTMS	Repetitive transcranial magnetic stimulation
tDCS	Transcranial direct current stimulation
fMRI	Functional magnetic resonance imaging
BOLD	Blood oxygenation level dependent
PET	Positron emission tomography
EEG	Electroencephalography
SSI	Somatosensory suppression index
ISI	Interstimulus interval
RSS	Repetitive somatosensory stimulation



# TABLE OF CONTENT

<b>INTRODUCTION.....</b>	<b>19</b>
CHAPTER I: THE SOMATOSENSORY SYSTEM: FROM THE PERIPHERY TO THE SOMATOSENSORY CORTEX.....	21
I- The peripheral tactile afferents.....	21
1) Primary-order somatosensory neurons.....	22
2) The A $\beta$ fibers and their associated mechanoreceptors.....	22
II- From the peripheral tactile afferents to the central somatosensory cortex.....	26
1) The pathway to the somatosensory cortex.....	26
2) The somatosensory cortex.....	33
CHAPTER II: LOW- AND HIGH-LEVEL SOMATOSENSORY PROCESSING ASSESSMENT.....	44
I- Tactile acuity: peripheral and central determinants.....	44
1) Tasks assessing tactile acuity.....	44
2) Afferent fibers involved in tactile acuity.....	46
3) Limiting factors of tactile acuity.....	48
4) Cortical areas underlying tactile acuity.....	51
II- Mental body representations (MBRs).....	54
1) The MBRs and their characteristics.....	55
2) Cortical areas underlying MBRs.....	62
3) Plasticity of MBRs.....	65
CHAPTER III: SOMATOSENSORY PLASTICITY & TACTILE LEARNING.....	70
I- Somatosensory deprivation-induced plasticity.....	70
1) Permanent deafferentation-induced plasticity.....	70
2) Temporary deafferentation-induced plasticity.....	74
II- Training-dependent plasticity.....	78
1) Tactile training-dependent plasticity and local perceptual consequences.....	78
2) Transfer of tactile learning to untrained body parts.....	80
III- Training-independent plasticity and tactile learning.....	84
IV- The Hebbian plasticity.....	84
CHAPTER IV: REPETITIVE SOMATOSENSORY STIMULATION (RSS).....	88
I- RSS: a tool for experimentally inducing Hebbian plasticity.....	88
II- Plasticity and local tactile improvement.....	89



1) Plastic changes in the somatosensory cortex.....	89
2) Perceptual changes at the stimulated body part .....	90
III- Transfer of tactile learning to unstimulated body parts.....	92
1) Hand to face transfer of tactile learning .....	92
2) Hand to hand transfer of tactile learning.....	93
IV- Relevance of RSS in research and clinical rehabilitation.....	95
SUMMARY & AIMS.....	97
<b>EXPERIMENTAL CONTRIBUTIONS.....</b>	<b>99</b>
STUDY 1: COGNITIVE STUDY.....	100
STUDY 2: PERCEPTUAL STUDY .....	126
STUDY 3: ELECTROPHYSIOLOGICAL STUDY .....	154
STUDY 4: CLINICAL STUDY.....	173
<b>GENERAL DISCUSSION.....</b>	<b>175</b>
I- How do somatosensory inputs feed MBRs? .....	175
II- Training-independent tactile learning spreads to high-level cognitive MBRs.....	178
III- A novel pattern of tactile localization bias at the finger.....	180
IV- Do 2PDT, 2POT and GOT similarly measure tactile acuity? .....	182
V- Does the 2PDT measure tactile acuity? Our contribution to the discussion .....	185
VI- Different patterns at stimulated and unstimulated fingers: different mechanisms? 187	
VII- Replication of RSS-induced remote effects in its electrocutaneous version.....	187
VIII- Inducing plasticity through RSS: methodological considerations .....	188
<b>CONCLUSION &amp; PERSPECTIVES .....</b>	<b>191</b>
<b>REFERENCES.....</b>	<b>193</b>





# INTRODUCTION

Somatosensation, often referred to as the sense of touch, is fundamental to human perception, action, and cognition. It plays a vital role not only in detecting external stimuli like pressure, temperature, and pain, but also in enabling fine motor skills, such as grasping objects, typing, or playing a musical instrument. By providing detailed feedback at the hands about the texture, shape, and size of objects, touch allows us to interact with our environment with precision and dexterity. Beyond its practical functions, somatosensation is key to bodily self-awareness, contributing to our understanding of body boundaries and position in space. Together, the sensory inputs are integrated in the brain, not only to guide physical actions but also to shape cognitive processes and mental representations of the body.

While sensory signals from our skin are constantly flowing into the brain, these inputs can fluctuate dramatically, either being reduced due to injury or increased during intense sensory experiences. When such changes occur, the brain must quickly adapt, a process made possible by somatosensory plasticity. This form of plasticity refers to the ability of the somatosensory system to adapt and eventually reorganize itself in response to altered sensory inputs, allowing us to maintain effective interactions with our environment. Whether to regain sensation after nerve damage or to enhance tactile sensitivity through repeated tasks or stimulation, somatosensory plasticity plays a pivotal role in maintaining the function of tactile perception. In the case of tactile enrichment, this adaptability leads to tactile learning, during which the somatosensory system refines its responses to sensory stimuli based on experience, allowing for improved tactile perception.

My doctoral work investigated somatosensation at cognitive, perceptual and physiological levels and answers theoretical questions about mental body representations and tactile acuity - two key behaviorally relevant processes within high and low levels of the somatosensory processing - through the induction of plasticity. In other words, I leveraged somatosensory plasticity to get answers to current questions about the somatosensory system. Part of my work also aimed at investigating the physiological mechanisms underlying tactile learning induced by somatosensory plasticity. Before delving into the experimental contributions of my work, I propose four introductory chapters reviewing current knowledge about the somatosensory system (chapter I), the low- and high-level somatosensory assessment through tactile acuity tasks and mental body representations respectively (chapter II), the somatosensory plasticity

induced by tactile deprivation or enrichment (chapter III), and plasticity specifically involved in training-independent tactile learning (chapter IV).

## **CHAPTER I: THE SOMATOSENSORY SYSTEM: FROM THE PERIPHERY TO THE SOMATOSENSORY CORTEX**

Touch is an essential sense that significantly impacts how we engage with the world around us. Particularly through the hands, it supports daily activities by facilitating not only practical tasks but also enhancing our sensory experiences and interactions with our environment. Its emergence in the brain involves a sequence of processing steps from the tactile receptors in the skin to the somatosensory cortex. This chapter aims at reviewing these somatosensory processing steps from the periphery to the somatosensory cortex. It will start with an overview of peripheral tactile receptors and afferents, followed by a description of the pathway that transmits and processes tactile information, concluding with a discussion of how this information is handled and processed in the primary somatosensory cortex (SI).

### **I- The peripheral tactile afferents**

The skin, constituting the interface between our body and the external environment, is the biggest of our organs and the mediator of our sense of touch. Across our body, two types of skin can be found: (i) the hairy skin covering most of our body, and (ii) the glabrous (hair-free) skin, mainly found on the palms of our hands, pulps of our fingers and toes, and soles of our feet. Structurally different, the hairy skin having a thicker epidermis than the glabrous skin, they have different functions. The skin is structured in three main layers (from the most superficial to the deepest): (i) the epidermis, composed of keratinized epithelial cells acting as a protection barrier against environmental threats and maintaining the body's hydration level, (ii) the dermis, composed of connective tissue containing collagen and elastin fibers giving the skin its tensile strength and elasticity, and (iii) the hypodermis composed of fat and connective tissue allowing to absorb pressure, store energy and anchor the skin to the underlying structures. Besides its many roles in protection, hydration- and thermo-regulation, the skin's function I am interested in is its sensitivity to tactile stimulations, mediated by somatosensory neurons whose endings (receptors) are located mostly in the dermis and the deepest layer of the epidermis. These receptors of the somatosensory system respond to a variety of stimuli: (i) mechanoreceptors respond to mechanical stimuli, (ii) nociceptors respond to noxious stimuli and (iii) thermoreceptors respond to temperature. In contrast to somatosensory neurons sensing pain, heat and cold, which endings in the skin are free, mechanosensory neurons at the glabrous skin end in specialized structures.

## 1) Primary-order somatosensory neurons

The somatosensory neurons associated with mechanoreceptors are classified according to their degree of myelination, axon diameter and axonal conduction velocity (see Handler & Ginty, 2021 for a recent review). Neurons which have heavily myelinated afferents have the largest axonal diameter and the fastest conduction velocity (16-100 m/s). They are named A $\beta$  fibers and are found in both glabrous and hairy skin. Neurons with less myelinated afferents, smaller diameter and slower conduction velocity (5-30 m/s) are called A $\delta$  fibers and are found exclusively in hairy skin. The third type of somatosensory neurons corresponds to neurons with unmyelinated afferents, the smallest diameter and the slowest conduction (0.2-2 m/s). Known as c-fibers, these neurons represent the majority of neurons innervating the skin and are found exclusively in hairy skin. As far as threshold of activation is concerned, these somatosensory neurons fall into two categories: (i) neurons with low activation threshold (0.5-2 mN) responding to innocuous mechanical stimuli, associated with low-threshold mechanoreceptors (LTMRs), and (ii) neurons with high activation threshold responding optimally (but not exclusively) to painful mechanical stimuli, associated with high-threshold mechanoreceptors (HTMRs). A $\beta$  fibers are mostly associated with LTMRs, thus considered light-touch receptors, while the majority of A $\delta$  fibers and c-fibers innervate HTMRs. For the purpose of this thesis work, mainly focusing on light touch at the pulp of the fingers, I will describe the A $\beta$  LTMRs found at the glabrous skin in further detail.

## 2) The A $\beta$ fibers and their associated mechanoreceptors

The LTMR-associated A $\beta$  fibers are further classified in two categories based on their velocity of adaptation (i.e. reduced sensitivity of the receptor to a stimulus after prolonged exposure to it). A $\beta$  fibers firing in a phasic way at the beginning and end of a static indentation are defined as rapidly-adapting (RA) and are particularly sensitive to vibrations and movement, while A $\beta$  fibers firing in a sustained manner during a stimulus indentation are called slowly-adapting (SA). Within each category, two types of afferents are distinguished based on the size of their receptive fields (RFs), partly defined by the depth of the LTMR they innervate: type I afferents innervate superficial LTMRs and have small and well-defined RFs, while type II afferents innervate deeper LTMRs and have large and poorly defined RFs. In this respect, four types of fibers, each innervating a different LTMR type are distinguished: RA type I and II, and SA type I and II (Figure 1).

Type I rapidly-adapting fibers (RAI) are associated with Meissner corpuscles. These end-organs are oval-shaped structures of stacked lamellar Schwann cells encapsulated in a layer of

fibroblasts. They are quite superficial as they are found at the apex of dermal papillae (protrusions of dermal tissue into the epidermis), which makes them highly sensitive to skin deformation by indentation as small as  $2\mu\text{m}$  (LaMotte & Whitehouse, 1986). Each Meissner corpuscle can be innervated by up to 3 RAI fibers and a single fiber can innervate many corpuscles. This makes RAI fibers' small RFs non-uniform, with many spots of sensitivity (also called hot spots or subfields). The area of their RFs depends on the indentation depth as it expands with deeper indentation. The impulse rate of RAI afferents also increases slightly with deeper indentations (Vega-Bermudez & Johnson, 1999a). They are maximally responsive to indentation by a single point, and additional neighboring stimuli reduce the impulse rate, thus reflecting a suppression mechanism making them sensitive to spatial variations in the stimuli (Vega-Bermudez & Johnson, 1999b). Besides static stimuli, they respond best to moving and low-frequency vibrations (optimal responses at 40-60 Hz; Freeman & Johnson, 1982; Muniak et al., 2007), triggering the sensation of flutter. These characteristics allow them to best respond to stimuli moving across the skin and to encode spatial patterns and textures.

Type II rapidly-adapting fibers (RAII) are associated with Pacinian corpuscles. These large oval-shaped onion-like structures are constituted of stacked lamellar Schwann cells encapsulated in layers of perineural cells are found deep in the dermis (mostly) and in the hypodermis. They are mostly found in clusters of 2-3 corpuscles (Wu et al., 1999). Due to their depth, RAII fibers have large and uniform RFs. They have a particularly low threshold of activation (as low as  $0.01\ \mu\text{m}$ ) and they respond to sudden changes in skin pressure and high-frequency vibrations (optimal responses at 200-300 Hz; Freeman & Johnson, 1982; Muniak et al., 2007), strongly responding to textured surfaces scanned across the skin. Because of their high sensitivity and depth in the skin, they were shown to respond to distant stimuli conducted through bone (Macefield et al., 2005) and are thought to provide information about digit and joint positions and facilitate the transmission of information about distant object during tool use (Johnson et al., 2001). Until recently, they were thought to convey little or no spatial information given the size and depth of their RF. Mostly investigated with multipoint stimulators applying stimuli at a given frequency with a background of steady pressure, the spatial resolution of RAII has consistently shown to be very low (Perez et al., 2000; Tannan et al., 2005; Zhang et al., 2008). However, as stated by Cataldo et al. (2023), these results may be influenced by mechanical interactions between propagation waves on the skin or by neural interactions between SAI and RAI/II afferents, due to the background steady pressure. To avoid these influences, Cataldo et al. (2023) investigated the spatial acuity of RA fibers using focused

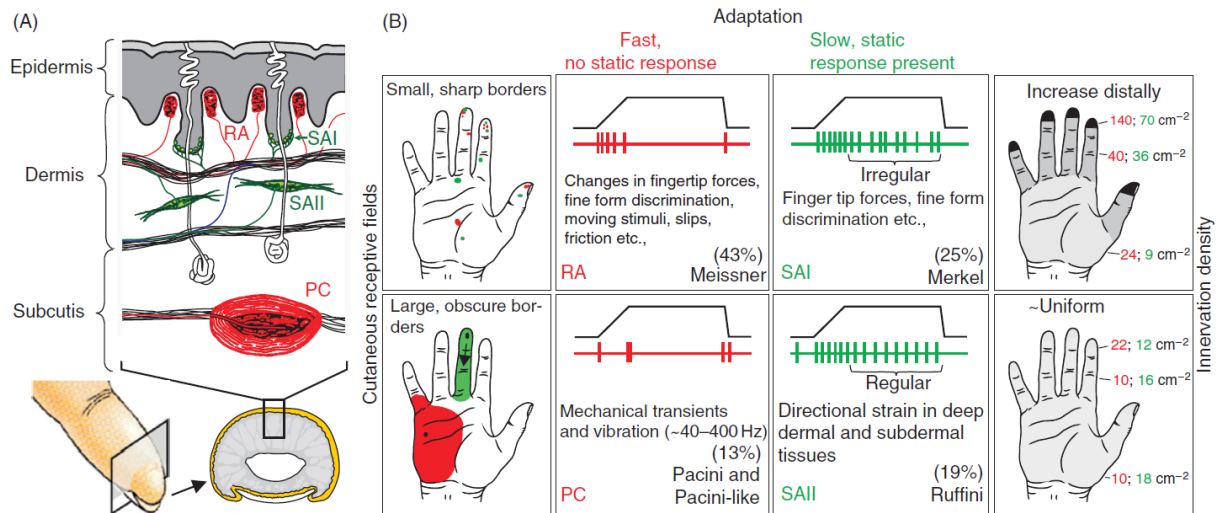


ultrasound to produce contactless precise frequency-resolved vibrotactile patterns specifically targeting each RA afferent (50 and 200 Hz preferentially activating RAI and RAII respectively). They revealed that the spatial acuity (as measured with the two-point discrimination task: 2PDT) found with the 50 Hz and 200 Hz stimuli were equivalent, indicating that RAII has higher spatial acuity than previously thought, and concluded that RAII may carry substantial spatial information (Cataldo et al., 2023).

Type I slowly-adapting fibers (SAI) end in Merkel cell-neurite complexes. These complexes are formed by an association of the SAI afferent with epithelial neuroendocrine cells called Merkel cells. Clusters of Merkel cells make synapse-like contacts with SAI fibers, with a single cluster containing up to 150 Merkel cells, and a single SAI fiber branching to contact several distinct clusters, contacting as many as 15 Merkel cells within each cluster. They are the most superficial as they are located in the basal layer of the epidermis, the *stratum basale*, mostly clustered at the base of *dermal papillae*, close to sweat ducts. The RF size of SAI fibers is comparatively the smallest, it is non-uniform with several subfields and increases with increasing indentation depth, to a much lesser extent than RAI's RFs. Sensitive to static indentation and low frequencies ( $< 10$  Hz), SAI fibers are highly responsive to contact with corners, edges and curvatures of objects, requiring very minimal skin displacement (less than 15  $\mu\text{m}$  in humans) to activate. Comprising two phases, their response to skin indentation consists in a sustained firing (dynamic phase; upon initial indentation) followed by irregular bursting (static phase; up to at least 30 min). SAI's response varies with velocity of displacement at the dynamic phase and with the amplitude (indentation depth) at both phases (Werner & Mountcastle, 1965; Vega-Bermudez & Johnson, 1999a) in a way that as the amplitude increases, the impulse rate increases as well, to a higher extent than RAI. Similar to RAI, though to a higher extent, they display a suppression mechanism when multiple points are indented, making them highly sensitive to spatial variations in the stimuli (Vega-Bermudez & Johnson, 1999b). Thus, with their higher suppression and higher responsiveness to edges, they convey a neural image of spatially patterned skin indentations with a higher spatial resolution than RAI.

Type II slowly-adapting fibers (SAII) are classically thought to end in Ruffini endings, though this is debated as they are elusive to human histology (Johnson et al., 2001; Parè et al., 2003). These spindle-shaped nerve terminals networks encased in layers of perineural tissue including Schwann cells and collagen fibers are found in the deep layers of the dermis. Each Ruffini ending is thought to be supplied by a single SAII fiber. Their RF size is large (about 5 times

larger than SAI's) and displays one central sensitive spot. As compared to SAI fibers, they are less sensitive to skin indentation and display a more regular inter-spike interval. Highly sensitive to skin stretch and tension, and densely innervating the skin around the nails (Johansson & Vallbo, 1979), they are believed to provide information about forces applied on and by the fingertips.



**Figure 1. The four classes of cutaneous afferents of the glabrous skin.** [Extracted from Delhaye, Long & Bensmaia, 2018] (A) Morphology of the different mechanoreceptors and their respective locations in the skin. (B) Adaptation properties and receptive field (RF) size of the four classes of cutaneous afferents. Rapidly adapting (sometimes referred to as fast adapting, particularly for humans) versus slowly adapting refers to responses to indentations (transient vs. sustained, respectively). Type I versus type II refers to the size of the RFs, determined in part by the depth of the mechanoreceptors in the skin: Type I fibers have small RFs whereas type II fibers have large ones. The density of innervation depends on the fiber type: Type I fibers innervate the skin more densely than do type II fibers. For example, rapidly adapting afferent type II (PC) afferents show rapidly adapting responses with large RFs and relatively low innervation density (type II).

Across the body, these mechanoreceptors are not uniformly distributed across the body, being most densely present in hands and lips, giving them their high sensitivity. At the hands, while SAII fibers innervate quite uniformly the palm and fingers, RAII innervation is higher at the fingertip than at the rest of the fingers and palm. Conversely, SAI and RAI display an increasing gradient of innervation from palm to fingertip, RAI being more densely distributed than SAI (Johansson & Vallbo, 1983; Vallbo & Johansson, 1984). While the number of SAI and RAI do not vary with the size of the hands, their densities do, with smaller hands displaying higher densities than larger hands (Bolton et al., 1966; Dillon et al., 2001; Peters et al., 2009). Overall, LTMRs of a given type often exhibit a non-overlapping arrangement across the skin (Kuehn et al., 2019; Neubarth et al., 2020) while among the different LTMR subtypes, there is significant territorial overlap (Johansson & Vallbo, 1979), which provides spatial and temporal information

about the tactile stimuli (Pruszynski & Johansson, 2014). For example, spatial patterns are encoded in the specific activation pattern they trigger in SAI and RAI fibers (Phillips et al., 1990), and possibly also in RAI fibers (carrying some amount of spatial information, see Cataldo et al., 2023). This suggests a population coding model for touch, where the central integration of various aspects of tactile stimuli give rise to our perception of the vast complexity of touch (Goodwin & Wheat, 2004).

## **II- From the peripheral tactile afferents to the central somatosensory cortex**

The tactile information encoded by each A $\beta$ -LTMR transits to the central nervous system (CNS) through the spinal cord, brainstem and thalamus to reach the somatosensory cortex. A specific characteristic of the somatosensory system is its topographic arrangement, which mirrors the spatial continuity of skin regions across the body (with some exceptions), a concept known as somatotopy. In other words, tactile stimuli encoded by different receptors across the body keep their spatial arrangement along the pathway, reaching the cortex with a somatotopic organization and giving rise to cortical somatotopic maps. This organization and the processing steps along the pathway will be reviewed in this section.

### **1) The pathway to the somatosensory cortex**

Depending on the body parts they originate from, tactile stimuli follow different afferent pathways to the CNS, with tactile stimuli from the head travelling through the sensory trigeminal pathway, while stimuli from the body travel through the dorsal column medial lemniscal pathway. Only the latter will be described as it is the only relevant for this thesis focusing on tactile perception at the hands. The following information is reviewed in Delhaye, Long & Bensmaia (2018).

#### **a. Somatotopy along the pathway**

As far as the afferent pathway is concerned, the above described A $\beta$ -LTMR afferent fibers are viewed as first-order tactile neurons. Afferent fibers that innervate nearby receptors group into fascicles, which progressively merge with other fascicles to form nerves, along with efferent (motor) fibers. The hands are innervated by three main nerves: the median and ulnar nerves innervate the palmar side of the hand and arm, while the radial nerve innervates the dorsal side (Figure 2). As these nerves approach the spinal cord, they divide into dorsal (sensory) and ventral (motor) roots. The cell bodies of the sensory neurons reside in the dorsal root ganglia (DRG). Upon entering the spinal cord via the dorsal root, afferent axons send (i) one projection to the dorsal horn (DH) where it synapses to postsynaptic dorsal column (PSDC) neurons which

project to the dorsal column nuclei (DCN) via the dorsal column (indirect dorsal column pathway), and (ii) another directly to the DCN via the dorsal column (direct dorsal column pathway). Neurons projecting from both direct (first-order neurons, exclusively A $\beta$ -LTMRs) and indirect (PSDC neurons) dorsal column pathways then synapse to second-order neurons in the DCN.

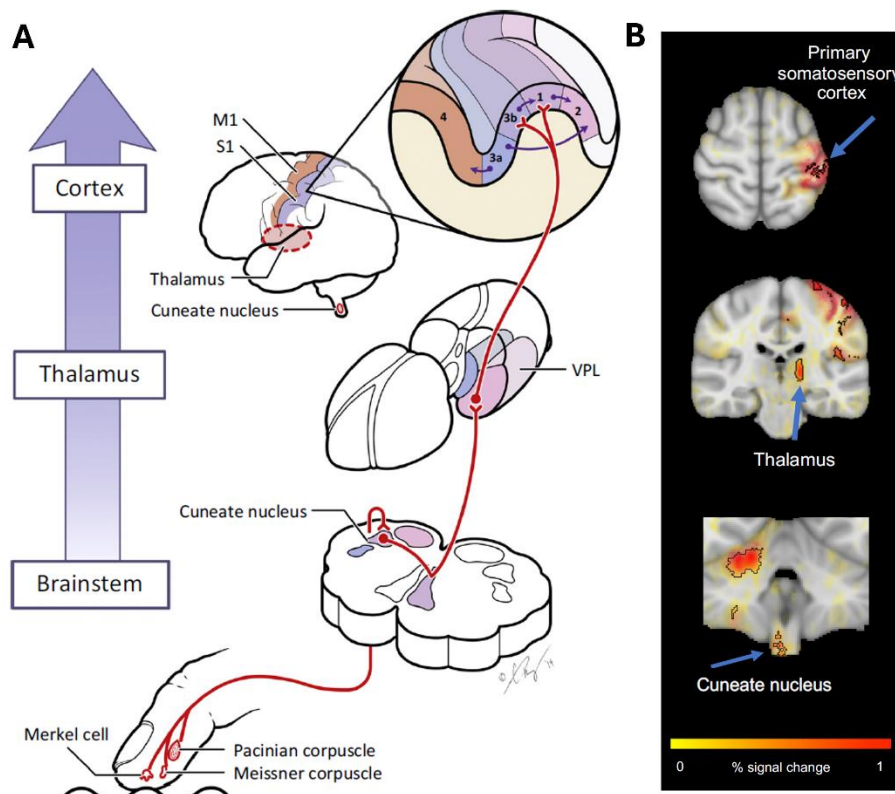
Recent findings in mice showed that the DH receives convergent inputs from both LTMRs and HTMRs and revealed an interconnected network (involving inhibitory interneurons) in the DH transforming the inputs into a diverse range of PSDC output channels (Chirila et al., 2022). The transformed LTMRs/HTMRs signal (indirect pathway) thus combines with the unmodified A $\beta$ -LTMRs signal (direct pathway) at the DCN. Furthermore, in mice, Turecek et al. (2022) unraveled the specific contributions of each of these pathways showing that the direct pathway conveys vibrotactile stimuli with high temporal precision while the indirect pathway primarily encodes touch onset and the intensity of sustained high-force indentation. They additionally showed that signals reaching the DCN from both pathways topographically realign to preserve precise spatial details. Finally, they showed that different combinations of inputs from both pathways in the DCN yield different specialized responses of the DCN neurons, distinguishing them into different subtypes of neurons. These recent results emphasize the importance of the indirect pathway in shaping the tactile information that is already processed as early as at the DCN level, before being transmitted to later stages of the afferent pathway.

Along the dorsal column in the spinal cord, the somatotopic arrangement is maintained. While it was first thought to be rudimentary, as suggested by the observation of human spinal cord samples showing a quite coarse topographic organization with extensive overlapping of fibers from different skin regions (Smith & Deacon, 1984), a more detailed topographic organization has been identified in the DH of macaques (Florence et al., 1989), squirrel monkeys (Florence et al., 1991), cats (Nyberg & Blomqvist, 1985) and rats (Molander & Grant, 1986) with the fingers represented along the rostrocaudal axis. Using optical activation of PSDC neurons, an elaborate somatotopic arrangement of digits has also been observed in mice (Turecek et al., 2022). The resemblance between the somatotopic organization across these species suggests that it is a common characteristic of the mammals' spinal cord.

Located in the medulla (in the brainstem), the DCN comprises two nuclei, the cuneate nucleus (CN) and the gracile nucleus, receiving inputs from neurons originating from the upper-body and the lower-body respectively. This thesis concerning upper-body only, the following descriptions of the pathway will consider CN only. A somatotopic organization has been

observed in the CN in marmoset monkeys, with the lower limbs represented in the medial part and the head in the lateral part of the DCN (Xu & Wall, 1996). Regarding the hands, unlike the glabrous skin, the hairy skin is represented in a discontinuous manner (Xu & Wall, 1996, 1999), and the digit regions are separated by myelin-dense cell-poor septa as observed in the CN of racoons (Johnson et al., 1968) and monkeys (Qi & Kaas, 2006).

Within the medulla, the second-order neurons decussate, i.e. cross the body midline, to reach the contralateral part of the medulla and ascend along the medial lemniscus through the pons and then the midbrain to reach the ventral posterolateral nucleus (or ventroposterior lateral nucleus; VPL) of the somatosensory thalamus, where they synapse to third-order neurons (Rasmussen & Peyton, 1948). In the VPL, a complete somatotopic map of the contralateral part of the body is represented with the upper body in the medial part and the lower body in the lateral part, as reported in macaque monkeys using injections of anatomical tracers and electrophysiological recordings (Padberg et al., 2009), as well as in humans using probabilistic tractography technique of diffusion tensor imaging (Hong et al., 2011) and deep brain stimulation (Rifi et al., 2024). As for the hand area, similarly to the CN, the digit regions in the VPL are separated by myelin-dense cell-poor septa as observed in racoons (Welker & Johnson, 1965) and non-human primates (Jain et al., 1998; Qi & Kaas, 2004; Qi et al., 2011). Third-order neurons then project to the somatosensory cortex (Figure 2).



**Figure 2. The somatosensory afferent pathway.** [A extracted from Saal & Bensmaia, 2014; B modified from Reddy et al., 2024] (A) Schematic representation of the dorsal column medial lemniscal afferent pathway with first-, second- and third-order neurons (red) relaying at the brainstem and thalamus. (B) Whole-brain fMRI signal evoked by brushing the right hand at brainstem, thalamus and SI in humans.

Overall, the somatotopic organization is preserved along the afferent dorsal column medial lemniscal pathway reaching the somatosensory cortex.

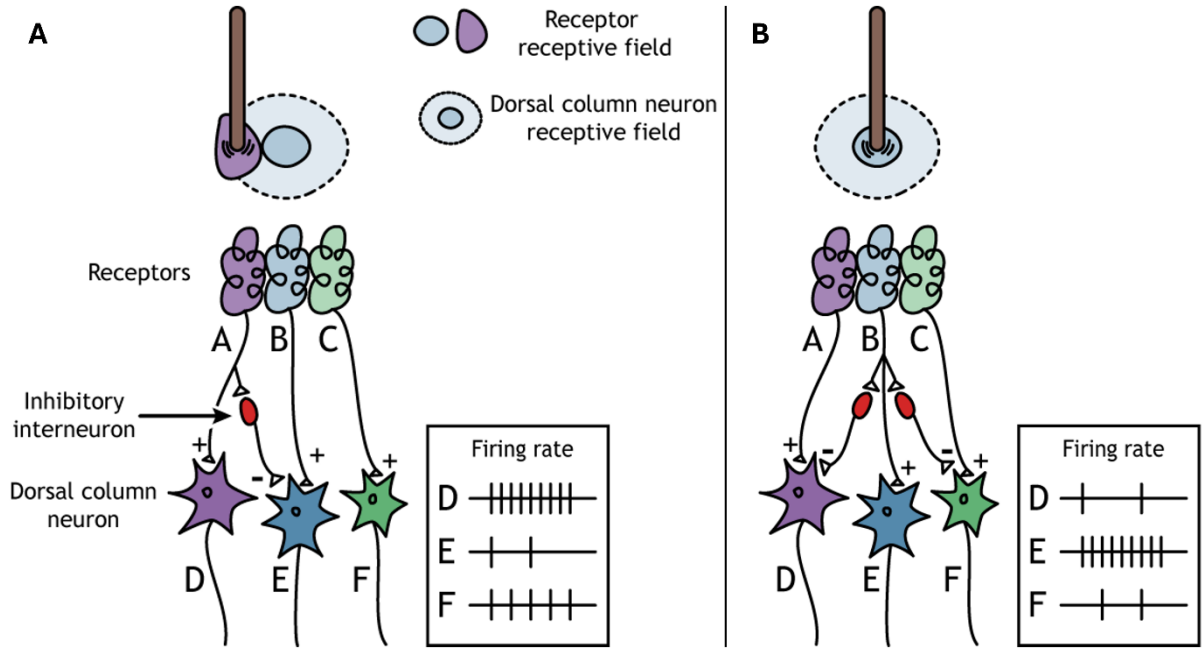
### **b. Somatosensory processing along the pathway**

Tactile information is processed while travelling from the peripheral nerves to the cortical neurons. Indeed, the signal arriving at the cortical neurons is filtered and refined, through a combination of excitatory and inhibitory mechanisms along the pathway. As it has been observed by Xu & Wall (1999) in squirrel monkeys, the tactile processing from the CN to SI preserves tactile responsiveness and somatotopic organization while involving transformations that lead to RFs sharpening, reduction of hand hairy skin inputs, amplification and refinement of hand glabrous skin inputs, and relocations of representations. More recently, Emanuel et al. (2021) used genetic manipulations and optogenetics in mice and brought evidence for extensive integration and transformation of tactile signal from different LTMRs along the pathway. Without detailing each of these processes, this section will outline the general processing along the pathway, with a particular emphasis on the role of inhibition (of interest in this doctoral work).

When a stimulus indents the skin, first-order neurons are excited and respond differently depending on their type, providing spatial and temporal information about the stimulus. They synapse to second-order neurons at the CN, each second-order neuron receiving inputs from many first-order neurons. The first stage of integration and processing of peripheral inputs occurs at this level, within the CN. Using a mechanical stimulation by differential traction (minimizing the uncertainty in the strain distributions induced in the skin) and single-neuron electrophysiological recordings in the cat, Hayward et al. (2014) delivered a wide range of precisely controlled spatiotemporal stimuli to the digital pads and showed that in the CN, the same second-order neuron responds differently (different time-course of spiking) to different spatiotemporal stimuli. This indicates that neurons in the CN are selectively sensitive to the spatial and temporal aspects of the stimuli. Additionally, using the same spatiotemporal stimulations, Jörtnell et al. (2014) revealed that despite their similar RFs and response properties, each CN neuron responds to a unique combination of inputs, suggesting that they encode distinct features of the stimuli. Beyond that, they were recently found to be selective for

specific features of tactile stimuli, as tested with a wide range of different stimuli (indentations, vibrations, random dot patterns, scanned edges) in macaque monkeys (Suresh et al., 2021). This study additionally showed that CN neurons receive inputs from multiple classes of afferent first-order neurons and have spatially complex RFs, making them more similar to cortical neurons than to the first-order neurons branched to them.

The RFs of second-order neurons are composed of the RFs of each first-order neuron branching to it. They are divided into excitatory and inhibitory regions that can be arranged in a variety of conformations, giving them a sensitivity to specific spatial features of their inputs (Suresh et al., 2021). For instance, an elongated excitatory region bordered on one side by an inhibitory one gives the neuron a selectivity for orientation. When a stimulus indents the excitatory region, the second-order neuron increases its firing rate, while when a stimulus indents the inhibitory region (i.e. it falls in the RF of a neighboring first-order neuron), the second-order neuron decreases its firing rate as a result of inhibition applied by inhibitory interneurons activated by the neighboring first-order neuron (Figure 3). This inhibition is referred to as lateral inhibition and constitutes the main contribution of neurons in the CN to tactile information processing, filtering the signal transmitted to the higher stages and thus sharpening the spatial details in the stimuli (Rongala et al., 2018).



**Figure 3. Schematic representation of lateral inhibition.** [Modified from Henley, 2021, licensed under CC BY-NC-SA] The conformation represented is an excitatory center and a surround inhibitory region, but other conformations exist (A) When a stimulus touches the

surround of the receptive field of Cell E, the firing rate decreases. Note that the stimulus is in the surround of Cell E's receptive field but is also in the center of Cell D, so the firing rate of Cell D will increase. (B) The point of a blunt probe pressing on the receptive field of Cell B will cause an increase in the firing rate of Cell E, but will also cause a decrease in the firing rate of Cells D and F. This increases the perceived difference between the point and the area next to the point that is not being stimulated.

By modulating the size of the RFs (Hicks & Dykes, 1983), lateral inhibition has been shown to be critical for tactile spatial resolution (or tactile acuity, i.e. the ability to distinguish fine spatial details) as it preserves the spatial distinction between two close stimuli on the skin (Mountcastle & Powell, 1959; Békésy, 1960) and enhances edge detection (Arkachar & Wagh, 2007). For example, when two punctate stimuli are widely spaced on the skin, two distinct neuronal populations are activated, making them distinguishable, while when they are brought close enough, the activity in the two populations would tend to overlap in the absence of lateral inhibition and would blur their distinction. Because of lateral inhibition, the inhibition produced by each stimulus attenuates the activity in the zone of overlap, sharpening the activity peaks in the two responding populations, thereby spatially separating them and allowing each stimulus to be perceived.

In a model of the spiking responses of second-order neurons to an edge indentation on a simulated mechanoreceptor, Parvizi-Fard et al. (2021) investigated the role of lateral inhibition for edge detection at the population-level by modulating the inhibitory currents in the CN. They showed that diminishing the amount of lateral inhibition leads to a decrease in the accuracy of the recognition of the indented orientations. Regarding spatial resolution, they also showed that an increase in lateral inhibition amplifies the process of spike filtering, allowing third-order neurons to be activated by a stronger and more consistent signal. As a result, the spatial resolution of the RFs is enhanced, which improves the ability to discriminate between two closely spaced simultaneous stimuli. They simulated the resulting responses at the cortical level and showed that their results are in agreement with the experimental cortical responses obtained when an edge indents the skin (Delhaye et al., 2019; Callier et al., 2019).

At the thalamic level, further inhibition occurs in the VPL. In addition to the lateral inhibition applied by interneurons (e.g., Poggio & Mountcastle, 1963; Andersen et al., 1964; Jänig et al., 1979), inhibitory signal in the thalamus also comes from astrocytes (Kwak et al., 2020). Such inhibition might play a role in tactile spatial discrimination, as recently suggested by Kwak et al. (2020). In mice, they showed that inhibition applied by thalamic astrocytes to somatosensory neurons in the thalamus was critically involved in tactile discrimination of textures, as the discrimination performance was significantly reduced when astrocytic thalamic inhibition was



blocked. This indicates that some processing of somatosensory information occurs in the thalamus, unlike what was previously thought (i.e. the thalamus has long been seen as a “passive” relay of information).

Besides, parallel to the thalamocortical feedforward information ascending the afferent pathway, feedback information travels down from SI and SII to the thalamus (Song et al., 2021). Although its mechanisms are not completely understood, this corticothalamic feedback tactile information - at least the one emerging from SI - seems to play a crucial role not only in sharpening the thalamic RFs and shaping thalamic responses (reviewed in Alitto & Usrey, 2003), but also in shaping thalamic firing modes and activity states (reviewed in Nicolelis & Fanselow, 2002). For instance, abolishing the corticothalamic feedback through a reversible inactivation of SI (barrel cortex) in rats (i) immediately altered the spatiotemporal structure of neurons’ activity in the ventroposterior medial nucleus (VPM; the nucleus receiving inputs from the face) of the thalamus in response to single-whisker stimulation (Krupa et al., 1999; Ghazanfar et al., 2001), (ii) altered RFs reorganization induced by peripheral deafferentation (Krupa et al., 1999), and (iii) altered the nonlinear summation of VPM neural responses to simultaneous stimulation of several whiskers (Ghazanfar et al., 2001). More recently, Hirai et al. (2018) showed that cortical lesions in SI in rats shifted the response of thalamic neurons towards bursting, increased the response probability and the gain of thalamocortical neurons, and altered the spontaneous activity of vibrissa-responsive thalamic neurons.

Corticothalamic feedback projections were shown to influence the relationship between neighboring thalamic neurons within the VPL. As has been shown recently in rats, within the VPL, adjacent pairs of neurons display specific correlations of spike firing activity, despite having access to near-identical afferent inputs, which suggests that the corticothalamic feedback information influences their response (Wahlbom et al., 2021a). Besides, the same team showed that following the stimulation of the right D2, responses were elicited through corticothalamic feedback projections not only in the VPL region specific to the stimulated finger, but also in other VPL regions (Wahlbom et al., 2021b). More precisely, they found that VPL neurons with short response latency times (responding to direct afferent inputs via the CN) were better decoders of specific spatiotemporal tactile input patterns than neurons with longer response latency times (likely to have received corticothalamic feedback information). Finally, Dimwama et al. (2024) lately found through optogenetic manipulations in mice that thalamocortical neurons dynamically modulate spiking activity in the VPM, either suppressing or enhancing it depending on their firing rate and synchrony.

As for the content of thalamocortical feedforward and corticothalamic feedback information, recent evidence showed that the direction of information between the thalamus and SI, as well as their synchronization, play a role in the perception of the stimuli (Tauste Campo et al., 2019). In this study, neurons from the VPL and SI of macaque monkeys were simultaneously recorded while monkeys judged the presence or absence of a tactile stimulus applied at their fingertip. They showed that the feedforward information increased with stimulus amplitude, while the feedback information remained unchanged. Besides, only the feedforward information was decreased during error trials, suggesting that perceptual detection might be related to the amount of stimulus information flowing from VPL to SI (feedforward). This indicates that feedforward information is sensory (tactile relevant information) while the feedback information is modulatory. More recently, Song et al. (2021) revealed distinct corticothalamic feedback regulations from SI and SII, with SI exerting inhibitory feedback regulation independent of external stimulation (coherent with the finding of Tauste Campo et al., 2019 showing that feedback information is not affected by the change in stimuli), and SII adding further inhibition to the thalamic activity specifically during tactile information processing. Using dynamic causal modeling combined with high-temporal-resolution fMRI in humans, the authors observed a significantly negative intrinsic connectivity from SI to the thalamus, which was not significantly influenced by somatosensory inputs. In contrast, the intrinsic connectivity from SII to the thalamus was not significant on its own, but external inputs strongly negatively modulated this connection. Altogether, the results of both these studies indicate that SI exerts a steady inhibitory influence on the thalamus that is independent of external stimuli, while SII's inhibitory effects on the thalamus are only triggered during external stimulation.

These inhibitory mechanisms at different stages of somatosensory processing allow to progressively sharpen the tactile information to be processed in the somatosensory cortex and in higher-level stages of somatosensory processing.

## **2) The somatosensory cortex**

From the VPL, thalamocortical projections convey the signal to the somatosensory cortex for further processing. The somatosensory cortex comprises the primary (SI) and secondary (SII) areas (Woolsey & Fairmain, 1946), with SI being located in the anterior parietal cortex, in the postcentral gyrus, and SII in the parietal operculum along the upper bank of the lateral sulcus (Figure 4). Within SI, four separate subregions are distinguished based on their cytoarchitectonic structure (Brodmann, 1909; Vogt & Vogt, 1919) and the type of information they receive and process (Powell & Mountcastle, 1959; Paul et al., 1972): (i) Brodmann's area

(BA) 3a processing mainly proprioceptive information, (ii) BA 3b processing low-threshold tactile information, (iii) BA 1 also processing low-threshold tactile information with an emphasis on texture discrimination, and (iv) BA 2 processing both proprioceptive and tactile information and specialized in size and shape recognition (Figure 4). These four areas receive inputs from thalamocortical projections and are highly interconnected. As for SII in the parietal operculum (BAs 40 and 43), it receives inputs mostly from SI and more sparsely directly from the VPL (Friedman & Murray, 1986; Krubitzer & Kaas, 1990). Within the human SII, four separate areas are distinguished based on their cytoarchitecture, namely OP1, OP4, OP3 and OP2, while only three areas compose the SII in non-human primates, the area S2, PV, VS corresponding to OP1, OP4 and OP3 respectively (Eickhoff et al., 2006).

#### **a. The primary somatosensory cortex (SI)**

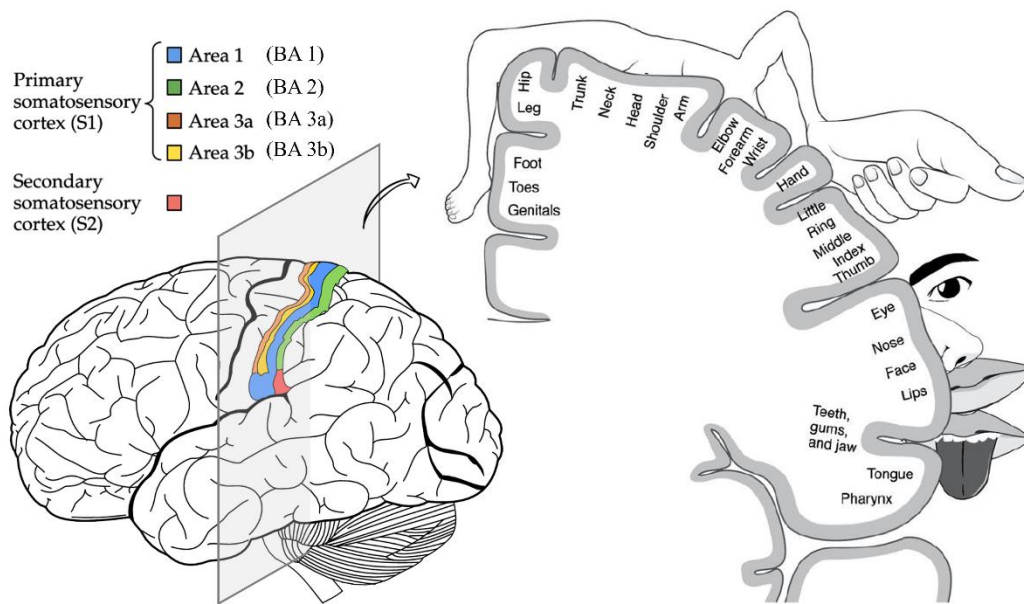
Most of the thalamocortical projections enter SI through BA 3b (but also sparsely project to the other areas), and from there, the information mainly sequentially transits to BA 1 and BA 2, and from BA 1 to BA 2, allowing for a progressive convergence and integration of information along the transit (Ruben et al., 2006). The integration of information from the CN to BA 1 is reflected in the structure and size of the RFs, evolving from the CN to BA 3b to BA 1, as they display progressively increasing surround inhibition and size (Sripati et al., 2006; Suresh et al., 2021) and decreasing response linearity (Sripati et al., 2006).

As suggested by many studies investigating SI neuronal responses in monkeys, SI neurons receive convergent inputs from both SA and RA afferents (Hyvärinen & Poranen, 1978; Sur et al., 1981, 1984; Pei et al., 2009; Kim et al., 2020). Indeed, SI neurons were found to display both a sustained firing during the static phase of an indentation (implying inputs from SA afferents) and an off response during the offset of the indentation (implying inputs from RA afferents). This allows these neurons to integrate the multiple features of a tactile stimulus carried by multiple afferent types. Touch is thus coded at a population level, both within and between afferent types (Saal & Bensmaia, 2014), and the population activity patterns consisting of neurons with weighted preferences for different types of stimuli allow to discriminate the type of stimulus.

Neurons in SI have been found to exhibit some sensitivity to features such as specific orientations (Bensmaia et al., 2008). Orientation-tuned neurons are the most prevalent in BA 1 (two third), then in BA 3b (half) and are less prevalent in BA 2 (one eighth) as found in monkeys (Bensmaia et al., 2008). When an edge indents the skin, these neurons fire based on the spatial

coincidence between the hot spots of their RFs and the local skin deformations induced by the orientation of the edge on the skin. Hence, the more spatial coincidences, the higher the firing intensity, which explains that for a given neuron, certain edge orientations (showing greater spatial coincidence) result in stronger responses. This way, the orientation of indented stimuli is coded through the firing intensity at the single-neuron level, while at the population scale it is coded through the spatiotemporal spiking patterns of neurons specifically tuned to it (Parvizi-Fard et al., 2021).

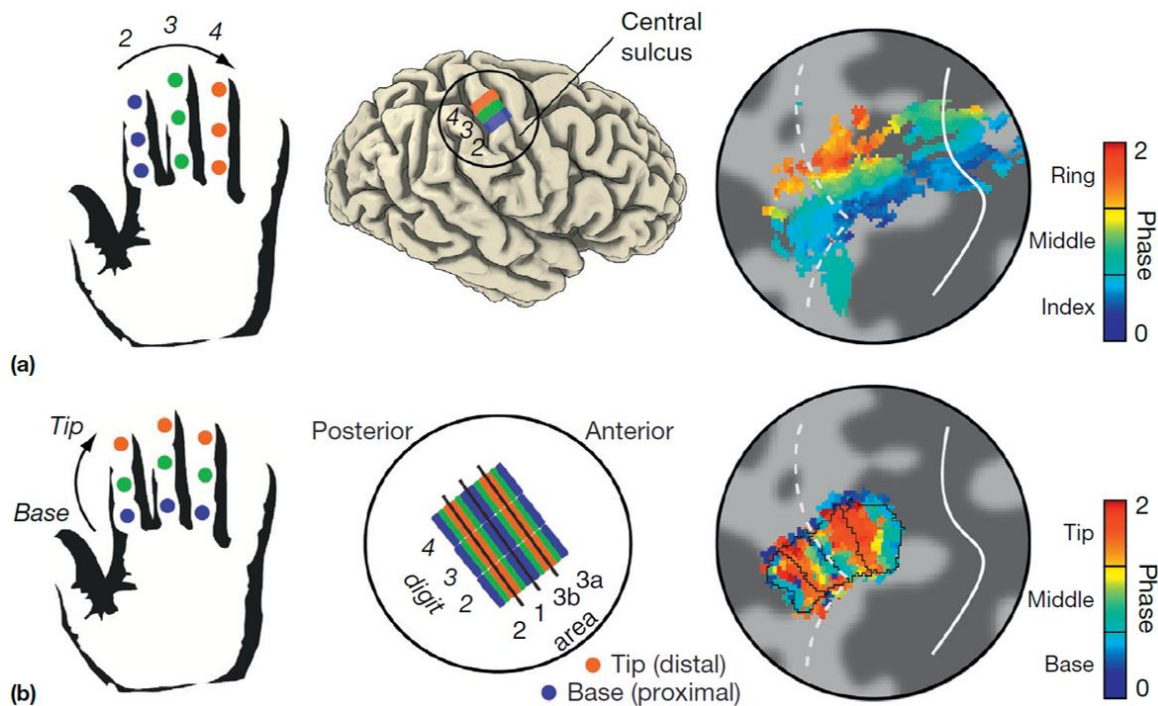
As for the topographic organization in SI, each of the four areas comprises a complete somatotopic map of the contralateral side of the body with the areas representing the foot located near the midline and the areas representing the face at the lateral end (monkeys: Pons et al., 1985, humans: Nakamura et al., 1998). A particularity of these maps is that the more densely innervated a body part is, the larger its cortical representation in SI areas is (i.e. fingers and lips have larger representations than arms and the back), a phenomenon known as cortical magnification (Sur et al., 1980). Considering both the somatotopy and cortical magnification, the overall map of the representations of all body parts has been illustrated as the sensory homunculus (Penfield & Boldrey, 1937; Figure 4). While the classical view advocates for a strong relationship between cortical magnification and innervation density (Catani et al., 2017), quantitative evidence was lacking. Recently, Corniani & Saal (2020) investigated this relationship and found that the correlation between these aspects is actually poor (non-significant) and additionally reported that some regions (among which the hand and face) exhibit larger magnification than expected from their innervation density alone. They hypothesized that this overmagnification might be due to the higher probability of receiving tactile stimuli on these regions or to their behavioral relevance.



**Figure 4. The somatosensory cortex and the sensory homunculus.** Left: the SI consists of the Area 1 (Blue), Area 2 (Green), Area 3a (Orange), and Area 3b (Yellow). The secondary somatosensory cortex (SII) is depicted in red. [Modified from Navarro-Guerrero et al., 2023]; Right: Sensory Homunculus of a human body [Extracted from Baweja, 2020].

Structurally, the representations of different body parts are histologically distinguishable as they form myelin-dense ovals separated by myelin-light septa (monkeys: Jain et al., 1998; humans: Geyer et al., 1999; Kuehn et al., 2017). Within the hand representation, fingers are represented latero-medially from thumb (D1) to little (D5) finger (monkeys: Jain et al., 1998; Qi & Kaas, 2004; humans: Schweisfurth et al., 2014; Sanchez-Panchuelo et al., 2018; Kolasinski et al., 2016; Puckett et al., 2020; Wang et al., 2021) and are separated by myelin-dense cell-poor septa in monkeys (Pons et al., 1985; Jain et al., 1998; Qi & Kaas, 2004). Contrasting with these findings, investigating the 3D structure maps of human individual finger representations in BA 3b through MRI, Doehler et al. (2023) recently found no structural differences, no low-myelin borders and high similarity of 3D structure profiles between finger representations, showing a difference in inter-finger organization between non-human primates and humans. As concluded by the authors, these results suggest that this lack of inter-finger structural difference could underly a high degree of flexibility for functional finger organization. Within finger's representations, in monkeys, the phalanges and palm represented rostro-caudally from fingertip to palm (Pons et al., 1985; Merzenich et al., 1978) are separated by myelin-dense cell-poor septa (Qi & Kaas, 2004). In humans however, such an ordered organization from fingertip to palm was less consistently observed, with a few fMRI studies showing such a pattern (Blankenburg et al., 2003; Sanchez-Panchuelo et al., 2012; Wang et al., 2021; Figure 5) and one

higher-resolution fMRI study on all fingers showing such an organized pattern only in D5 and a more variable pattern in the other fingers (Schweisfurth et al., 2014).



**Figure 5. Within hand somatotopic organization in SI.** [Extracted from Schluppeck & Francis, 2015] (a) Somatotopy ('between-digit') of finger representation in the cortex measured by stimulating different digits in sequence. Middle panel: rendering of a cortical hemisphere showing the approximate location of S1 and how digits 2 (index), 3 (middle), and 4 (ring) are mapped (colors). Right panel: map of fMRI response phase, corresponding to preferred stimulation site (colors) on a flattened cortical map (gray) in example subject. (b) Map of 'within-digit' somatotopy measured by stimulating corresponding distal to medial sites on digits 2, 3, and 4. Middle panel, diagram illustrating the orthogonal orientation of 'between-digit' and 'within-digit' maps and putative relationship to cytoarchitectonic subregions 2, 1, 3a, and 3b (fMRI data collected at 7 T with 1.25 mm isotropic spatial resolution).

Despite the body part's representations in SI being organized in a somatotopic manner with quite strong selectivity within body part's representations (Cunningham et al., 2013; Huber et al., 2020), a growing number of studies tend to indicate that the information about a stimulus touching a given body part is primarily contained in the corresponding SI area but can be also found to a lesser extent in other areas. For instance, in owl monkeys, Reed et al. (2010) showed that applying a stimulus in a nonpreferred location of a given neuron, simultaneously to or before applying a stimulus in its preferred location, suppresses its response as measured by a reduction of magnitude. The suppression occurred even between non adjacent digits and even when stimuli were separated by long durations (up to 500 ms, the longest interval tested), indicating that BA 3b is involved in widespread stimulus spatiotemporal integration. Additionally, Lipton et al. (2010) showed in monkeys that a given digit representation responds

to stimulation of all other digits tested. Similarly in rats, Enander & Jörntell (2019) applied different tactile inputs to a digit and showed that information from these stimuli could be decoded from the representation of other adjacent and non-adjacent digits. Using multivariate fMRI analysis in humans, Muret et al. (2022) showed that SI regions (e.g., the foot region) also contain relevant information about cortically distant body parts (e.g., the hand and face). Altogether, these findings indicate that even though each cortical neuron in SI responds preferentially to stimuli in a certain skin region, they are influenced by tactile stimuli applied at distant skin regions.

### **b. The secondary somatosensory cortex (SII)**

At a higher-level, SI (all areas, but mostly BA 1 and 2) sends projections along two parallel streams for further tactile processing: (i) the ventral stream in the lateral parietal cortex (LPC), transiting through SII responsible for higher-level feature extraction and cognitive functions such as attention and decision-making (Jiang et al., 1997; Mima et al., 1998; Romo et al., 2002) and the posterior parietal cortex (PPC) including BA 5 and BA 7, and (ii) the dorsal stream in the PPC, linked to shape and object recognition to serve motor behavior (Murata et al., 2000; Gharbawie et al., 2011). In parallel, SI and SII also project to the primary motor cortex (MI) to provide tactile information to be used for the control of finely tuned movements and complex motor skills (Tamè et al., 2015a; Shelchikova et al., 2023; Martinetti et al., 2024). Finally, SI and SII also send projections to the cerebellum, and the interaction between both is critically involved in somatosensory attenuation of self-touch (Kilteni & Ehrsson, 2020). This section focusses on processing and somatotopic arrangement in SII specifically.

As briefly stated in section II.2.a., besides receiving cortical inputs from SI, SII also receives direct thalamocortical inputs from the VPL, suggesting not only a serial processing of tactile information in SI then SII (Pons et al., 1987, 1992), but also a parallel processing in SI and SII simultaneously (Rowe et al., 1996; Chung et al., 2014). Using fMRI and dynamic causal modeling (DCM) analysis in humans, Khoshnejad et al. (2014) showed evidence for a serial processing of tactile information in SI then SII in response to stimulations of sural nerve (innervating the ankle and foot) in humans. In contrast, compelling neuroimaging and electrophysiological evidence for the parallel processing in SI and SII has been provided in humans (Avanzini et al., 2016). Applying DCM and Bayesian model selection to fMRI data collected during stimulation the superficial peroneal nerve (innervating the ankle) in humans, Liang et al. (2011) showed that the neural responses to the stimuli were best explained by models in which the fMRI responses in both SI and SII depend on direct thalamocortical

projections, thus supporting a parallel processing of tactile information in SI and SII. Additionally, intracranial recordings of median nerve stimulation-evoked high-frequency gamma oscillations revealed simultaneous (accuracy of 10 ms) phasic responses in all four SI areas and OP1 area of SII, followed by tonic responses in all four SII areas (Avanzini et al., 2016). Although the authors recommended that these results be treated with caution as the temporal resolution is of only 10 ms, these results suggest a parallel processing in SI and OP1 area of SII and a serial processing from OP1 to the other SII areas. A last study (Klingner et al., 2016) addressed this question using fMRI and DCM applied to magnetoencephalography (MEG) data collected during sustained tactile stimulations. Using Bayesian model comparisons, they showed that the neural activity in the first 100 ms is best explained by models supporting parallel processing while the subsequent activity is best explained by models supporting serial processing. As a result, they concluded that both SI and SII receive simultaneously tactile inputs, and then the processing in SII is mostly based on signals received via (and preprocessed by) SI.

SII is involved in higher-order processing of tactile inputs such as shape and texture discrimination (Health et al., 1984; Henderson et al., 2023), tactile learning (Pleger et al., 2003; Hodzic et al., 2004), and sensory decision making (Romo et al., 2002; Romo & de Lafuente, 2013). Such processing is possible in SII thanks to the features of its neurons. Indeed, SII contains orientation-tuned neurons (Thakur et al., 2006) which - unlike SI orientation-tuned neurons - have large RFs spanning multiple pads on multiple digits (Hsiao et al., 2002; Fitzgerald et al., 2004) allowing to integrate features across the whole hand which is critical for shape and haptic object recognition. As for texture discrimination, roughness-selective areas were found in SII of primates (Roland et al., 1998; Simões-Franklin et al., 2011) and humans (Sathian et al., 2011; Stilla & Sathian, 2008). Although SI areas are activated during texture perception tasks (O'Sullivan et al., 1994; Servos et al., 2001), SII was found to be also activated and has recently been proposed to be more critically involved in texture discrimination (Henderson et al., 2023). In a recent activation likelihood estimate meta-analysis on fMRI data collected during texture perception tasks in humans, Henderson et al. (2023) accounted for non-textural haptic elements and revealed that SII - and not SI - may play a key role in encoding textural properties.

Each subregion of SII contains a somatotopic map of the body (Eickhoff et al., 2007; Sanchez-Panchuelo et al., 2018). As far as topography is concerned, SII differs from SI in that its somatotopy is less selective (Del Gratta et al., 2000; Ruben et al., 2001; Simões et al., 2001)



and its RFs are larger and more complex (Fitzgerald et al., 2006), both findings indicating that from SI to SII the signal is further processed and integrated (Pons et al., 1987, 1992; Iwamura, 1998). An example of the coarser somatotopic organization of SII is shown by a study using ultra-high-field fMRI in humans (Sanchez-Panchuelo et al., 2018). The authors observed that in contrast to SI, distinct individual finger representations could not be decoded in SII due to highly overlapping representations. Similarly, using multi-voxel pattern fMRI analysis in humans, Beauchamp et al. (2009) found that touches closely spaced on the body surface (e.g., fingers of the same hand) were more accurately decoded in SI than in SII, while touches widely spaced (e.g., hand vs. foot) were decoded equally accurately in both regions. As suggested by the authors, the less well-organized somatotopy in SII than SI may be responsible for these findings.

Last but not least, a particularity of SII as compared to SI is its more prevalent bilateral representations. Indeed, bilateral activations of SII were observed following unilateral tactile stimulation (Disbrow et al., 2000; Del Gratta et al., 2002). Essential for dexterous and coordinated bimanual tasks, this integration across hemispheres is conducted through interhemispheric communications.

### **c. Intra- and inter-hemispheric communication**

Within each hemisphere, the representations of body parts interact. For example, within the hand representation in SI, the interaction between the SI representations of digits of the same hand were found to rely on lateral inhibition. The representations of individual fingers in SI are laterally connected via inhibitory (but also excitatory) interneurons (Forss et al., 1995; Reed et al., 2008). Gandevia et al. (1983) recorded the evoked potentials in human SI through electroencephalography (EEG) while stimulating two neighboring fingers either simultaneously or individually. They found that the potential evoked by the simultaneous stimulation had lower amplitude than the sum of the potentials evoked by individual stimulations, revealing a suppressive interaction between the afferent signal from the two fingers. Since then, these results have been replicated in humans (Biermann et al., 1998; Hoehstetter et al., 2001; Severens et al., 2010) and primates (Chen et al., 2003; Friedman et al., 2008) and have been attributed to intracortical lateral inhibition between fingers' representations. Indeed, in addition to the measured suppression induced by the simultaneous stimulation, a reduction in the activated areas as well as a decrease in amplitude of activation were shown in primates (Friedman et al., 2008). Moreover, when investigated across neighboring and distant fingers, the suppression was systematically found to be stronger

between neighboring than distant fingers suggesting a gradient of inhibition related to cortical proximity (Biermann et al., 1998; Hoechstetter et al., 2001; Friedman et al., 2008; Severens et al., 2010). Although similar lateral inhibition processes occur earlier in the somatosensory afferent pathway (i.e. at the brainstem and thalamus level, e.g. Rongala et al., 2018; Jänig et al., 1979), the inhibition observed in the cortex is stronger (Hsieh et al., 1995).

In contrast to SII, SI was long thought to receive and process exclusively information from the contralateral part of the body. However, studies in animals (Iwamura et al., 1998, 2001, 2002) and humans (e.g., Kakigi & Jones, 1985; Tan et al., 2004; Tommerdahl et al., 2006; Sutherland & Tang, 2006) challenged this notion by revealing bilateral activations in SI. As an example, using a source separation algorithm on EEG data collected during unilateral median nerve stimulation in humans, Sutherland & Tang (2006) showed an ipsilateral SI activation consistently detected across all ten subjects, weaker and delayed compared to the contralateral SI activation. Besides ipsilateral activations following a stimulus, ipsilateral deactivations were also revealed. As an example, applying a long-lasting tactile stimulation on a finger was shown to deactivate the ipsilateral SI finger representation in addition to activating the contralateral SI finger representation, as revealed through fMRI in humans (Hlushchuk & Hari, 2006). Similarly, stimulating one limb has been shown to decrease the activity of the ipsilateral SI as observed in fMRI (Eickhoff et al., 2008; Klinger et al., 2011). Besides ipsilateral response to a stimulus, interactions were found between the right and left SIs (e.g., Lipton et al., 2006; Reed et al., 2011). As shown in owl monkeys, stimulating a finger (conditioning stimulus) simultaneously to or before a second stimulation (test stimulus) on the other hand suppressed the contralateral SI response to the second stimulation (Reed et al., 2011). Based on these and many other studies hinting to a bilateral processing of touch in SI, Tamè et al. (2016) proposed to revisit the notion of exclusively contralateral processing in SI and advocated for an early integration of tactile inputs from both body sides. As for SII, its bilateral representations are well-established, as a bilateral activation was repeatedly observed following unilateral stimulation in primates (eg. Sakata et al., 1973) and humans (e.g., Forss et al., 1995; Hari et al., 1993). These bilateral responses in SI and SII to unilateral stimulations imply that the two hemispheres communicate during tactile processing.

Behaviorally, these interhemispheric communications, either suppressive (i.e. worsening tactile performance) or facilitatory (i.e. improving tactile performance) were observed since long in humans, as revealed by conditioning-test stimuli paradigms, i.e. by applying touches simultaneously or sequentially at the hands (e.g., Craig, 1985; Fukuda et al., 2023). As an

example of facilitatory interaction, Craig (1985) showed that the identification of a vibrotactile pattern improved when the pattern was presented on different hands (homologous fingers) compared to when it was presented on fingers of the same hand. In contrast, as an example of inhibitory interaction, Fukuda et al. (2023) showed that the perceptual threshold of the index finger was increased (i.e. impaired tactile perception) when the homologous finger was stimulated 40 ms before (conditioning stimulus) as compared with the perceptual threshold obtained in absence of a conditioning stimulus. Additionally, they found that suppression occurred only when the conditioning stimulus was applied on the homologous finger and not on any other finger of the other hand, recalling (though not exactly replicating) previous findings displaying a stronger inhibitory interaction between homologous than non-homologous fingers (Tamè et al., 2012, 2015b). Interestingly, because of the longer interstimulus interval (ISI; 40 ms) than needed if the interhemispheric transmission would occur between the contralateral and ipsilateral SIs (20 ms), the authors suggested that the interhemispheric transmission occurred between the SIIs. At the cortical level, more recent work (Norata et al., 2024) used a similar paradigm with bilateral median nerve stimulations applied consecutively (at various ISIs) and measured the amplitude of the evoked response (N20) and the high frequency oscillation (HFO) bursts in SI on both hemispheres. They found that the ipsilateral stimulation significantly inhibited the evoked response (lower amplitude) at ISIs between 5 and 40 ms and suppressed HFO burst at ISIs of 5 and 10 ms, which suggests that the interhemispheric transmission occurred between the SIs. This is coherent with the findings of Tamè et al. (2015b) showing an interaction between the hands, as measured as a suppression in MEG signal when two fingers of different hands were stimulated consecutively in SI at short delays (25 ms), but not at longer delays, indicating that the interaction between hands would occur in SI.

The somatosensory areas (both SI and SII) of the two hemispheres interact through the corpus callosum, with callosal connections denser for body parts anatomically situated at body midline (e.g., trunk, lips) than for body parts at the periphery (e.g., hands, feet; Iwamura, 2000; Killackey et al., 1983). A direct consequence of this difference in callosal connections density is the quicker interhemispheric transfer of information between the two sides of body parts at the midline (forehead) than at the periphery (forearms and fingers), as revealed through a tactile detection task in humans (Tamè & Longo, 2015). Both homologous and non-homologous regions of SI and SII are connected through callosal fibers (Conti et al., 1986; Clarke & Zaidel, 1994). Interhemispheric callosal connections are known to be excitatory and inhibitory. The

type of interhemispheric interaction (excitatory or inhibitory) is hypothesized to be dependent on the task demands (Tamè et al., 2016).

A similar hypothesis has been formulated regarding lateral (intrahemispheric) inhibition between the SI representations of adjacent fingers of the same hand, except that instead of switching from excitatory to inhibitory interaction, the hypothesis postulated that the strength of the lateral inhibition is modulated by the task demands (Arslanova et al., 2020). Recording EEG activity while delivering two simultaneous tactile motion trajectories to two adjacent fingers in humans, Arslanova et al. (2020) instructed the participants to compare the motion directions or to combine them to report their average direction. They found that the inhibition between the two fingers was significantly reduced in the combination condition as compared with the comparison condition, confirming that the strength of inhibition is modulated by the task demands. Although these results were found within the same hemisphere, they provide evidence that the strength of inhibition can be modulated by the task demand, giving more weight to the possibility of such an inhibition/excitation modulation between hemispheres. A more recent work of the same team (Arslanova et al., 2022) compared the performance at averaging between motion directions (combination condition) of tactile stimuli simultaneously applied at (i) both hands and (ii) different fingers of the same hand. They found that the participants were better at averaging stimuli applied on different hands than on different digits of the same hand, and that the performance was not affected by adjacency of the fingers of the same hand or by homology between fingers of both hands. These findings demonstrate a bimanual perceptual advantage in multi-touch integration that might be explained by the distributed resources across hemispheres due to interhemispheric integration of information. Taken together, all these results tend to indicate that applying tactile stimuli on two hands would be beneficial to performance in tasks requiring combination of information (averaging information or identifying a pattern), while it would be detrimental to performance in detection tasks.

---

In brief, tactile stimuli are detected by mechanoreceptors and transmitted to the brain via the somatosensory afferent pathway. As this information ascends, it follows a somatotopic organization and undergoes refinement and processing before it reaches the contralateral somatosensory cortex. Once in the cortex, the information undergoes additional processing and interacts with the opposite hemisphere, enabling the integration of tactile information.

## **CHAPTER II: LOW- AND HIGH-LEVEL SOMATOSENSORY PROCESSING ASSESSMENT**

From the peripheral mechanoreceptors to the highest levels of somatosensory processing, the tactile signal is processed. At the behavioral level, different tasks may reflect relatively low to higher level aspects of tactile perception. The most commonly used measures of somatosensory processing are tactile acuity tasks and tasks assessing mental body representations (MBRs). Indeed, because of its direct dependency on SI, measuring tactile acuity is often seen as a way to investigate low-level somatosensory processing, while because MBRs are the result of multisensory integration, measuring them is seen as reflecting higher-level somatosensory processing.

This chapter will not only present the different tasks used to measure tactile acuity and MBRs, but also the relations between the different paradigms and models, as well as their neural correlates for a comprehensive view of these measures of somatosensory processing.

### **I- Tactile acuity: peripheral and central determinants**

A specific aspect of touch this thesis is interested in is tactile acuity (or tactile spatial resolution), which consists in discriminating fine spatial details in tactile stimuli. Being the highest at the fingertips, tactile acuity is crucial for everyday seemingly trivial, but highly skillful acts such as buttoning a shirt, looking for keys in a bag without vision, as well as grasping a small object without letting it slip. Indeed, it is an aspect of touch that is tightly linked to fine motricity as detailed tactile feedback is required to perform dexterous actions. Tactile acuity relies both on peripheral and central mechanisms. In this section, I will first briefly describe several tactile acuity tasks that are relevant for this thesis (specifically focusing on static tasks), then I will present the afferent fibers thought to convey spatial information, as well as the limiting factors of tactile acuity, and I will finally give an overview of the brain areas shown to be involved in these tasks.

#### **1) Tasks assessing tactile acuity**

Various tasks are used to assess tactile acuity, in which stimuli can be static or dynamic and are either punctate probes or edges.

The original and most classical tactile acuity task is the Two-Point Discrimination Task (2PDT). Consisting in discriminating between one or two points (separated by various distances)

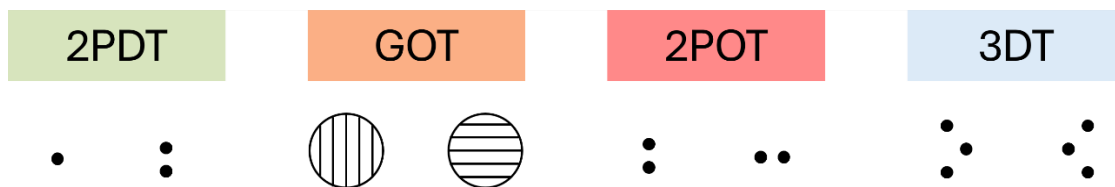
touching the skin (Figure 6), this task has been extensively used since Weber's landmark work (1978) and is still used nowadays, not only in fundamental research (Schmidt-Wilcke et al., 2018; Sasaki et al., 2023), but also in clinical practice to diagnose deficits and assess recovery (Lundborg & Rosén, 2004; Van Boven & Johnson, 1994a; Van Nes et al., 2008). However, several concerns have long been raised about this task, particularly when used with subjective methods whereby participants receive only two point stimulations (at different separations), but no single point stimulation (objective method, see Johnson et al., 1994; Johnson & Phillips, 1981): (i) to solve the task, participants must set a personal criterion (i.e. arbitrarily split their sensation continuum into two categories), which increases variability among participants, (ii) and the "one" and "two" stimuli differ in intensity (one pin being perceived as more intense than two close pins), providing a non-spatial cue to solve the task. In this task, the threshold corresponds to the smallest distance between the two points necessary for them to be perceived as two distinct points 50% of the times.

The most prominent alternative method to assess tactile acuity is the Grating Orientation Task (GOT) which consists in discriminating orientations of gratings of varying width (ridges and grooves carved in a plastic dome) touching the skin along and across the axis of the finger (Figure 6; Johnson & Phillips, 1981). This task is considered more reliable than the 2PDT (Holmes & Tamè, 2023) since it is immune to intensity cues as both the along and across stimuli have the same intensity. However, the afferent fibers were shown to be differently sensitive to the two orientations (Bensmaia et al., 2006; Phillips & Johnson, 1981). This difference in sensitivity is likely involved (at least partly) in the perceptual anisotropy with better performance reported for the "across" than the "along" orientations (Wheat & Goodwin, 2000; Vega-Bermudez & Johnson, 2004). In this task, the threshold represents the smallest grating width for which the orientation can be correctly perceived 50% of the times.

Half-way between the 2PDT and the GOT lies the Two-Point Orientation Task (2POT), more recently proposed by Tong et al. (2013), where participants have to discriminate the orientation of two points touching the skin along and across the axis of the finger, with the distance between the points varying across trials (Figure 6). This task, merging features of both the 2PDT and the GOT, has the advantage of accounting for the "intensity issue". Similarly to the GOT, the 2POT threshold represents the smallest distance between the two points for which the orientation can be correctly perceived 50% of the times.

A last task of interest here (as it is used in many studies cited in this doctoral work) is the Three-Dot Task (3DT). Originally developed in vision and known as the three-dot vernier task (Beck

& Schwartz, 1979), it was adapted to the tactile modality and consists in discriminating the direction of an “arrow” formed by three raised bumps (engraved onto a plate) touching the skin (Figure 6). The central bump is slightly offset along the axis (with a varying offset across trials), and subjects are instructed to report whether the central bump is offset to the left or right. In this task, the threshold corresponds to the smallest offset allowing to correctly identify the direction of offset 50% of the times.



**Figure 6. Illustration of the stimuli used in the 2PDT, GOT, 2POT and 3DT.** These tasks consist in discriminating between one and two points (2PDT), two points oriented along or across the proximo-distal axis of a body part (2POT), gratings oriented along or across the proximo-distal axis of a body part (GOT), or discriminating the direction of an “arrow” formed by three raised bumps.

Although these tasks are all considered to assess tactile acuity, and are used interchangeably in research and clinical practice (although the 2PDT is preferred for ease of administration in clinical contexts), they are likely to measure different aspects of tactile acuity because of the different nature of their stimuli and the difference in the inherent task. As such, they may not be similarly affected by the same clinical condition or experimental manipulation. As an example, nerve injured patients were shown to recover faster in the 2PDT than in the GOT (Van Boven & Johnson, 1994a). In contrast, in cerebral palsy patients, an intensive bimanual training was found to significantly improve their performance in GOT but not in 2PDT (Kuo et al., 2016). These differences in the effect of a single process or intervention on different tactile acuity tasks might additionally be explained by the difference in the aspects of tactile acuity that these tasks rely upon (see section I.4). To date, no study comprehensively investigated whether the different tasks measure similar aspects of tactile acuity. I have investigated this in my doctoral work (see Experimental contributions, Study 2).

## 2) Afferent fibers involved in tactile acuity

At the peripheral level, spatial information of touch has historically been understood to be conveyed by SAI and RAI only. With their relatively small RFs, shallow position within the skin, and high density at the fingertips, both afferents are suited to convey spatial perception, with SAI fibers responding with higher spatial resolution but lower sensitivity than RAI fibers. They are thus being seen as playing complementary roles in tactile discrimination (Abraira &

Ginty, 2013), though due to their higher spatial resolution, SAI fibers are seen as setting the limits of tactile spatial acuity (Phillips & Johnson, 1981). Indeed, Phillips et al. (1988) statically applied alphabet letters on the fingertips of monkeys while recording afferent responses and showed that SAI responses exhibit finer spatial details than RAI responses, and RAI responses seemed to carry almost no spatial information. An additional argument in favor of the involvement of both SAI and RAI fibers in spatial acuity is the relationship between the discrimination thresholds obtained with different measures of spatial acuity and their densities (Peters et al., 2009; Tong et al., 2013; Vallbo & Johansson, 1978) as well as their RF spacing (Craig & Lyle, 2001, 2002). In this respect, the ratio between the 2PDT thresholds measured on the distal phalanx of the index finger and those on the two more proximal phalanges (2.31/1; Vallbo & Johansson, 1978) has been found to match the ratio of SAI density at these locations (2.37/1; Johansson & Vallbo, 1979). Moreover, RAI and SAI are more densely distributed in the fingertips (Johansson & Vallbo, 1979) shown to have smaller 2PDT (Vallbo & Johansson, 1978) and GOT thresholds (Craig, 1999) - i.e. higher acuity - as compared to the rest of the fingers and palm. Finally, the 2PDT and 2POT thresholds measured at the index fingertip, finger base, palm and forearm were found to correlate with the estimated spacing between centers of the RF of the SAI afferents of these areas (Tong et al., 2013).

The involvement of RAI and SAI in spatial acuity is further supported by the link between age-related decline of tactile acuity and the peripheral changes in these fibers-LTMRs. In aging, reduced tactile acuity (Stevens & Choo, 1996; Stevens & Patterson, 1995; Stevens et al., 2003), as well as changes in RAI and SAI fibers' innervation density and in morphology, size and depth of their associated LTMRs were shown (Shaffer & Harrison, 2007; Bolton et al., 1966; Garcia-Piqueras et al., 2019), while less consistent changes were found in RAI fibers (Cauna & Mannan, 1958; Garcia-Piqueras et al., 2019). This deterioration of tactile acuity (2PDT) has been revealed to be partly caused by the reduction of innervation of RAI and SAI fibers (but not tested for RAI) among other structural skin-related factors (Deflorio et al., 2023), though the contribution of central and peripheral factors in age-related decline in tactile acuity is not clear to date. Such a link between the loss of afferents and decline in tactile acuity can also be made in clinical populations. As an example, patients with complex regional pain syndrome, known to have an impaired tactile acuity (Catley et al., 2014) were recently shown to have a reduction of RAI associated-Meissner corpuscles while the number of SAI associated-Merkel cells are unaffected (Mehling et al., 2024), which suggests a potential link between their loss of RAI fibers and their altered tactile acuity.



Besides considering peripheral afferent types, it is worth considering that tactile information is also coded in the central nervous system at the population level (Goodwin & Wheat, 2004), which opens the possibility that afferents with relatively large RFs and deep mechanoreceptors (such as the RAI afferents) may be partly involved in spatial discrimination. Indeed, a quantitative model of RAI afferents suggests that population coding can improve spatial information, when accounting for clusters of Pacinian corpuscles versus individual ones (Vasudevan et al., 2020). This could explain the aforementioned findings of Cataldo et al. (2023) showing that tactile acuity (2PDT) at the index finger obtained when stimulating specifically RAI afferents is equivalent to when stimulating specifically RAI afferents (displaying smaller RFs and more superficial mechanoreceptors). Also, when using an OPTACON, a device consisting of arrays of vibrating pins, to apply statically the stimuli in a letter recognition task, both the RAI and RAI afferents were shown to activate while SAI were not (Gardner & Palmer, 1989). The performance of letter recognition with this device was still comparable to the performance in classical (non-vibrating) letter recognition task. This result has been interpreted as indicating that the resolution of the task involves only RAI (because RAI afferents' spatial resolution was thought to be too poor), but in the light of the recent results of Cataldo et al. (2023), a contribution of RAI in the resolution of this task cannot be excluded. Using optical imaging, Tommerdahl et al. (1999) revealed that inputs from RAI afferents in SI cause activation followed by widespread inhibition of cortical neurons, which might lead to a sharpening of its spatial response profile (Tommerdahl et al., 2005). It is however worthy to mention that although RAI afferents were shown to carry some spatial information, the extent to which they contribute to tactile acuity is not clear yet.

### **3) Limiting factors of tactile acuity**

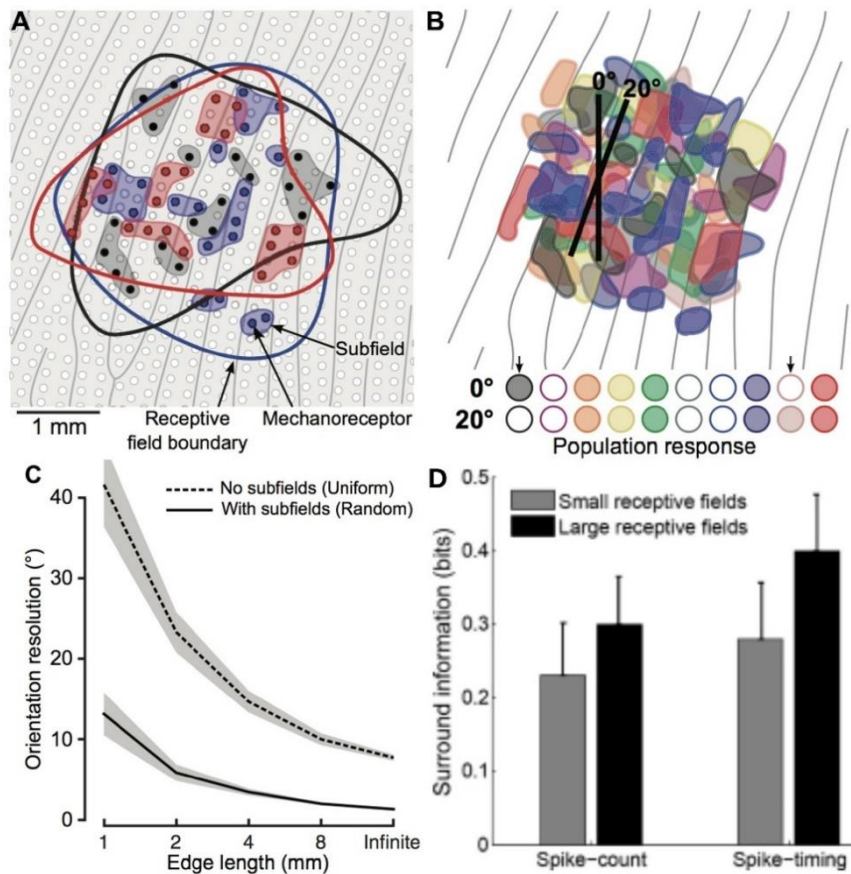
Partly due to the abovementioned correlations between type I afferents innervation density and tactile acuity, as well as because of the known involvement of lateral inhibition in tactile acuity (see Chapter I, section II. 1. b), the classical view establishes that tactile acuity is limited by the afferent innervation density and the center-to-center spacing between RFs (Van Boven & Johnson, 1994b; Goodwin & Wheat, 1999). Despite this, hyperacuity performance, i.e. spatial discriminations finer than predicted solely by innervation density, has been reported (Loomis & Collins, 1978; Loomis, 1979; Wheat et al., 1995; Sathian & Zangaladze, 1998), suggesting additional factors contribute to tactile acuity.

Indeed, recent models indicate that, beyond the RF spacing, the complex shapes of SAI and RAI afferents' RFs with multiple hotspots accounts best for the behavioral spatial resolution

(Pruszynski et al., 2018; Jarocka et al., 2021; Deflorio et al., 2022). Pruszynski et al. (2018) proposed a model in which they implemented complex heterogeneous RFs and a model with simple homogeneous RFs. They compared the ability of each model to resolve edge orientations, with edges of different lengths. Their simulations showed that the complex RFs model can resolve finer details than the homogeneous RFs model at all edge lengths, which better accounts for the behavioral results they obtained in a tactile pointer-alignment task in which participants are required to rotate a pointer to a target orientation using tactile feedback from a raised edge. They also showed that this advantage of the complex RFs model over the homogeneous RFs model is higher for shorter edges, which suggests that the complex RFs are particularly beneficial in tasks requiring tactile stimuli approaching the limits of the system's spatial resolution (Figure 7C). Because of the subfields of high sensitivity in the RFs, and the overlap between RFs of first-order neurons in a given skin area, different ensembles of neurons are activated by edges oriented - even slightly - differently. As illustrated in Figure 7A-B, an edge indenting the skin at a certain location and orientation excites primarily the neurons whose subfields are contacted by the edge, while an edge indented at a slightly different orientation contacts different subfields and thus primarily excite a different ensemble of neurons. The same reasoning can be applied to punctate probes applied to the skin. More recently, Jarocka et al. (2021) presented additional evidence that the spatial resolution of SAI and RAI fibers is determined by the complex structure of their RFs rather than solely by their spacing. Scanning raised dots at the fingertips of human subjects while recording SAI and RAI afferents responses, they showed that the measured subfield acuity ( $\approx 0.4$  mm) would enable the resolution of details finer than the innervation density alone. Considering the impact of the complexity of RFs on the neurons' spatial resolution, the less complex RFs of RAI afferents, along with their low density of innervation, potentially account for their lower spatial resolution when compared to RAI and SAI afferent's.

The size of the RFs was also considered a critical factor involved in tactile acuity, with the smallest RFs thought to convey the highest spatial resolution (Johansson & Vallbo, 1979). However, many examples in the literature weaken the link between RF size and tactile acuity. For instance, studies reporting a learning-induced improvement of tactile acuity in a given body part also report a parallel increase in the size of the corresponding RFs (e.g., Godde et al., 1996). Indeed, large RFs in SI do not automatically imply low tactile acuity. Recording SI single-neuron responses to tactile stimuli of the forelimbs in rats, Foffani et al. (2008) showed that the discrimination between close locations is allowed not only thanks to the spike count code (i.e.

the number of neuronal discharges), but also to the spike timing code (i.e. the latency differences within the neural responses). They demonstrated that the spike timing code is particularly informative when RFs are large, or when discriminating between close locations (Figure 7D), allowing for a good tactile acuity even with large RFs.



**Figure 7. The complex shape of RFs and the spike-timing code affect tactile acuity.** [A-C modified from Deflorio et al., 2022, reproduced from Pruszynski et al., 2018; D modified from Foffani et al., 2008] (A) Schematic of skin patch with papillary ridges (grey lines) and mechanoreceptors (white and colored dots). Blue, black and red dots represent receptors innervated by one of three first-order tactile neurons. Colored contour represents first-order neurons' receptive field, while shaded area behind the colored dot represents subfields. (B) Color-coded subfields for 10 first-order tactile neurons. Representation of 10 first-order tactile neurons with overlapping receptive field and subfields (color-coded). First-order neurons are activated if the edge falls on one subfield. Here, the activation response is shown for 10 neurons and 2 edges of 2 mm with different orientation (0 and 20). Colored circles are filled if the neuron is active and empty otherwise. (C) Output of the two tested models (subfields vs. uniform sensitivity). The lines indicate the mean and the shaded areas represent the 95% confidence interval. (D) Large vs. small receptive fields. Surround responses conveyed more information about stimulus location and the additional information conveyed by spike timing over spike count was greater in subpopulations of neurons with large receptive fields compared with subpopulations of neurons with small receptive fields. Whiskers represent 95% confidence intervals.

Overall, recent key findings challenge our understanding of tactile acuity. While it was long believed that precise tactile spatial information was primarily conveyed by densely distributed afferents associated with superficial mechanoreceptors and small RFs (SAI and RAI), recent advances suggest that it may also involve less densely distributed afferents with deeper mechanoreceptors and larger RFs (RAII). In addition to the long-held view that tactile acuity is primarily determined by afferent innervation density and the size and spacing of RFs, recent advances suggest that the complex shape of RFs and the temporal coding of spatial information are equally critical in shaping tactile acuity.

#### **4) Cortical areas underlying tactile acuity**

Tactile spatial resolution is thought to rely on lateral inhibition occurring between close regions on the skin at different stages of the somatosensory processing in subcortical (brainstem, thalamus) as well as cortical areas (SI; see section II. 1 for details). This section specifically focusses on cortical areas involved in tactile spatial acuity. In SI, both structural and functional aspects of these cortical areas were found to be associated with tactile acuity thresholds.

From a structural perspective (i.e. size of cortical areas), intracortical mapping in monkeys consistently documented a positive correlation between tactile acuity at the fingers and the size of the cortical areas representing these fingers in SI, especially in BA 1 and 3b, suggesting that higher tactile acuity is associated with larger areas (Xerri et al., 1996; Xerri et al., 1999). In humans, similar results were reported using fMRI. Duncan & Boynton (2007) showed that the increase in the size of cortical representation across fingers in SI correlates with the decrease in tactile thresholds from the index finger to the little finger, as measured with the 3DT. Härtner et al. (2021) showed that the distance between the representational maps of thumb and little finger in BA 1 and 3b (a proxy of the representation size) is positively correlated with tactile acuity at these fingers as measured with GOT and partially with 2PDT (measured only at the thumb). Other studies investigated the relationship between tactile acuity and gray matter volume. Schmidt-Wilcke et al. (2018) observed that the tactile acuity, as measured with 2PDT, was positively correlated with gray matter volume in SI, including parts of area 1 and 3b, as well as in the thalamus, and negatively correlated with primary visual cortex. Recently, Onishi et al. (2023) showed that the 2PDT performance was negatively correlated with gray matter volume in the inferior parietal lobule (IPL) and middle temporal gyrus.

From the functional perspective, using resting-state fMRI, Haag et al. (2015) showed that higher baseline cortical activity (blood oxygenation level dependent (BOLD) signal amplitudes) and

synchronicity at rest in the SI hand region are related to better tactile acuity - as measured with the 2PDT - of the contralateral hand. Additionally, a MEG study revealed that the beta band resting-state functional connectivity between SI and superior parietal lobule, IPL and superior temporal gyrus predicts tactile acuity as measured with the 2PDT, with stronger connectivity associated with better performance in 2PDT (Sasaki et al., 2023). Using paired pulse electrocutaneous stimulation, they additionally showed that a weaker somatosensory gating (i.e. a weaker attenuation of the second cortical response by the first stimulus, reflecting weaker inhibition) is associated with better performance in 2PDT, suggesting that SI local inhibitory network plays a role in tactile acuity. In contrast, in an older population, a weaker somatosensory gating was found to be associated with a worse performance in 2PDT, indicating that an increased excitability of SI is associated with impaired tactile acuity (Lenz et al., 2012). This discrepancy can be attributed to the age difference between the two populations, suggesting that the reliance of tactile acuity on SI cortical inhibition may vary with age.

Besides somatosensory cortices SI and SII, as well as areas involved in somatosensory processing, attention, and working memory (involved in all cited tasks, so not mentioned in this section), other cortical areas have been shown to be involved in the resolution of the different tactile acuity tasks (described above). Some of these areas are shared across tasks, while others seem task-specific. These will be briefly reviewed in the next paragraphs and summarized in Figure 8.

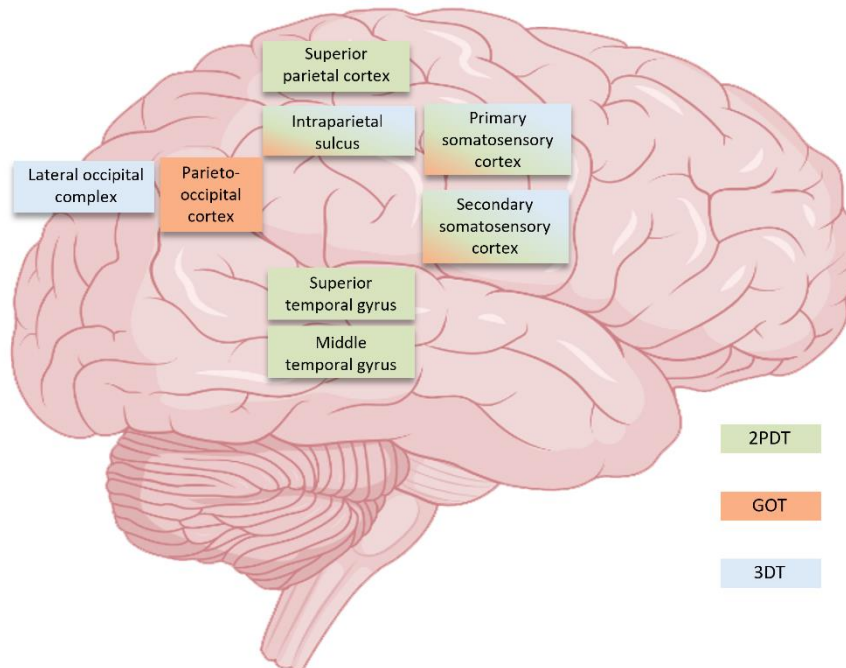
Despite the extensive use of 2PDT in the literature, very few studies investigated the cortical areas involved during this task. In fMRI, Akatsuka et al. (2008) found that the left IPL is specifically activated during the 2PDT, as compared to during a control task (intensity discrimination task). According to the authors, this result suggests that early automatic discrimination takes place in SI and SII (Akatsuka et al., 2007), and the next higher-order judgment process takes place in the IPL. When inspecting closely the coordinates the authors provided for the activated IPL ( $x, y, z = -46, -40, 48$ ) in an online brain atlas (Siibra explorer by Ebrains), I found that this area is located closer to the intraparietal sulcus (IPS) than to IPL. Besides, it is worth adding here that even though the performance in the 2PDT has been shown to negatively correlate with the gray matter volume in the primary visual cortex (Schmidt-Wilcke et al., 2018), this finding was not replicated (Onishi et al., 2023; described above). In addition, this area was not found to be activated during the 2PDT in fMRI (Akatsuka et al., 2008), suggesting that it is very unlikely involved in the task.

Concerning the GOT, multiple studies showed that its performance involves of the left intraparietal sulcus (IPS). Using fMRI, Van Boven et al. (2005) found that in comparison to a control task (discrimination of location), performing the GOT selectively activated the IPS, with significantly greater activity in the left than the right IPS, regardless of the tested hand. Using fMRI, Zhang et al. (2005) revealed that in comparison to a control task (discrimination of grating spacings), the GOT performed with the right index finger activated the left anterior IPS and left parieto-occipital cortex. Contrasting the activities measured in positron emission tomography (PET) imaging during GOT versus during a control task (discrimination of grating spacings) performed with the right index finger, Sathian et al. (1997) also revealed a selective activation of the left parieto-occipital cortex (bordered by the IPS), which suggested the involvement of this visual area in GOT. Later transcranial magnetic stimulation (TMS) studies confirmed that this area is crucial for the task, as disrupting its activity through TMS impaired the performance in GOT, while it did not affect the performance in the control grating spacing task (Zangaladze et al., 1999; Sathian & Zangaladze, 2002).

During the 3DT, areas shown to be involved in this task performance include the right posterior IPS, as revealed both through fMRI (Stilla et al., 2007; performed with the right index finger; contrasted with a temporal discrimination version of the task) and EEG combined with source reconstruction techniques (Adhikari et al., 2014; performed with the right index finger). Other regions such as the right precuneus (in the superior parietal lobule; Stilla et al., 2007) and the right lateral occipital complex (LOC; Adhikari et al., 2014) were shown to be involved as well. The activity in the right posterior IPS and right precuneus significantly predicted the individual performance (Stilla et al., 2007). Interestingly, in the visual version of the 3DT, the IPS was also found to be specifically activated, while the LOC was specifically activated during the extrapolation control task (Tibber et al., 2008). Considering the results of both these studies, one can hypothesize that the LOC - known to be involved in shape perception and object recognition (Mazer & Gallant, 2000) - activated during the tactile but not the visual 3DT, would reflect a process of mentally imagining a visual image of the orientation of the touched dots (i.e. similar to an extrapolation), while the IPS, activated both during the tactile and visual 3DT would reflect the spatial acuity.

While the IPS (or IPL close to IPS) seems to be involved in all three tasks (in addition to other somatosensory, attentional and working memory areas), suggesting that it is involved in the processing of discriminating between fine spatial details in tactile stimuli, the temporal gyrus seems more specific to the 2PDT, and visual occipital cortical areas seem more specific to tasks

involving orientation judgement (GOT and 3DT). No neuroimaging data during the 2POT are so far available in the literature, but one can hypothesize that because of the orientation aspect of the task, the involved areas would be similar to those involved in the GOT. The Figure 8 summarizes the neural bases of the tactile acuity tasks described in this section.



**Figure 8. Neural bases of the tactile acuity tasks.** While the IPS (or IPL close to IPS) seems to be involved in all three tasks (in addition to other somatosensory, attentional and working memory areas), the temporal gyrus seems more specific to the 2PDT, and visual occipital cortical areas seem more specific to the GOT and 3DT, involving orientation judgement.

## II- Mental body representations (MBRs)

As briefly mentioned earlier (see section II.2.b.), the processed tactile information from SI and SII reach the PPC (including BA 5 and BA7), known to house representations of our body parts, called mental body representations (MBRs). Besides receiving tactile inputs, these representations are also nourished by proprioceptive, visual, auditory, and motor inputs, making them multisensory (Bremner et al., 2012; Azañón et al., 2016). To achieve a unified perception of the external world (Bremner et al., 2012) and a coherent sense of body ownership (Klaver & Dijkerman, 2016), sensory signals must be processed with reference to these representations.

Some authors distinguish between short- and long-term MBRs, the former referring to very short lived MBRs that are built up, stored in working memory, and erased within a very short delay, while the latter refers to MBRs storing content that is never erased, but only updated (de Vignemont, 2010; Gadsby, 2019). Note that in this thesis work, only long-term MBRs will be

discussed and studied. Importantly, no consensual number of MBRs has been agreed upon in the literature, many of them carrying multiple definitions and being articulated in different classifications and models. In this section, I will deliberately select the models appropriate for this thesis and I will attempt to present them highlighting their correspondences and will propose a theoretical working model to be used in my thesis work. I will then briefly present the known neural basis of these MBRs and conclude this section with evidence showing how plastic they are.

## **1) The MBRs and their characteristics**

### **a. Body schema & Body image**

The first known classification of MBRs (referred to as the dyadic model) is the distinction between the body schema, a representation of body parts used for action, and the body image, a representation of body parts used for bodily perception (Sattin et al., 2023). The evidence of such a distinction first came from studies of double dissociation showing that some patients with brain injuries were unable to localize a tactile stimulus on their body while being still able to verbally indicate where they were touched (Head & Holmes, 1911). Similarly, a stroke patient was unable to detect a tactile stimulus on their hand while being still able to point towards it (Paillard et al., 1983). Further support for this distinction was provided by quite similar double dissociation observations (Gallagher & Cole, 1995; Paillard, 1997; Paillard, 1999; Anema et al., 2009; Ro & Koenig, 2021). These dissociations were interpreted as originating from distinct processes mediated by two distinct MBRs, namely the body schema, thought to be disrupted when patients were not able to point towards a tactile stimulus, as in deafferented patients, and the body image, thought to be impaired when patients could not consciously detect a tactile stimulus, as in numbness or personal neglect (Paillard, 1999; Ro & Koenig, 2021). Dijkerman & De Haan (2007) then attributed action-oriented sensory processing to the body schema and perception-oriented sensory processing to the body image, and postulated that the former is part of the dorsal somatosensory stream while the latter is part of the ventral somatosensory stream. This model is known as the perception-action model.

The body schema's definition varies slightly depending on the authors, but the consensual idea is that it is an implicit sensorimotor representation containing knowledge of the positions of body parts, continuously updated as the body moves, involved in guiding actions unconsciously (Head & Holmes, 1911; Medina & Coslett, 2010). It is seen as nourished mainly (but not exclusively) by proprioceptive inputs and motor outputs, drawing on past sensorimotor experiences to represent the body's typical sensorimotor configurations and using this to assess



the current state of the body (Berlucchi & Aglioti, 1997). The body schema can be assessed through tasks like pointing to one's body parts (Paillard, 1999; Rossetti et al., 1995), localizing a tactile stimulus on one's own body by pointing towards it (Anema et al., 2009), hand laterality tasks and motor imagery (Schwoebel & Coslett, 2005) and reaching and grasping (de Vignemont, 2010).

Often defined in opposition to the body schema, the body image, involved in explicit perceptual judgments, is a conscious visuospatial representation of the body and its parts, responsible for perceptual identification and recognition of the body (e.g., body part judgements; Dijkerman and De Haan, 2007; Paillard, 1999), containing information about the shape and size of the body parts. According to some authors, the body image encompasses this perceptual aspect (size, shape, weight of our body parts), as well as other aspects such as cognitive components (beliefs regarding body shape and appearance) and affective (feelings, satisfaction or dissatisfaction about the body) ones (Gallagher, 2005), which are mainly studied in clinical cases of body image disturbance (Yamamoto et al., 2017). In this thesis work, the term body image will consistently refer to the perceptual aspect of this MBR.

The body image can be measured through two main types of methods (Longo & Haggard, 2012a): (i) depictive methods, in which participants are instructed to compare their own body to a picture, or drawing of a body (2D), including tasks such as the distorting mirror, the distorted photograph technique, and the template matching task, and (ii) metric methods, in which participants are asked to compare their own body to a physical length (1D), including tasks such as the moving caliper, the image marking procedure, and the line length. Depending on the type of task used to assess it, the body image appears either accurate or distorted. As an example, the body image of the hand was consistently found to be accurate when measured through depictive methods (Longo & Haggard, 2010, 2011; Berlucchi & Aglioti, 2010; Cash & Deagle, 1997; Van der Looven et al., 2021). Instead, the use of metric methods revealed a quite distorted body image, with an underestimation of the finger length and an increasing underestimation along a radial-ulnar gradient, matching the SI maps distortions (Longo & Haggard, 2012a). This discrepancy between depictive and metric methods also stands for other body parts (Linkenauger et al., 2015) and in clinical populations such as anorexia (Cash & Deagle, 1997; Smeets et al., 1997). As proposed by Longo & Haggard (2012a), these findings suggest that metric methods may not be pure measures of the body image, but instead a mixed measure tackling both the body image and another MBR likely nourished by additional somatosensory information (i.e. the body model, described in section II.1.c.).

Since the establishment of the concepts of body schema and body image, much work has been done in trying to clarify their distinction and studying their functional relationships (e.g., Gadsby, 2017; Pitron & de Vignemont, 2017; Pitron et al., 2018), with the co-construction model arguing that body image and body schema co-construct and reshape each other (Pitron & de Vignemont, 2017). In contrast with the classical view of independent body schema and body image, associated with two distinct functions (perception and action), some authors argued that it is possible to switch from the body schema to the body image in case of unreliability of one source of information (Ionta et al., 2016; Scandola et al., 2019). This issue, however interesting, will not be further developed as it is beyond the scope of this work.

### **b. Body structural description & Body semantics**

The second well-established model of MBRs is the triadic model (Sirigu et al., 1991; Schwoebel & Coslett, 2005), that keeps the body schema, but splits the body image into two distinct MBRs, namely the body structural description and the body semantics. Thought to be primarily based on visual inputs, and to a lesser extent on somatic perception, the body structural description contains information about the relationships between body parts (spatial configuration of the body) and is updated as a function of position of body parts in space. More conceptual and linguistic, the body semantics contains information about the names of body parts, their functional purpose, as well as the categorical relationships between them. Support for this triadic model comes from the dissociation between the following clinical conditions. The body structural description would be disrupted in autotopagnosic patients, who are not able to point to named body parts on themselves or others, or to match pictured body parts across changes in viewing angles while being still able to point to parts of animals and inanimate objects (Sirigu et al., 1991; Buxbaum & Coslett, 2001). In contrast, the body semantics would be disrupted in body-specific aphasic patients, who are unable to understand body part names despite being able to understand words from other semantic categories and to point to visually identified body parts on themselves (Suzuki et al., 1997).

The body structural description can be assessed through tasks such as matching body parts by location, in which participants should find the body part closest to a target body part (Schwoebel & Coslett, 2005), or the in-between task, in which participants are instructed to estimate the number of unstimulated fingers between two touched fingers (Rusconi et al., 2014). The body semantics can be assessed through tasks such as matching body parts by function (finding the body part most similar in function to a target body part), or matching body parts to clothing and objects (Schwoebel & Coslett, 2005).

### **c. Superficial schema & Body model**

Besides the classical dyadic and triadic models, more recent models include other MBRs. Longo et al. (2010) argued that localizing a tactile stimulus on our body requires a MBR connecting the locations in SI somatotopic maps to the locations on the skin surface of the body, which they proposed to be the superficial schema, first described by Head & Holmes (1911). Support for the existence of this MBR can be found in cases of brain damaged patients (i) unable to localize where they were touched while still being able to report that they had been touched, suggesting that a process beyond SI could be involved in tactile localization (Head & Holmes, 1911) and (ii) brain damaged patients displaying systematic shifts when localizing tactile stimuli on their hand, with still preserved somatotopic arrangement between the perceived locations of stimuli, suggesting a disrupted linking function between the SI somatotopic maps and the corresponding skin regions (Rapp et al., 2002). The superficial schema can be assessed through tasks such as localizing a tactile stimulus on a drawing or picture of the body part (Longo et al., 2015; Mancini et al., 2011). According to the models of Longo et al. (2010, 2015), the superficial schema is involved in the somatic localization of touch (localizing touch on the skin), which is then combined with spatial localization of the touched body part, to localize touch on the external space (spatial remapping). Beyond this view, somatic localization of touch has also been shown to integrate location estimates of the touched body part. Indeed, alongside anatomically coded spatial information, current research indicates that tactile localization relies on externally coded spatial information as well (see Badde & Heed, 2016 for a review). Additionally, recent evidence further indicates that the default location of a touched body part, in addition to its current location, is also involved in the computation of the location of touch. Badde & Heed (2023) showed that prior information about the location of the hand (i.e. hand's default location) influenced tactile localization on a limb.

In addition, Longo & Haggard (2010) introduced another MBR to account for the ability to localize a body part in space (what is known as position sense), as this requires not only information about the posture (angles of joints, from proprioceptive inputs) stored in the body schema, but also information about the distance between the joints, putatively stored in another representation which they called the body model. Because it contains metric properties of the body parts, this MBR would also be required for perceiving metric properties of tactile stimuli. The body model can be measured through landmark localization and tactile distance judgement tasks. In the landmark localization task, participants are asked to localize joints and extremities on a board covering the body part. The perceived metrics of the hand can be derived from these

judged locations. In the tactile distance judgement task, participants are instructed to estimate the distance between two tactile punctate stimuli applied simultaneously on their body part.

Using a tactile localization task, Mancini et al. (2011) reported consistent distal and radial biases on the hand dorsum (towards fingertips and thumb) and less striking proximal biases on the hand's palmar surface. These findings were replicated at the hand (Margolis & Longo, 2015; Medina & Duckett, 2017; Kang & Longo, 2023) and localization biases were also found at the forearm (Azañón et al., 2010; Cholewiak & Collins, 2003), abdomen (Cholewiak et al., 2004) and back (Pratt et al., 2024), which indicates that the superficial schema is distorted in the healthy population. Interestingly, similar distortions were found when assessing the body model with both landmark localization and tactile distance judgement tasks. Using landmark localization tasks, Longo et al. (2010) found that the hand width was consistently overestimated while the finger length was underestimated, with larger distortions on the dorsal than on the palmar surfaces of the hand (Longo & Haggard, 2012b). Coherent findings were observed when the body model was assessed through a tactile distance judgement task, in which distances across the hand were systematically perceived as larger than along the hand (Longo & Haggard, 2011).

These distortions were hypothesized to stem from the shape of the RFs of neurons representing the limbs which tend to be oval-shaped, elongated along the proximo-distal axis of the limb (e.g., Powell & Mountcastle, 1959; Brooks et al., 1961), but because the SI-related distortions are larger than those seen in the tasks, they would be partly corrected before impacting the behavioral performance in the tasks. Further support for this hypothesis was brought by Tamè et al. (2021). Using fMRI and multidimensional scaling to reconstruct the internal geometry of tactile space in SI when punctate stimuli were applied on the hand dorsum, they revealed a distorted pattern in SI tactile space that is similar to the distorted pattern of perceived tactile distances. Recently, these perceptual distortions were proposed to arise from near-optimal Bayesian integration of somatosensory inputs, instead of reflecting an inherent feature of these MBRs (Peviani et al., 2024).

This distorted pattern has been extensively replicated on the hand with both the landmark localization task (e.g., Tamè et al., 2021; Longo & Haggard 2012a; Peviani & Bottini, 2018; Van der Looven, 2021) and the tactile distance judgement task (Longo & Haggard, 2011; Longo, 2020, 2022; Mainka et al., 2023), and other distortions (over and underestimation) were also found with both tasks on the arm (Engel et al., 2021; Chang & Longo, 2022), face (Longo & Holmes, 2020), upper-back (Nicula & Longo, 2021), leg (Stone et al., 2018), feet (Manser-

Smith et al., 2021), the lower-back (Nicula & Longo, 2021), the belly (Engel et al., 2021; Longo et al., 2019) and the full body (Caggiano & Cocchini, 2020). Taken together, these results indicate that the body model, the MBR supposedly involved in both landmark localization and tactile distance perception, is distorted for most of the body parts.

Originally, Longo et al. (2010) introduced the body model into their model of MBRs to account for both the position sense (as measured through the landmark localization task) and tactile distance perception (as measured through the tactile distance judgement task). While the distortions found in both these tasks were found to be similar, suggesting the involvement of a common MBR (the body model), a study comparing directly both tasks in the same individuals called this into question, as they found no correlation between the magnitudes of distortions found in each task (Longo & Morcom, 2016). The authors concluded that while it is possible that two distinct MBRs would underlie position sense and tactile distance perception (in this case, the similar patterns would stem from the oval-shaped RFs in SI maps), the possibility of a common MBR could not be excluded, and the different patterns of individual differences would be accounted for by the specific task demands. In the remainder of this dissertation outside this chapter, the term body model will refer to the MBR involved in tactile distance perception.

Because of these distortions in the body model, one could wonder how can distorted representations lead to accurate actions, an issue known as the “hand paradox”. The question is currently debated in the literature (Bassolino & Becchio, 2023; Longo, 2023), and one of the proposed explanations is that correction of the distortions would take place during action (Longo, 2023). Studies supporting this hypothesis showed that when assessed during movement (dynamic task), the body model is less distorted than when assessed in the absence of movement (static task), suggesting that the kinesthetic feedback would reduce body model distortions (Peviani & Bottini, 2018; Peviani et al., 2020).

Although the body model was originally thought to be perception-oriented (Longo et al., 2010) along with the body image and in contrast to the body schema, a recent view argues that the body model would be both action- and perception-oriented and would inform both the body image (thought to rely on the ventral stream) and the body schema (thought to rely on the dorsal stream), suggesting a hierarchical organization between the body model (upstream) and the other two MBRs (Coelho & Gonzalez, 2024).

#### **d. Matching the models**

The MBRs described in the previous sections are articulated differently under “categories of MBRs” in the multiple models the authors proposed. As presented above, the dyadic model only includes the body schema and body image, while the triadic model includes the body schema, the body structural description and the body semantics.

In the models of Longo et al. (2010, 2015), the body schema (often called the postural schema), the body image (which they define as the perceptual body image, excluding the conceptual or affective components), the superficial schema, and the body model are part of a broad category they call *Somatoperception* which consists in the perception that involves the online construction of higher-level percepts related to the body, ensuring somatic perceptual constancy. Instead, the body structural description and the body semantics (along with general knowledge about bodies and emotions about the body) are part of another category they call *Somatorepresentation*, which refers to the cognitive process of constructing semantic knowledge and attitudes about the body.

Recently, De Haan & Dijkerman (2020) revised their model opposing perception-oriented and action-oriented MBRs (Dijkerman & De Haan, 2007) and proposed a new model of somatosensory processing architecture featuring five multimodal partially-overlapping networks, each of which relies in part on somatosensory information and serves a specific function: haptic object recognition, body ownership, affective processing, body perception, and action. According to my view and based on the descriptions of these networks, two of these networks would involve the MBRs described in the previous sections: MBRs related to action and MBRs related to body perception, with the latter split into spatial body representations and structural body representations, based on literature showing that both are dissociable (Sirigu et al., 1991; Schwoebel & Coslett, 2005), even though they share some parts of their networks. They describe spatial representations as representations used to get the location of, distance between, and speed of touch sensation, while structural representations would concern knowledge and awareness of the positions of body parts, as well as knowing the left and right sides of the body.

Based on the description of the functions underpinned by the different networks, I attempt here to highlight correspondences (though not perfectly fit) between De Haan & Dijkerman’s recent model and the MBRs described in the sections above. To my understanding, the MBR related to action would correspond to the body schema in all models. Spatial representations would

correspond to the body model and superficial schema, from the model of Longo et al. (2010) and structural representations would correspond to the body structural description, from the triadic and Longo et al. (2010)'s model. The body image, acknowledged by De Haan & Dijkerman's model though not explicitly included in one of the networks, would correspond to both the body image from Longo et al. (2010)'s model and the body semantics from the triadic and Longo et al. (2010)'s models. The Figure 10 below presents my best attempt to match the MBRs terminologies across the models.

Dyadic model	Triadic model	Longo et al. (2010, 2015)	De Haan & Dijkerman (2020)
<b>Body image</b> Visuospatial representation of the body used for perception	<b>Body structural description</b> Visuospatial representation of the relations between body parts (spatial configuration of the body)	<b>Body structural description</b> Visuospatial representation of the relations between body parts (spatial configuration of the body)	<b>Structural body representations</b> Knowledge and awareness of the positions of body parts, knowing left and right sides of the body
	<b>Body semantics</b> Semantic and lexical representations of the body including body part names and functions	<b>Body semantics</b> Semantic and lexical representations of the body including body part names and functions	<b>Body image</b> Conscious representation of the body used for building and maintaining a sense of self
<b>Body schema</b> Sensorimotor representation of the relative positions of body parts, used for action	<b>Body schema</b> Sensorimotor representation of the relative positions of body parts, used for action	<b>Postural schema</b> Sensorimotor representation of the relative positions of body parts, used for action	<b>Action-related representation</b> Representation of position of body and limbs
		<b>Superficial schema</b> Representation of the body surface used to localize somatic stimuli	<b>Spatial body representations</b> Representation of the location of, distance between, speed of touch sensation
		<b>Body model</b> Representation of the metric properties of body parts, used to perceive metric properties of tactile stimuli	

**Figure 9. Working model matching the MBRs described in the dyadic, triadic, Longo et al. (2010, 2015), and De Haan & Dijkerman (2020) models.**

## 2) Cortical areas underlying MBRs

Quite consensually, the MBRs are thought to be housed in PPC areas (Serino & Haggard, 2010) or underpinned by networks mostly involving the PPC. However, the areas specific to each MBR have not been completely determined, mainly because most neuroimaging and neuropsychological studies focused on one MBR at a time usually using different tasks depending on the authors. Based on the neural bases identified in the recent reviews by Longo et al. (2010), De Haan & Dijkerman (2020), the meta-analysis of Di Vita et al. (2016), as well as a few additional neuroimaging studies (e.g., Hamamoto et al., 2023), the cortical areas underlying each MBR described above are briefly presented in the following paragraphs, without detailing each study. As argued by De Haan & Dijkerman (2020), all MBRs are based on a common foundation composed of the thalamus, SI and SII, and their neural bases diverge at a higher level.

Lesions of the superior parietal lobe were observed in stroke patients suffering from deficits in tasks supposedly involving the body schema (Wolpert et al., 1998). The more frequent involvement of the right hemisphere additionally suggests a higher dependency of the body schema on this hemisphere (Sterzi et al., 1993). PET and fMRI studies showed that tasks involving motor imagery and postural representations of the upper limb activated the superior parietal cortex (Parsons et al., 1995; Pellijeff et al., 2006). Monkey studies further revealed that visual information modulated postural information in the lateral intraparietal area (LIP) in the IPS (Snyder et al., 1998) and an area thought to correspond to the LIP was found to process changes of head position in relation to the rest of the body in humans (Fasold et al., 2008). Besides, an ALE meta-analysis on human data (Di Vita et al., 2016) showed the specific involvement of MI and the right extrastriate body area (EBA) in the occipital cortex in the body schema. According to the model of De Haan & Dijkerman (2020), the action network involving the body schema comprises the superior parietal cortex, the IPS, the premotor cortex and MI, as well as the cerebellum.

The body image involves more distributed areas across the brain as it involves the PPC, as well as occipital and frontal areas. In the PPC, it relies on the anterior IPS (Ehrsson et al., 2005), the inferior parietal lobule (IPL; Esposito et al., 2016; Gaudio & Quattrocchi, 2012) and the precuneus (Mohr et al., 2010, 2011). In the occipital lobe, the volume of the EBA and its functional connectivity to the PPC have been linked to susceptibility to the finger stretch illusion (Moayedil et al., 2021). Additionally, the connectivity between the EBA and the insula was found to positively correlate with the degree of perceived distortion when comparing our own body to a pictured body of varying width (Hamamoto et al., 2023). In the frontal lobe, the middle frontal gyrus was found to be associated with estimating the size of the body (Mohr et al., 2010, 2011). Moreover, the activity in the anterior cingulate cortex was found to be positively correlated with the degree of perceived distortion when comparing our own body to a pictured body of varying width (Hamamoto et al., 2023). Finally, a meta-analysis revealed the involvement of the supramarginal gyrus in the parietal cortex in the body image or body structural description (the authors did not distinguish between them; Di Vita et al., 2016).

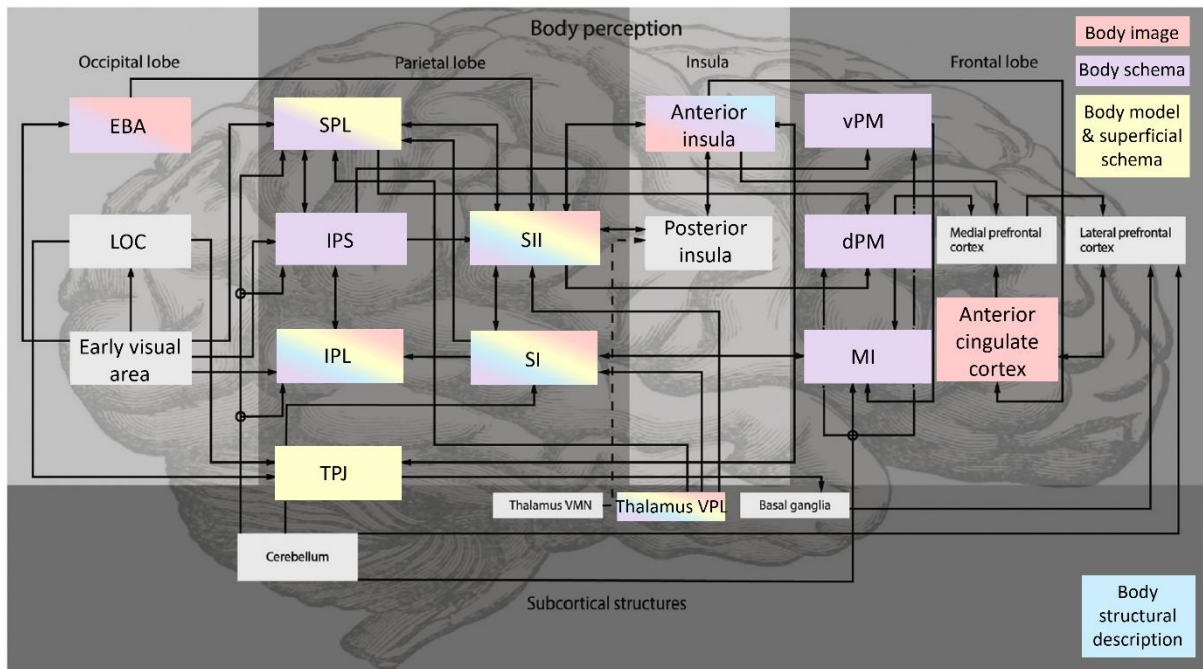
The body structural description and the body semantics seem to be especially linked to the left hemisphere. The body structural description was found to rely on the left posterior IPS as shown in fMRI during the assessment of spatial relationship between body parts (Corradi-Dell'Acqua et al., 2008) and mental rotation task (Corradi-Dell'Acqua et al., 2009) as well as the left superior parietal cortex (Felicjan et al., 2004). The body semantics is thought to involve the left



parietal cortex (Laiacona et al., 2006; Suzuki et al., 1997), and more specifically the left inferior parietal cortex, the inferior frontal cortex (Kemmerer & Tranel, 2008), as well as the anterior temporal cortex (Dennis, 1976), because patients impaired in naming body parts were found to have lesions in these regions. According to the model of De Haan & Dijkerman (2020), the structural representation network (which would correspond to the body structural description) involves the inferior parietal cortex and the anterior insula.

Finally, the superficial schema and the body model would involve exclusively parietal areas. Indeed, tactile localization involving the superficial schema was found to activate the right temporoparietal junction (TPJ; Van Boven et al., 2005), and to be altered when TMS was applied over the anterior parietal cortex (Porro et al., 2007). In addition, tactile distance judgement involving the body model was found to activate the right angular gyrus and the right parieto-occipito-temporal junction (Spitoni et al., 2010), and to be altered after transcranial direct current stimulation (tDCS) over the right angular gyrus (Spitoni et al., 2013). According to the model of De Haan & Dijkerman (2020), the spatial representation network (which would correspond to the body model and superficial schema) comprises the superior and inferior parietal cortex, as well as the TPJ.

Overall, while the body schema and body image seem to rely on distributed areas in the parietal, occipital and frontal cortices, the body semantics seem to involve parietal, temporal and frontal areas, and the body structural description, the superficial schema and the body model seem more specific to the posterior parietal cortex. The areas involved in the body image, body schema, body model and superficial schema are recapitulated in the following Figure 10.



**Figure 10. Cortical areas involved in MBRs.** [Modified from De Haan & Dijkerman, 2020] While all MBRs rely on SI, SII and the inferior parietal lobule (IPL), the body image (pink) would additionally rely on the extrastriate body area (EBA), the anterior insula and the anterior cingulate cortex, the body schema (purple) would rely on the superior parietal lobule (SPL), intraparietal sulcus (IPS), EBA, the ventral and dorsal premotor cortex (vPM & dPM) and the primary motor cortex (MI), the body structural description (blue) would rely on the anterior insula, and the body model and superficial schema (yellow) would rely on the superior parietal lobule (SPL) and the temporoparietal junction (TPJ).

### 3) Plasticity of MBRs

Far from being fixed, MBRs are highly plastic as they were found to evolve during development (Bremner et al., 2016; De Klerk et al., 2021), change with healthy ageing (Riemer et al., 2019; Sorrentino et al., 2021; Dupin et al., 2022), and be altered in clinical conditions such as following brain lesion but also in anorexia nervosa (e.g., Keizer et al., 2012; Risso et al., 2020), bulimia (e.g., Mohr et al., 2011 ; Mölbert et al., 2017) or complex regional pain syndrome (e.g., Tajadura-Jimenez et al., 2017a; Reinersmann et al., 2021). In addition, changes in MBRs were also observed following manipulations of somatosensory inputs such as altering tactile inputs (e.g., Gandevia & Phegan, 1999), tool-use (e.g., Cardinali et al., 2009), or when conflicting multisensory information as in sensory illusions (e.g., Botvinick & Cohen, 1998).

As mentioned earlier, MBRs were found to be continuously updated by SI inputs (Serino & Haggard, 2010). It is therefore not surprising to find them altered following temporary (anesthesia or stimulation) or permanent (amputation) changes in tactile inputs. An increased perceived size of a body part indicating an alteration of the body image has been consistently shown following anesthesia, for the thumb (Gandevia & Phegan, 1999; Paqueron et al., 2003),

lips (Gandevia & Phegan, 1999; Türker et al., 2005) and limbs (Paqueron et al., 2003). Additionally, Gandevia & Phegan (1999) showed that similarly to anesthesia (reduction of inputs), three short trains of electrical cutaneous stimulation (increase of inputs) of digital nerves also induced an increased perceived size of the stimulated finger (though smaller than following anesthesia). When somatosensory inputs (as well as the sight of the limb) are permanently removed through amputation, studies revealed shorter tactile distances on the stump than on the healthy limb (Canzoneri et al., 2013a), impaired performance in a motor imagery task (Nico et al., 2004) and an impaired ability to represent relations among different body parts as compared with healthy controls (Palermo et al., 2014), suggesting an alteration of the body model, the body schema, and the body structural description, respectively.

Following both anesthesia and amputation, the alterations of MBRs are thought to be mediated by the plasticity in SI maps induced by these peripheral changes (Calford & Tweedale, 1991; Merzenich et al., 1984). Interestingly, a more common case in which a peripheral intervention can affect MBRs is tool use (see Martel et al., 2016 for a recent review). Recording hand movement kinematics before and after tool use, Cardinali et al. (2009) showed that after using a mechanical (arm-shaped) grabber for ten minutes, the kinematic profile of hand reaching movements was significantly altered in a way that corresponds to the kinematic pattern of long-armed people. The grasping component of the same movements was not affected. These results are coherent with a modification of the body schema affecting the forearm, but not the hand, suggesting that the tool was selectively incorporated into the body schema of the forearm (de Vignemont & Farnè, 2010). In another study, pointing to anatomical landmarks where participants were touched on the forearm or hand after arm-shaped tool-use revealed a performance consistent with an elongated forearm but not hand (Cardinali et al., 2011), suggesting a specific alteration of the forearm's body model. In contrast, when the tool used to grasp an object was a hand-shaped grabber, tool use altered the perceived tactile distance on the hand, but not on the forearm (Miller et al., 2014), indicating a selective alteration of the hand's body model. Additionally, it selectively affected the grasping component of the movement while the reaching component was unchanged (Cardinali et al., 2016), indicating a selective alteration of the hand's body schema. Curiously, while the results described above tend to indicate that tool-use increased represented arm length, other studies (Canzoneri et al., 2013b; Miller et al., 2014) found that tool-use affected tactile distance on the forearm in the direction of a reduction. This discrepancy was explained by the authors to either arise from differences

in the tasks used, or to be related to the fact that as one's body part is perceived as larger, external objects appear smaller in comparison (e.g., van der Hoort et al., 2011).

Beyond that, MBRs were also found to be altered when central SI activity was temporarily disrupted by TMS or repetitive TMS (rTMS). Applying TMS over the right sensorimotor cortex, Seyal et al. (1997) observed deficits in both detection and localization of tactile stimuli applied at the hand, with more profound and long-lasting impairments for localization, suggesting an altered superficial schema. Applying rTMS over the hand SI area in both hemispheres (in different experiments), Giurgola et al. (2019) showed that the participants perceived their hand as larger than at baseline, as assessed through a template matching task, suggesting that their body image was altered.

Because MBRs are built from multiple sources of sensory information from different modalities, they can be altered under certain conditions of conflict or artificial concordance between multiple sensory information (for a recent review, see Kilteni et al., 2015). The most famous case is the visuo-tactile Rubber hand illusion (Botvinick & Cohen, 1998) during which a rubber hand can be felt as our own when the tactile (feeling our hand being stroked) and visual (seeing the rubber hand being stroked) information are repeatedly synchronized to create the illusory feeling that the rubber hand is our own even though these information are incongruent with proprioceptive information from our real hidden hand. Additionally, the illusion results in the real hand being perceived as closer to the rubber hand than it really is. Some studies found that reaching or grasping is also affected (Botvinick & Cohen 1998; Holmes et al., 2006; Kammers et al., 2010) while others found no effect of the illusion on reaching and grasping (Kammers et al., 2009). The former results indicate that the body schema would incorporate the rubber hand (Heed & Röders, 2012) alongside the body image, while the latter indicate that only the body image would be affected by the illusion.

Other sensory manipulations affecting MBRs consist in visually magnifying or minifying a body part to induce a change in the perceived size of the body part. Interestingly, this illusion was found to alter not only the perceived length of the body part (Taylor-Clarke et al., 2004; Bratch et al., 2021), but also the perceived distance between two points applied on this body part suggesting a subsequent alteration of the body model (Taylor-Clarke et al., 2004). Reaching and grasping were also affected, suggesting an alteration of the body schema (Marino et al., 2010; Ambron et al., 2017). The illusion was also found to induce a change in motor cortex excitability (Ambron et al., 2018).

When considering illusions induced by manipulating proprioceptive information, the classical one is the Pinocchio illusion (Lackner, 1988). It consists in stimulating the tendon of a limb muscle while the participant uses this limb to touch another body part, which induces an illusory movement of the stimulated limb accompanied by a change in the perceived size of the touched body part, suggesting an alteration of the body image (Lackner, 1988; Ehrsson et al., 2005). For instance, when the nose is touched while the biceps tendon is vibrated, the hand touching the nose is perceived as moving away from the face, and the nose is thus perceived as elongated. In contrast, when the nose is touched while the triceps tendon is vibrated, the hand is perceived as moving towards the face, and the nose is perceived as shorter (Lackner, 1988). Using a variant of this illusion consisting in biceps tendon vibration while the participants grasped their index finger, de Vignemont et al. (2005) showed that inducing an illusory lengthening of the finger increased the perceived tactile distance between two points applied on this finger, suggesting that both the body image and the body model were affected by the illusion.

More recently, MBRs were found to be also altered by auditory illusions. In a series of studies by Tajadura-Jiménez et al. (2012, 2015), participants tapped on a surface while progressively extending their arm sideways, hearing a tapping sound in synchrony with each tap. When the sound was manipulated to originate at double the distance at which they tapped, the arm was perceived as being longer than its actual length (Tajadura-Jiménez et al., 2015) and the tactile distance between two points applied on the arm was perceived either as larger (Tajadura-Jiménez et al., 2012), or as smaller (Tajadura-Jiménez et al., 2015) than before the illusion. This discrepancy in the effect's direction on tactile distance judgement recalls the discrepancy in tool-use-induced changes in perceived tactile distance described above, and shows that it is important to account for factors that may affect how tactile information is used when making tactile distance judgments (Miller et al., 2014). In other studies (Tajadura-Jiménez et al., 2017b; Nava & Tajadura-Jiménez, 2020) the authors manipulated the pitch of sounds to manipulate space in order to produce an “auditory Pinocchio illusion”, as pitch has been found to be mapped onto a mental representation of space, with high pitches mapped to high positions in space (Rusconi et al., 2006). As participants pulled on their right index finger with their left hand in either the vertical or horizontal direction (without seeing it), they heard brief sounds of rising pitch, and consequently perceived their finger to be longer than before in the vertical (Tajadura-Jiménez et al., 2017b; Nava & Tajadura-Jiménez, 2020), but not the horizontal direction condition (Nava & Tajadura-Jiménez, 2020). Taken together, all these findings suggest that auditory illusions alter the body image as well as the body model.

Though not exhaustive, the experimental findings described in this section demonstrate that MBRs, built with integrated multisensory information, are highly plastic and can be rapidly altered by altered SI processing, tool use, and sensory unimodal or multimodal manipulation.

---

In summary, the studies discussed in this chapter offer valuable insights into the current understanding of tactile acuity and MBRs. Recent findings about the determinants of tactile acuity challenge our understanding of it, and nourish reflections about the various features that contribute to it, as well as the most effective ways to measure it. At a higher level, the multisensory MBRs are diverse and serve different purposes. Although they share certain cortical foundations, they also appear to involve distinct cortical areas. Due to their reliance on diverse sensory inputs, they exhibit high plasticity and can be rapidly altered by peripheral and central interventions.

## **CHAPTER III: SOMATOSENSORY PLASTICITY & TACTILE LEARNING**

Throughout life, experiences deeply influence and shape somatosensory maps. This experience-dependent plasticity is crucial for acquiring new tactile skills and adapting to changing environments. Such plasticity generally occurs in response to changes in environmental stimuli, either in cases of reduction or absence of tactile inputs (deprivation-induced plasticity) or in cases of increase of tactile inputs (enrichment-induced plasticity). In the former case, tactile deprivation can be either permanent (following nerve transection or amputation) or temporary (nerve crush or anesthesia). In the latter case, inputs can be increased either by actively training on a tactile task (training-dependent plasticity), or through passive exposure to tactile stimuli (training-independent plasticity).

In this section, I will present the plastic changes and the associated behavioral effects in each of these cases, starting with cases of somatosensory deprivation and moving progressively towards the passive training-independent plasticity, of utmost relevance for this work.

### **I- Somatosensory deprivation-induced plasticity**

Sensory deprivation has been shown to induce somatosensory plasticity along with perceptual changes. Two cases can be distinguished: (i) permanent lesion-induced plasticity, through deafferentation by nerve transection or limb amputation, and (ii) reversible non-lesion induced plasticity through deafferentation by pharmacological, or ischemic nerve blockade (i.e. local anesthesia).

#### **1) Permanent deafferentation-induced plasticity**

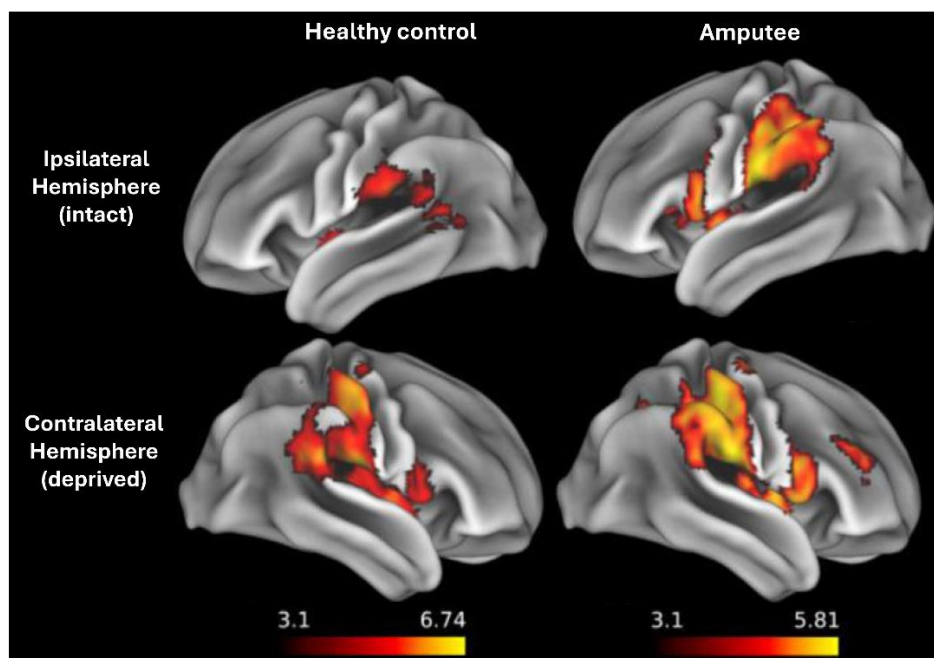
Following amputation of a digit, SI cortical neurons originally receiving tactile inputs from the digit do not receive them anymore. Instead of remaining permanently silent, they become responsive to stimuli applied at neighboring skin regions as first shown through electrophysiological recordings in rodents and monkeys. Indeed, as observed in flying-foxes and rats, within a few minutes after amputation of one or a few digits, the RFs of these SI neurons, deprived of inputs from the removed digits, enlarged to include skin regions adjacent to the removed digits (Calford & Tweedale, 1988; Byrne & Calford, 1991), before shrinking back to their original size within a week (Calford & Tweedale, 1988). Similar plastic changes were observed in monkeys following amputation of one or multiple digits, though on a longer timescale (Rasmusson, 1982). After an initial period of a few weeks of unresponsiveness, SI

neurons of the deprived cortical region became responsive to stimuli applied to neighboring skin areas within two months. The enlarged RFs then shrank back, but still included neighboring skin areas (Rasmusson, 1982). This plasticity was understood to come from a disinhibition followed by a homeostatic restoration of the inhibitory balance in the deprived cortical area. Besides changes at the scale of RFs, cortical representations of the neighboring regions were also found to expand into the deprived representation, leading to remapping of the cortical maps following median nerve transection (Merzenich et al., 1983) and multiple digit amputation (Merzenich et al., 1984). Cortical remapping was also observed at a larger scale when a whole limb was deafferented through transection of dorsal root in monkeys (Pons et al., 1991). Twelve years after transection, the deprived arm representation was found to be responsive to stimuli applied to neighboring skin regions, including the chin and the lower jaw (which cortical SI areas neighbor the hand cortical area). These large-scale plastic changes were consistently reported after nerve transection or limb amputation in monkeys (Florence & Kaas, 1995; Florence et al., 1998, 2000; Jain et al., 2008). Similar plasticity has also been observed along the afferent pathway at the brainstem (e.g., Jain et al., 2008), the somatosensory thalamus (e.g., Florence et al., 2000), as well as at higher-level cortical areas such as SII (Tandon et al., 2009).

Coherent with the remapping observed in monkeys, the cortical representation of the lip in the deprived hemisphere was found to be shifted medially after arm amputation in humans (e.g., Karl et al., 2001; Makin et al., 2015). However, a major difference between the amputation-induced remapping in monkeys and humans is that in humans, the lip representation does not annex completely the missing limb representation (Makin et al., 2015; Root et al., 2022) and instead, the deprived area also responds to body parts that are overused to compensate for the lost limb, which is usually the contralateral intact limb (Makin et al., 2013; Philip & Frey, 2014). Indeed, following amputation of an upper or lower limb in humans, responses to the opposite intact limb were shown to be increased in the deprived SI area, ipsilateral to the intact hand (Figure 11; Lotze et al., 2001; Simões et al., 2012; Valyear et al., 2020; Philip & Frey, 2014; Tucciarelli et al., 2024). A recent study in human amputees additionally showed that despite increased responses to the intact hand in the deprived SI area, the intact hand's motor performance was not improved (Tucciarelli et al., 2024). This suggests that the increased response to the intact hand may not reflect the intact hand function, but rather indicates that both hand areas work together more collaboratively than in healthy participants (Tucciarelli et al., 2024). The fact that the deprived area responds to stimuli applied to body parts that are cortically non adjacent would mean that cortical remapping is more driven by the use of the



intact body part than by its cortical proximity. A hypothesis has been proposed to explain the difference between cortical remapping in monkeys and humans stating that while humans usually use their intact hand to compensate for the lost hand, monkeys may use more their mouth (Makin & Bensmaia, 2017). Besides cortical remapping at the deprived SI hand area, cortical plasticity has also been reported in the intact SI hand area (ipsilateral to the missing hand) in monkeys with the enlargement of RFs (Calford & Tweedale, 1990), in rats with the expansion of the intact representation (Bahia et al., 2019). Similarly in humans, Elbert et al. (1997) observed an enlargement of the intact hand representation and Valyear et al. (2020) reported increased responses to stimuli applied at the intact hand (Figure 11). These changes at the intact SI hand area were proposed to be caused by a compensatory over-use of the intact limb (Elbert et al., 1997; Makin et al., 2013).



**Figure 11. Amputees display increased responses in bilateral sensorimotor cortex during hand stimulation.** [Modified from Valyear et al., 2020]. Areas exhibiting statistically significant effects are displayed on semi-inflated surface rendering. Left: Areas exhibiting significant increases for stimulation of the “left” hand in controls relative to baseline. Right: Areas exhibiting significant increases for stimulation of the intact “left” hand in amputees relative to baseline. This difference includes the deafferented former sensory hand territory and extends caudally across the lateral convexity of the postcentral sulcus, and into the supramarginal gyrus.

While they consist in representational enlargement of neighboring and homologous contralateral cortical areas and RFs, these cortical changes did not affect tactile perception at the corresponding intact skin areas. Indeed, after amputation of a finger or upper limb, no change in tactile acuity was found in the adjacent intact fingers (Vega-Bermudez & Johnson,

2002), or in the intact hand (Valyear et al., 2020), as measured by the letter recognition task and the GOT respectively. However, one of the most characteristic perceptual consequences of amputation-induced cortical remapping is painful sensation referred to the missing limb, also known as phantom limb pain (Flor et al., 1995, 2006). This phenomenon was initially found to be strongly correlated with the degree of cortical remapping (Flor et al., 1995, though see Makin & Flor, 2020; Root et al., 2022). Besides, non-painful referred sensations on the missing hand (phantom sensations) have been shown to be elicited by stimuli applied at the face (Ramachandran, 1993) and at many body sites whose cortical representations are not necessarily neighboring the deprived area (Knecht et al., 1996). Because these areas are not close to each other in SI, one possibility is that they may be closer to each other in structures along the afferent somatosensory pathway, as proposed by Makin & Bensmaia (2017). They suggested that the patterns of referred sensations may reflect somatotopic organization along the pathway (though see Amoruso et al., 2023).

While the deprived SI cortical area became responsive to stimuli from other body parts, it was still able to respond to stimuli applied to the residual injured nerve, as has been observed in humans (Anani & Körner, 1979; Dhillon et al., 2004). This suggests that the original pathway from the peripheral nerves to their target SI area may still be preserved (Merzenich et al., 1984), possibly due to the spontaneous reinnervation of the stump by the residual nerve of the missing limb (Makin & Bensmaia, 2017). In the other direction, intracortical microstimulation (ICMS) of the deprived SI hand area in a long-term spinal cord injured patient was found to elicit sensations in the missing hand, but not in any other body part (Flesher et al., 2016), which suggests that the original representation was still there and was not replaced. Besides, the topography within the missing hand's representation was also shown to be preserved despite the remapping (Kikkert et al., 2016, 2021).

Overall, after lesion-induced deafferentation of a limb, plastic changes were reported in the contralateral deprived SI, along the afferent pathway, and in the ipsilateral intact SI. These plastic changes were not translated in functional tactile benefits but were rather accompanied by phantom sensations elicited by stimuli applied on many skin regions, not necessarily cortically neighboring the deprived area. The mechanisms proposed to support these plastic changes and related perceptual consequences will be discussed in section I.3.

## 2) Temporary deafferentation-induced plasticity

Because amputation and nerve transection consist in a lesion not only in the afferent sensory system, but also in the efferent motor system, the effects of sensory loss are confounded with the effects of motor loss on SI maps. Although in a shorter timescale, the effects of loss of sensory inputs can be specifically investigated through deafferentation by anesthesia, which disrupts only the afferent sensory system. Importantly, the methods used to induce anesthesia are not equivalent. While ischemic nerve block disrupts both the somatosensory and motor inputs and induces pain, pharmacological nerve block (through injection) or superficial anesthesia (through injection or cream application) disrupts only somatosensory inputs and is not painful.

Following anesthesia, animal studies showed that the RFs of the SI neurons neighboring the neurons deprived of inputs enlarge to include the anesthetized skin regions. For example, pharmacological anesthesia of a toe in rats was shown to trigger rapid expansion of the RFs of the other toes (Byrne & Calford, 1991; Calford & Tweedale, 1991). After the withdrawal of the anesthetic, the RFs shrank, but did not return back to their original size, suggesting potential longer-lasting effects. At the scale of cortical representations of body-parts, neighboring cortical areas were observed to expand into the deprived area following local anesthesia both in animals (e.g., Byrne & Calford, 1991; Katz et al., 1999) and humans (e.g., Tinazzi et al., 1997). In humans, pharmacological anesthesia of the right forearm revealed an expansion of the neighboring SI hand area towards the deprived forearm area (Björkman et al., 2009). Similarly to amputation induced deafferentation, plastic changes were also observed along the afferent pathway. Indeed, following local anesthesia in animals, expansion of RFs (and representations) was found in the brainstem (Pettit & Schwark, 1993; Faggini et al., 1997) and thalamus (Shin et al., 1995; Katz et al., 1999).

At the perceptual level, these plastic changes were found to be paralleled by tactile changes. Similarly to amputation-induced referred sensations, touch is also mislocalized following anesthesia. For instance, after radial and median nerve pharmacological block in humans, tactile sensations were perceived at the anesthetized middle finger when stimuli were applied at the intact skin of the neighboring ring finger (Weiss et al., 2004). In contrast, unlike in the case of amputation, perceptual improvements were observed at the opposite intact limb, as well as at intact skin areas whose cortical representations neighbor the deprived area. Indeed, tactile acuity improvements were found at the opposite intact hand as measured through the GOT (Werhahn et al., 2002) and the 2PDT (Björkman et al., 2004) after hand anesthesia through

ischemic nerve block. In Björkman et al. (2004)'s study, tactile detection was also improved, but for a shorter period (less than 15 minutes) in comparison to the 2PDT improvements (at least 15 minutes). Tactile acuity at the lip was also found to improve after hand anesthesia, when measured through the 2PDT (Weiss et al., 2004), but not the GOT (Werhahn et al., 2002). Besides the difference in acuity tasks they used, these two studies also differ by the method and extent of anesthesia. While Weiss et al. (2004) pharmacologically blocked two out of the three nerves of the hand, Werhahn et al. (2002) anesthetized the whole hand through ischemic nerve block.

When the left forearm was superficially anesthetized through anesthetic cream, tactile acuity (GOT), but not tactile detection was improved on the neighboring left hand (Petoe et al., 2013). However, a more recent study failed to replicate the perceptual improvement at the hand after forearm and upper arm anesthesia through anesthetic cream (Sehle et al., 2016). Interestingly, when one finger was anesthetized through pharmacological block, tactile acuity (GOT) was improved at the neighboring finger, but not at non-neighboring fingers of the same hand or of the opposite hand (including the homologous finger; Dempsey-Jones et al., 2019). Thus, it appears that while anesthetizing the whole hand (or most of it) induced tactile improvement on the opposite hand (Werhahn et al., 2002; Björkman et al., 2004), anesthetizing one finger induced tactile improvement only on the neighboring finger, but not on the opposite hand (Dempsey-Jones et al., 2019). This suggests that the extent of the perceptual effects may depend on the extent of the anesthetized skin area.

Besides tactile improvements, motor improvements were observed as well. Indeed, hand anesthesia through ischemic nerve block was reported to transiently improve the grip strength of the intact hand. This motor improvement was paralleled by an increased cortical activity in the corresponding MI as measured through fMRI (Björkman et al., 2004). After anesthesia of the left forearm via anesthetic cream, the neighboring left hand had better performance in a manual dexterity task than after application of a placebo cream (Petoe et al., 2013).

Overall, anesthesia-induced deafferentation of a body part triggers plastic changes similar to those triggered by lesion-induced deafferentation in the deprived SI area and along the afferent pathway. In contrast to lesion-induced deafferentation however, these plastic changes are accompanied by perceptual changes such as improvements in tactile detection and acuity, as well as motor improvements. The mechanisms proposed to support these plastic changes and related perceptual consequences will be discussed in the following section.

### **3) Mechanisms involved in deafferentation-induced plasticity**

Though no consensus has been made regarding the mechanisms supporting plastic changes following deafferentation (lesion-induced and anesthesia-induced), a few mechanisms of functional and structural nature are considered the most likely. While the functional ones are associated with both lesion-induced and anesthesia-induced plasticity, the structural ones are rather associated with lesion-induced plasticity, occurring on a longer timescale.

As mentioned in chapter I, the topographical organization between adjacent cortical SI areas representing different body parts is thought to be maintained through intracortical lateral inhibition (e.g., Jones, 1993; Paullus & Hickmott, 2011). After removal of inputs to the area representing the deafferented limb, lateral inhibition exerted by this area onto its neighbors (in the contralateral hemisphere) would cease and consequently the thalamocortical and cortico-cortical connections that are usually silent due to lateral inhibition would become functional (Jones, 1993; Jones et al., 1997). Indeed, pre-existing subthreshold inputs may be raised to suprathreshold levels, as it has been observed following the suppression of GABAergic inhibition (e.g., Li & Waters, 1996). This functional plasticity, often referred to as unmasking of tactile inputs, is supported by evidence of reduced intracortical inhibition (e.g., Hordacre et al., 2015), decreased GABA neurotransmitter levels (Capaday et al., 2000; Levy et al., 2002) and increased excitability (e.g., Schweinkreis et al., 2000; Dettmers et al., 2001) following limb deafferentation in humans. Further support is provided by findings showing the suppression of anesthesia-induced plasticity by GABA antagonists (Jung & Shin, 2002).

Structurally, another mechanism, potentially occurring after the disinhibition and accounting for longer-term plastic changes, is axonal sprouting, that is the growing of new neuronal connections between neurons. This hypothesis is supported by multiple evidence both at cortical and subcortical levels. A first anatomical tracing study in monkeys with long-standing injury to a forelimb revealed expanded lateral connections in the deprived areas in BA 1 and 3b, but normal thalamocortical projections (Florence et al., 1998). This suggests that the cortical remapping could be supported by sprouting in SI but not in the thalamus. More recent evidence was provided by an anatomical tracing study in monkeys who underwent upper cervical spinal cord lesion (Liao et al., 2016). After tracer injections in the deprived hand region, more labeled neurons in the face and shoulder BA 3b regions were found in these monkeys than in normal monkeys. After tracer injections in the face region, these monkeys had more labeled neurons in the hand region. These findings indicate that intracortical connections are altered, potentially through sprouting (Liao et al., 2016). They also revealed that after injections in the face area in

one monkey, they found no labeled terminals in the cuneate nucleus even though they did find a face representation in the deprived hand region. This suggests that the cortical response in the deprived hand region to stimuli on the face may be mediated by intracortical connections from the hand to the face area within BA 3b.

However, other studies failed to demonstrate that this face activity in the hand area would be mediated by intracortical connections. For example, no cortico-cortical axonal projections were observed between the hand and face BA 3b areas in monkeys after lesion of the dorsal column (Chand & Jain, 2015). Additionally, inactivating the SI face representation after dorsal column lesions in monkeys did not alter the face-elicited activity in the deprived hand cortical area suggesting that it is not mediated by intracortical connections between these areas (Kambi et al., 2014). In contrast, in the same study, the authors found that inactivating the cuneate nucleus abolished the hand-face plastic remapping in SI, suggesting that the brainstem would be critically involved in the SI remapping, potentially through axonal sprouting in the cuneate nucleus. Indeed, at the subcortical level, sprouting has also been reported in the spinal cord and cuneate nucleus of monkeys after amputation of the arm (Florence & Kaas, 1995) and transection of the dorsal roots from the hand (Darian-Smith, 2004). In addition, growth of afferents from the chin representation specifically from the trigeminal nucleus (receiving inputs from the face) into the cuneate nucleus was reported in monkeys after dorsal column lesions (Jain et al., 2000) which could account for the expansion of the face responses into the hand representation. Taken together, these results suggest that the deafferentation-induced remapping would occur (at least partly) via axonal sprouting in both SI and the brainstem, potentially more critically at the brainstem than at SI.

As for plastic changes observed at the intact ipsilateral SI area, they were proposed to be driven by interhemispheric disinhibition (Werhahn et al., 2002; Simões et al., 2012; Bramati et al., 2019). Evidence supporting this hypothesis lies in the decreased interhemispheric resting-state functional connectivity between bilateral sensorimotor regions revealed through fMRI following lower-limb amputation in humans (Bramati et al., 2019) and forelimb amputation in rats (Pawela et al., 2010). Additionally, following unilateral whisker denervation in mice, Petrus et al. (2020) found that the neurons from the deprived contralateral barrel cortex that project to the ipsilateral intact barrel cortex were hyperexcitable, had stronger responses and reduced inhibitory input to corpus callosum stimulation. On a structural level, the corpus callosum under the deprived SI-MI of lower-limb amputated humans displayed changes in myelin integrity, as evidenced through a reduced fractional anisotropy as observed through MRI (Simões et al.,

2012). More recently in forearm-amputated rats, Bahia et al. (2019) reported an expansion of the callosal terminal arbors from the deafferented area, with increased number of terminal boutons within the homotopic representation.

In summary, the deprivation-induced plastic changes are mostly proposed to rely on intra- and interhemispheric disinhibition, as well as axonal sprouting at both cortical and subcortical levels. One or several of these mechanisms can be co-occurring or occurring at different timescales to account for both rapid and longer-term plastic changes.

## **II- Training-dependent plasticity**

As briefly mentioned in the previous section, following the use (or over-use) of a limb, hand or digit, plasticity can also be induced by both somatosensory and motor activity. Among the most well-established examples of this plasticity are the changes observed in string players and Braille readers. Indeed, playing a musical instrument requiring individual finger movements induces enlargements of the SI cortical representations of the preferentially used fingers (e.g., Elbert et al., 1995). Similarly, braille reading with multiple fingers induces enlargement and merging of the SI cortical representations of the co-used fingers (e.g., Sterr et al., 1998).

A more relevant case for this thesis work, is tactile training-dependent plasticity, involving more the somatosensory aspect and containing less (or no) motor component. This section will focus on this kind of plasticity, which has been reported to be associated with tactile learning not only on the trained body part but also on untrained ones.

### **1) Tactile training-dependent plasticity and local perceptual consequences**

Animal studies first revealed that tactile training induces cortical somatosensory plasticity. Indeed, when monkeys were trained in a frequency discrimination task on a single digit for weeks, the BA 3b representation corresponding to the trained skin areas expanded and even replaced the corresponding BA 3a representation (Recanzone et al., 1992a). This indicates that cutaneous representations were “replacing” proprioceptive ones as a consequence of the cutaneous training. Additionally, changes in the temporal response properties of BA 3b neurons were observed in these monkeys and were found to correlate to improvements in frequency discrimination performance (Recanzone et al., 1992b). As for the RFs, when the training was repeatedly made on the same finger, but not specifically the same skin patch, RFs were found to shrink (Jenkins et al., 1990), whereas when it was performed on the exact same skin patch, RFs enlarged and became more overlapping (Recanzone et al., 1992c). This differential pattern

may indicate that different mechanisms support the shrinking and enlargement of RFs induced by training on variant and invariant skin regions respectively.

Besides training a single finger or skin area, other animal studies trained multiple fingers at the same time, promoting synaptic integration of temporally coincident inputs, and revealed interesting patterns of plasticity translating in tactile learning. For instance, Wang et al. (1995) trained monkeys to perform a temporal discrimination task with a tactile bar applied on three adjacent fingers synchronously at the distal phalanx, but asynchronously at the other two phalanges. They found that additionally to the enlargement of the RFs in BA 3b from single to multiple fingers, the cortical representations of the phalanges stimulated synchronously were “merged” while the representations of the phalanges stimulated asynchronously were more segregated. This showed that temporal correlation between inputs is crucial to the induced plasticity as it defines its pattern. The authors additionally found no changes in the VPL, suggesting that this plasticity would be specifically cortical. Similar merged SI finger representations and enlarged RFs were found in monkeys after they were trained for one month to detect temporal differences in tap pairs applied to two adjacent fingers, even with stimulus asynchronies from 100 to 200 ms, indicating that imprecise synchrony is sufficient to induce this plasticity (Blake et al., 2005). In humans, EEG recordings before and after training two fingers simultaneously on the 3DT (a tactile spatial discrimination task, see Chapter II, section I. 1. for the description) revealed a reduction of the distance between the cortical representations of the trained fingers (Braun et al., 2000), coherent with the merging of representations observed in animal studies.

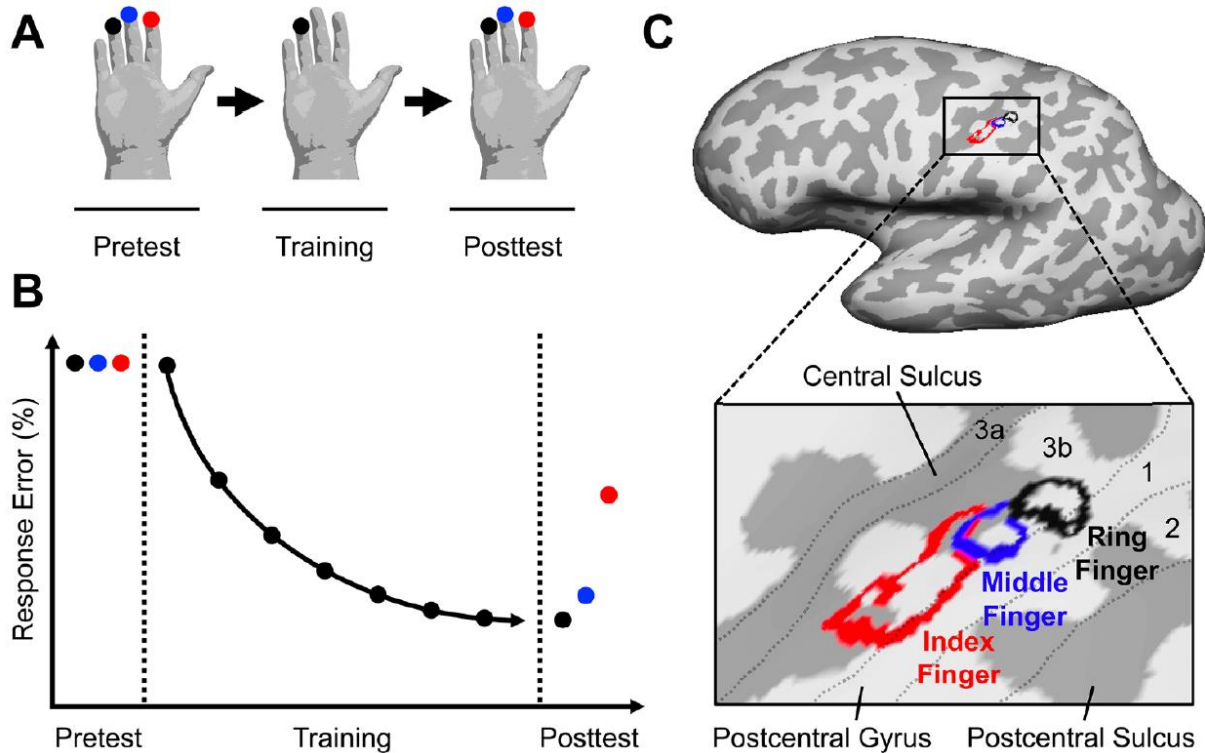
Behaviorally, plasticity was found to be accompanied by an improved performance in the trained tasks, or in tasks involving the same stimuli, as it has been shown in humans trained in spatial (Braun et al., 2000; Dempsey-Jones et al., 2021) and temporal discrimination tasks (Trzcinski et al., 2016). For instance, when trained for nine days to detect consecutive indentations (temporal discrimination) of tactile bars spanning multiple fingers, participants’ performance improved across the trained fingers in this task, as well as in another temporal discrimination task (Trzcinski et al., 2016). This indicates that the improvement in discriminating the temporal order of multi-digit stimuli transferred to temporal discrimination of other tactile stimuli. Similar transfer of improvement between tasks was found when the training and testing tasks used the same stimuli but were different in task instructions. When trained on an orientation discrimination task (judging whether two consecutive gratings display the same orientation) on the middle finger, participants had better performance in the GOT



(judging whether the single grating is oriented along or across; Dempsey-Jones et al., 2021). Interestingly, when an N-methyl-D-aspartate (NMDA) receptor agonist was given before the training sessions, tactile learning was delayed. Instead of showing immediate improvement like the placebo group, participants receiving the agonist only exhibited progress the next day, whereas the control group showed no additional enhancement in performance (Dempsey-Jones et al., 2021). Showing for the first time that training-dependent perceptual learning can be modulated by an NMDA receptor agonist, these findings suggest that training-dependent tactile learning may involve NMDA receptors.

## **2) Transfer of tactile learning to untrained body parts**

Following tactile training, perceptual improvement does not limit to the trained finger or limb, but also transfers to untrained body parts. A first study showed that when participants were trained on a temporal discrimination task (discriminating sequentially applied multi-finger stimuli) on three adjacent fingers, they had better performance not only on the trained fingers but also on the opposite untrained fingers, suggesting a transfer of improvement across hands (Spengler et al., 1997). When one finger was trained, similar transfer of improvement to the homologous finger (the only tested finger) was reported by Sathian & Zangaladze (1998). Testing more untrained fingers, Harris et al. (2001) showed that improvements in tactile roughness discrimination transferred almost entirely to adjacent and homologous fingers, and partially to other fingers, suggesting that the transfer follows a topographic gradient (Figure 12). Harrar et al. (2014) observed a more restricted pattern of transfer as the improvement of a finger trained on the GOT was transferred only to the adjacent and homologous fingers, but not to the other fingers tested. The authors proposed that plastic changes in neurons which RFs span adjacent and homologous fingers, such as those in BA 2 (Iwamura, 2000) or some RFs in BA 3b (Trczinski et al., 2023), serve as the neural basis for such a transfer. In other words, the neuronal population responsible for improvement in the trained finger would be shared between both the trained and adjacent and homologous untrained fingers.



**Figure 12. Transfer of tactile learning between trained and untrained fingers of the same hand.** [Extracted from Frank, 2024] (A) Experimental design. The tip of the ring finger of the right hand was trained in a tactile learning task. During the pre- and post-tests, performance in the tactile learning task or a related task involving the trained tactile feature was measured at the tips of the ring finger, adjacent middle finger, and nonadjacent index finger. (B) Theoretical learning and transfer results. Pretest performance is similar among fingers, but post-test performance follows a somatotopic transfer pattern, as evidenced by few errors being made with the trained ring finger and the adjacent untrained middle finger, but more errors with the nonadjacent untrained index finger. These results would suggest that tactile learning involved cortical areas with a somatotopic body map in which the middle finger is represented closer to the ring finger than the index finger. For results supporting such a behavioral pattern of transfer of tactile learning, see Harris and others (2001). (C) Cortical representations of the tips of the right ring, middle, and index fingers in one participant. Each fingertip was mapped with tactile stimulation during functional MRI: the representation of each fingertip was calculated by contrasting activation during stimulation of this fingertip with activation during stimulation of the other fingertips. The representations of the fingertips are shown on the participant's inflated left hemisphere by color-coded outlines. Approximate borders among areas 3a, 3b, 1, and 2 (dashed lines) are derived from the cortical parcellation proposed by Glasser and others (2016).

As for the magnitude of learning transfer, both the adjacent and homologous untrained fingers were found to benefit from the same amount of improvement observed at the trained finger (Harris et al., 2001; Harrar et al., 2014), suggesting a complete transfer. However, a more recent study showed rather a gradient of transfer after the middle finger was trained on the GOT, with a higher magnitude of transfer to the adjacent index finger, followed by the homologous finger and finally the adjacent middle finger (Dempsey-Jones et al., 2016). Though sharing the same proximity to the trained finger, the two adjacent untrained fingers differed in their co-use

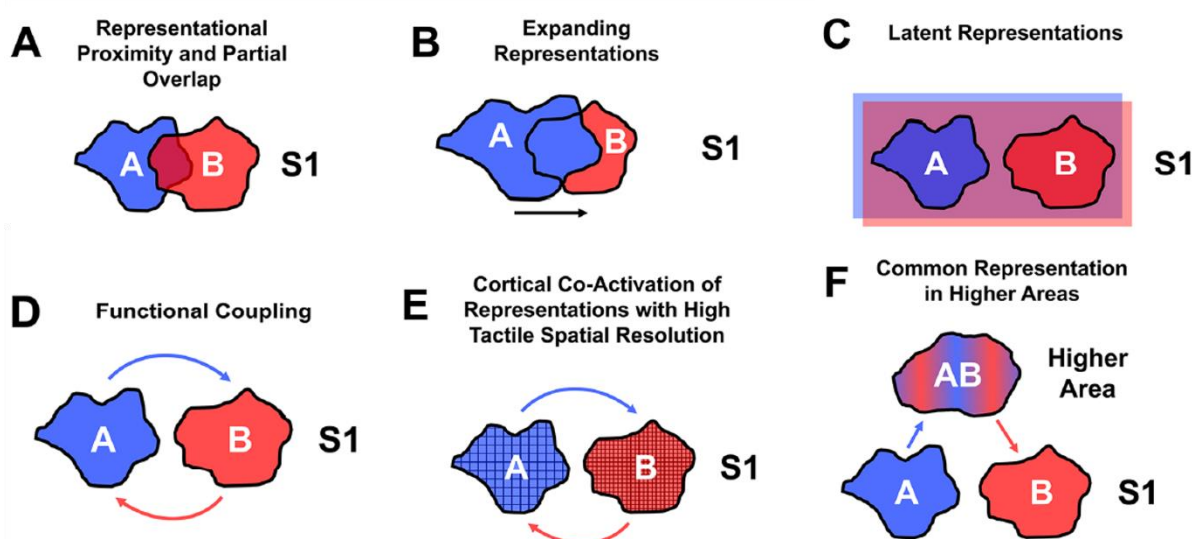
patterns with this finger. These results suggest that the transfer could be supported by greater representational overlap between the fingers that are usually co-used as compared to less co-used fingers (Glasser et al., 2016), supporting the idea that tactile coactivation patterns between fingers influence the transfer of tactile learning.

Besides transfers within and across hands, whose cortical representations are close and strongly related, learning transfers were found also between the hands and the foot, which are cortically distant. Training the palm of the right hand or the sole of the right foot on a spatial discrimination task (discriminating between tactile movement patterns), Frank et al. (2022) found that training one body part resulted in improved task performance in both body parts, suggesting that the improvement transferred from the trained to the untrained body part. As for the amount of transfer, they found it to be asymmetrical, as the transfer from the foot to the hand was significantly greater than the transfer in the reverse direction. Interestingly, using multivariate analysis on fMRI data, they found that stimulating one of the two body parts triggered coactivation of both SI representations, with the hand activation in foot representation being more pronounced than the foot activation in hand representation. In addition, when the foot was stimulated, the activation at the hand representation was associated with both the performance and the amount of improvement transfer. The greatest hand activations were associated with the lowest performance at the foot and the greatest transfer of improvement at the hand. However, in the reverse coactivation case, when the hand was stimulated, the activation at the foot representation was not associated with performance or the amount of transfer. As hypothesized by the authors, these results suggest that the SI area of an untrained body part could be coactivated to assist in processing tactile cues presented to the trained body part. This would be the case especially when the untrained body part displays a higher spatial resolution than the trained one, as to recruit higher-resolution areas to help solve the task on the trained lower-resolution body part. Additionally, this coactivation may play a crucial role in facilitating the transfer of tactile learning from the representation of the trained body part to the untrained one in SI.

In contrast to training to discriminate simple stimuli (varying along only one dimension), training on with more complex tactile stimuli, such as tactile letter recognition, allows for a wider pattern of transfer to emerge (Arnold & Auvray, 2014). Participants trained in a letter recognition task on either their belly, thigh or shin improved not only the trained body part, but also the untrained ones. All body parts were found to display the same amount of improvement, regardless of the skin and cortical closeness of the body parts, suggesting that cortical proximity

is irrelevant for the transfer to occur. As opposed to simple discrimination tasks displaying a transfer of improvement driven by the cortical proximity of body parts or the functional coupling between them, more complex discrimination tasks display a more generalized transfer of improvement across physically and cortically distant body parts. As suggested by the authors, this difference likely lies in the difference of cortical areas involved in the tasks. Indeed, while simple discrimination tasks involve mostly low-level somatotopically organized areas, more complex discrimination tasks (requiring the spatiotemporal integration of different features into a unique percept) involve higher-level, and less topographically organized areas. This suggests that, while the mechanisms underlying both types of transfer (i.e. shared cortical RFs between the trained and untrained body parts) may be the same, the cortical area in which this transfer occurs is likely different, with the former occurring at low-level areas (S1) and the latter at higher-level areas.

The mechanisms supporting the transfer of tactile learning across body parts are not established yet, but some have been proposed and recently reviewed by Frank (2024; Figure 13). He argued that multiple mechanisms could explain a single case of transfer, and his suggestions can be summarized as follows. Transfers to cortically close body parts may be supported by the cortical proximity and partial overlap (e.g., Harrar et al., 2014), while transfers to cortically distant body parts could be supported by latent information, functional coupling of the two body parts due to co-use, and cortical coactivation. In contrast, transfer of tactile learning in tasks involving processing in higher areas (complex tactile features), showing a more generalized pattern, would involve common representations between the trained and untrained body parts in higher areas (e.g., Arnold & Auvray, 2014).



**Figure 13. Schematic representation of mechanisms proposed by Frank (2024) to explain the transfer of tactile learning between trained and untrained body parts and skin locations.** [Extracted from Frank, 2024] Blue and red blobs correspond to cortical representations of two different body parts labeled A and B. Blue is the trained body part. Red is the untrained body part. (A) Transfer due to adjacent and partially overlapping representations of trained and untrained body parts in S1. (B) Modulation of transfer with the expansion of the representation of the trained body part into the representation of the untrained body part in S1. (C) Transfer due to the latent representation of the untrained body part within the representation of the trained body part and vice versa in S1 (signified by red and blue highlighted rectangles, respectively). (D) Transfer due to functionally coupled representations of trained and untrained body parts in S1. (E) Transfer due to coactivation of the representation of the untrained body part with higher tactile spatial resolution than the trained body part in S1. (F) Transfer due to projections from S1 to higher areas with overlapping or common representations of trained and untrained body parts.

### **III- Training-independent plasticity and tactile learning**

In contrast to explicit training, requiring repeated active tasks, passive exposure to tactile stimulations have also been shown to induce somatosensory plasticity accompanied by behavioral alterations of tactile perception.

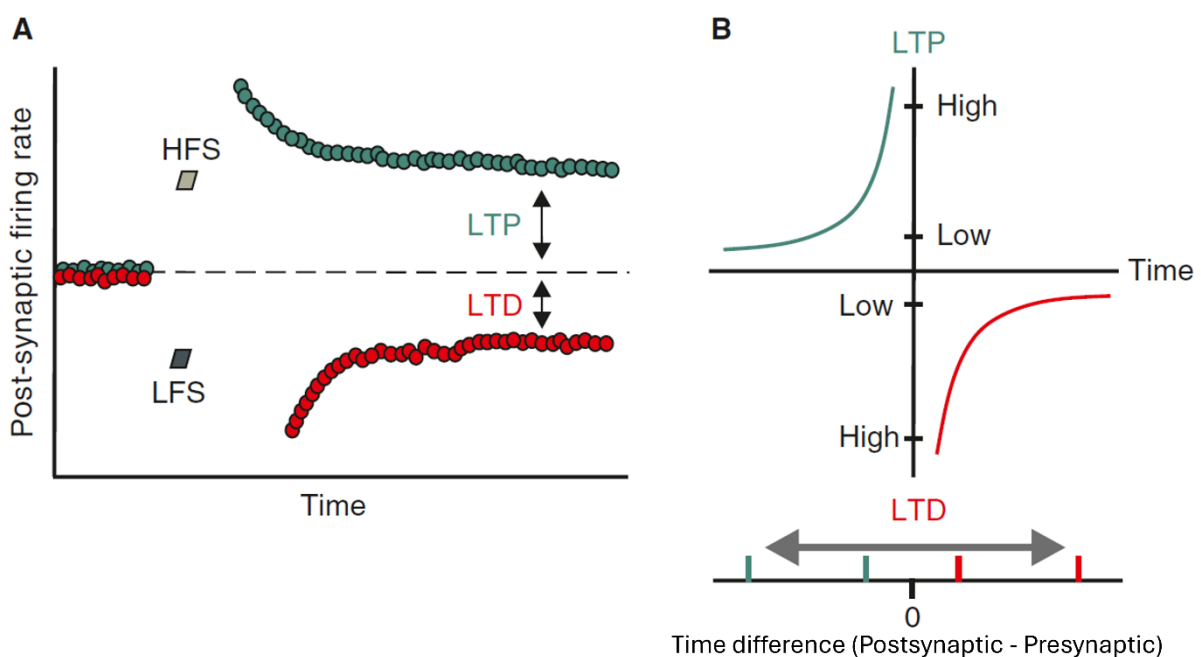
When monkeys maintained regulated fingertip pressure on a rotating textured disk with one or two digits across many sessions for ten days, the BA 3b representations of these digits were found to be enlarged, with their borders shifted laterally and towards BA 3a representations (Jenkins et al., 1990). Similarly, after weeks of tactile stimulations applied at the forearm through stimulators, Craig (1993) observed tactile mislocalization to skin regions close to the forearm, such as the palm and upper arm (Craig, 1993). These mislocalizations are coherent with an enlarged forearm SI representation expanding to neighboring cortical areas. Shorter stimulation periods of a few hours of tactile stimulations were also found to induce tactile acuity improvements not only at the stimulated body part (Pleger et al., 2001) but also at unstimulated body parts (Muret et al., 2014). Such stimulation protocols are referred to as repetitive somatosensory stimulation (RSS) and their cortical and perceptual effects will be detailed in the next chapter.

### **IV- The Hebbian plasticity**

At the level of synaptic connections, Hebbian plasticity is considered a leading mechanism for explaining cortical plasticity resulting from an increase in inputs (training-dependent or training-independent). This form of plasticity is grounded in the principle that repeated simultaneous activation of presynaptic and postsynaptic neurons leads to the strengthening of their synaptic connection. This phenomenon, identified by Donald Hebb and captured in the

phrase “neurons that fire together wire together” (Hebb, 1949), is considered to be fundamental for brain learning processes.

The most typical examples are long-term potentiation (LTP), consisting of synapses strengthening, and long-term depression (LTD), consisting of synapses weakening. While LTP is typically induced in brain slices through high-frequency stimulation (10 Hz or above), LTD can be consistently triggered by low-frequency stimulation of approximately 1 Hz (Figure 14A; Bliss & Collingridge, 1993). Coherent with the frequency, the timing between the firing of presynaptic and postsynaptic neurons dictates which one of the two occurs. This phenomenon, called spike-timing-dependent plasticity (STDP), follows a specific temporal pattern, with LTP occurring when the presynaptic neuron fires just before the postsynaptic neuron (within tens of milliseconds) while LTD occurs when the neurons are activated in the reverse order (e.g., Markram et al., 1997; see Feldman, 2012 for a review). The proximity in time between the activity of both neurons determines the magnitude of LTP and LTD effects; the closer their firing occurs in time, the stronger the effects (Figure 14B).



**Figure 14. Principles for inducing LTP and LTD.** [Modified from Beste & Dinse, 2013] (A) Long-term potentiation (LTP) is induced using high-frequency stimulation (HFS) and leads to increases in post-synaptic firing rate. Opposed to this, long-term depression (LTD) is induced using low-frequency stimulation (LFS) and leads to decreases in post-synaptic firing rate. (B) The principles underlying spike-time-dependent plasticity (STDP). If spiking in the pre-synaptic neuron occurs closely to activity of the post-synaptic neuron, LTP and LTD effects are strong. When the time difference in pre-synaptic neuron spikes and activity of the post-synaptic neuron is more, the LTP or LTD effect is weaker. LTP and LTD effects depend on whether the presynaptic neuron fires before or after the postsynaptic neuron.

At the postsynaptic neuron, the glutamatergic NMDA receptor plays a critical role in the induction of LTP. Considered “coincidence detectors”, these receptors require both presynaptic glutamate release and postsynaptic depolarization to open their ion channels, triggering the molecular events that lead to LTP. In contrast, because of a smaller postsynaptic depolarization, LTD involves a less important activation of NMDA receptors, which leads to molecular mechanisms reducing the synapse's responsiveness to presynaptic signals (Bear & Malenka, 1994). For these reasons, increasing NMDA receptors functioning or reducing the inhibition favors LTP and makes it more pronounced.

An experimental way of inducing LTP at the cortical level is through repetitive ICMS, which consists in repetitive electrical pulse trains that activate almost simultaneously pre- and postsynaptic neurons in the stimulated cortical area. When applied on SI of rats and monkeys, a few hours of ICMS have been shown to transiently (for several hours) induce an enlargement of the cortical representation corresponding to a small skin area (Recanzone et al., 1992d; Spengler & Dinse, 1994). This stimulation also leads to changes in RF locations, as well as to an increase in the size and overlap of RFs (Recanzone et al., 1992d). More recently, repetitive ICMS applied at the forelimb SI area of rats increased evoked firing activity at the corresponding homotopic site in the other hemisphere, and induced the emergence of an ipsilateral RF similar to the normally evoked contralateral RF in response to stimuli at the forelimb (DeCosta-Fortune et al., 2020). In other words, repetitive ICMS applied on SI in one hemisphere strengthened the interhemispheric connection between SI homotopic sites, allowing for the expression of previously ineffective inputs from the ipsilateral forelimb (DeCosta-Fortune et al., 2020).

At the periphery, Hebbian plasticity occurs when tactile inputs are paired in time because stimulating two neighboring skin areas in quick succession increases the likelihood of synchronous firing in adjacent neurons. Studies in monkeys (Recanzone et al., 1992a; Wang et al., 1995) and humans (Spengler et al., 1997; Liu et al., 2000) have shown cortical reorganization following such paired stimulation through training. This was initially reported in experiments involving syndactyly (i.e. fusing the skin of two adjacent fingers through surgery) and webbing. In monkeys, fusing the skin of two adjacent fingers through surgery induced an extension of some RFs across the limit between the two fingers because of the synchronous co-stimulation patterns across the fingers (Clark et al., 1988; Allard et al., 1991). Comparable observations were reported in humans with webbed fingers who displayed non-somatotopic hand cortical representations (Mogilner et al., 1993). Inspired from these experiments, studies reported similar cortical changes after a few hours of passive multifinger

stimulation (Pilz et al., 2004; Vidyasagar et al., 2014). While synchronous multifinger stimulations were found to bring closer together (or merge) the corresponding cortical representations, asynchronous multifinger stimulation rather resulted in a segregation of their representations (Pilz et al., 2004; Vidyasagar et al., 2014). Importantly, synchronous stimulations on the index and ring fingers were found to increase the temporal coherence of the fMRI signal, reflecting a strengthening of the neuronal connections between the two fingers regions (Pilz et al., 2004). In contrast, asynchronous stimulation had no effect on this parameter, suggesting that the coherence increase was driven by the temporal coincidence between the inputs applied on the two fingers (Vidyasagar et al., 2014). These cortical changes were found to be accompanied by perceptual changes. After synchronous stimulations on three adjacent fingers, the number of tactile mislocalizations increased, while after asynchronous stimulations, it decreased as compared to the baseline (Pilz et al., 2004).

Based on the abovementioned mid-90's findings, Godde et al. (1996) developed a protocol of associative pairing tactile stimulation, consisting in simultaneously stimulating skin regions to alter the tactile synergy and likelihood of coactivation between them. The authors found that tactile coactivation applied on rats' digits enlarged the corresponding RFs and cortical representations in SI. When applied to human fingers, it was found to produce a behavioral effect by improving tactile acuity, as assessed through the 2PDT (Godde et al., 1996). This protocol is nowadays known as RSS and is used to investigate somatosensory plasticity and its relationship with perceptual improvement. These studies will be reviewed in the next chapter.

---

Overall, the studies reviewed in this chapter show that reducing or increasing tactile inputs triggers somatosensory plasticity, whose pattern depends on the amount and spatiotemporal distribution of tactile inputs. As a matter of fact, while depriving a cortical SI area from tactile inputs induces its shrinking and concurrent enlargement of the neighboring representations, increasing tactile inputs in a coherent manner (through training or passive stimulation) induces an enlargement of the representation of the trained or stimulated skin region, paralleled by perceptual alterations (tactile mislocalization, discrimination and detection) that can be transferred to untrained or unstimulated body parts.



## CHAPTER IV: REPETITIVE SOMATOSENSORY STIMULATION (RSS)

Designed to induce Hebbian-like plasticity in a non-invasive way, repetitive somatosensory stimulation (RSS) consists of simultaneous stimulation of several cutaneous RFs, for a duration ranging from about half an hour to three hours (see Beste & Dinse, 2013; Parianen Lesemann et al., 2015; Dinse & Tegenthoff, 2019 for reviews). Administered either in a mechanical or electrocutaneous form, the main advantage of this protocol is its passive nature as it does not require attentional or physical efforts. RSS induces training-independent cortical plasticity (e.g., enlarged BOLD activity in response to tactile stimuli) and perceptual changes (e.g., improvement in tactile acuity), observed both at the site of stimulation (local effect) and at unstimulated body parts (remote effect).

After a brief explanation of how RSS fits the framework of Hebbian plasticity, this chapter will explore its cortical and perceptual effects at the stimulated site, followed by its perceptual impact at unstimulated body parts. The chapter will conclude by highlighting the significance of RSS as a tool for research and clinical rehabilitation.

### **I- RSS: a tool for experimentally inducing Hebbian plasticity**

The basic idea behind RSS design is Hebb's principle, according to which the simultaneous activation of multiple RFs (here cutaneous ones) generates temporally correlated inputs, driving plastic changes in the somatosensory cortex. Since its development, many studies have brought evidence of its Hebbian nature.

Both cortical and behavioral effects of RSS were shown to depend on NMDA receptors (Dinse et al., 2003) and cholinergic mechanisms known to be involved in NMDA receptor-dependent plasticity (Bliem et al., 2008). Indeed, these studies showed that the RSS-induced cortical plasticity and improvements in tactile acuity were hindered by the administration of a cholinergic antagonist and a NMDA receptor antagonist. NMDA receptors being crucially involved in LTP induction (see Chapter III, section IV), these findings suggest that RSS effects are mediated by LTP processes.

The coactivation of multiple RFs has been demonstrated to play a crucial role in driving plasticity and perceptual improvements. Indeed, comparing the effects of the same stimulation applied either through a single-site tiny actuator (0.2 mm<sup>2</sup>), or through an actuator that spans multiple RFs (50 mm<sup>2</sup>) on the index finger, Pleger et al. (2003) and Ragert et al. (2008) found

that unlike the large actuator, the tiny one did not elicit any perceptual or cortical change. This suggests that multiple RFs need to be coactivated to trigger the plastic changes and the subsequent perceptual improvement.

On the temporal aspect, the frequency of the stimulation was found to influence its perceptual effects. While applying RSS at a high-frequency (20 Hz) improved tactile acuity, applying it at a low-frequency (1 Hz) led to its impairment (Ragert et al., 2008). These results recall closely both LTP and LTD processes and effects. Notably, researchers consistently observed that the effects of RSS were transient (Pleger et al., 2001, 2003), lasting less than 8 hours (Godde et al., 2000) or up to 24 hours (Ragert et al., 2008), depending on the frequency.

Overall, the cortical and perceptual effects of RSS (described below) are critically dependent on NMDA, the stimulation of multiple RFs, the frequency and temporal pattern, highlighting the reliance of RSS-induced effects on LTP-like mechanisms. Moreover, its effects are reversible. In light of these findings, RSS is considered to induce Hebbian-like mechanisms.

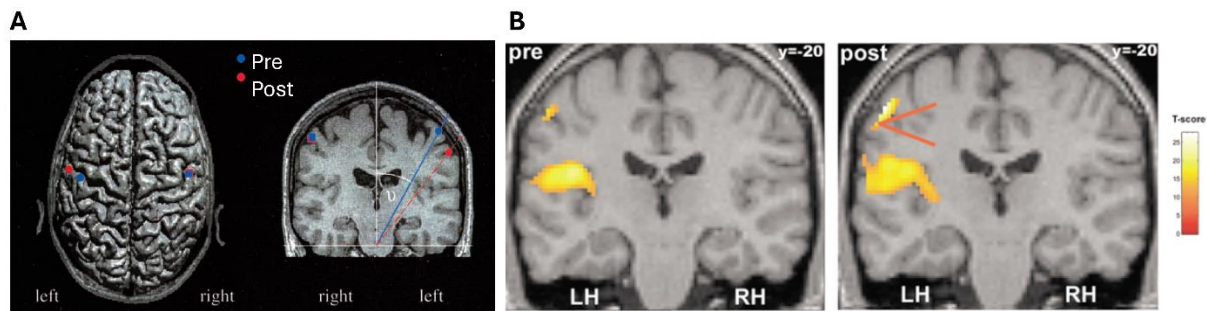
## **II- Plasticity and local tactile improvement**

### **1) Plastic changes in the somatosensory cortex**

As briefly mentioned in the last chapter, the first RSS study conducted on rats showed that this stimulation protocol induced an enlargement of the RFs and SI cortical representation corresponding to the stimulated hindpaw (Godde et al., 1996). Similarly, an enlargement of SI cortical representation of the stimulated fingers, usually the right index fingertip, were consistently reported following RSS in humans, either as an area enlargement (Figure 15A; Pleger et al., 2003; Hodzic et al., 2004) and/or a shift of center of gravity in fMRI studies, or as a dipole source displacement towards the thumb representation in MEG/EEG studies (Figure 15B; Pleger et al., 2001; Dinse et al., 2003; Godde et al., 2003; Hodzic et al., 2004; Muret 2016). Additionally, similar changes were observed in SII (Pleger et al., 2003; Hodzic et al., 2004). At the structural level, RSS was reported to increase SI gray matter volume (Schmidt-Wilcke et al., 2018).

Besides, RSS increases cortical excitability, as measured through dipole strength in EEG (Pleger et al., 2001), BOLD signal intensity in fMRI (Pleger et al., 2003), or paired-pulse SEP recordings (Höffken et al., 2007; Gatica Tossi et al., 2013). Moreover, it was found to strengthen intrinsic functional connectivity within the corresponding SI hand area while reducing it in the insula, a higher-order associative region (Heba et al., 2017). The latter finding suggests that RSS effects may not be limited to the relatively low-level tactile processing taking place in SI

and SII and instead spread to higher-level processes subtended by associative brain regions. I have investigated this possibility in my thesis work (see Experimental contributions, Study 1).



**Figure 15. Enlargement of SI and SII cortical representations of the stimulated hand following RSS.** [A modified from Pleger et al., 2001; B extracted from Pleger et al., 2003] (A) Schematic projection of the average locations ( $n=10$ ) of the single equivalent N20-dipoles of the index fingers pre-coactivation (blue symbols) and post-coactivation (red symbols) onto an axial (Left) and a coronar MR slice (Right) of an individual subject. The average difference (pre-post) for the Euclidean distances of the N20 of the index finger of the coactivated and of the control hemisphere are shown (Left). (Right) The average positions of the N20-dipoles are given by the polar angles showing a coactivation-induced shift toward the lateral and inferior aspects of the postcentral gyrus. A comparable effect is lacking on the non-coactivated hemisphere. (B) Fixed-effects analysis shows BOLD signals detected pre (Left) and post (Right) coactivation in the contralateral SI and in the contralateral and ipsilateral SII. Coronal slices are viewed from the back (LH, left hemisphere; RH, right hemisphere;  $y$  values, MNI coordinates). Activations are projected on coronal T1-weighted MRI slices.

## 2) Perceptual changes at the stimulated body part

Following RSS on the (typically right) index fingertip, the main perceptual change that was repeatedly reported is an improvement in tactile acuity at this finger, ranging from 13% to 29%. While most studies used the 2PDT and consistently observed improved performance (Godde et al., 2000; Pleger et al., 2001, 2003; Dinse et al., 2003, 2006; Godde et al., 2003; Gatica Tossi et al., 2013; Erro et al., 2016; Schmidt-Wilcke et al., 2018; Timm & Kuehn, 2020), other studies used the GOT and either found an improvement (Hodzic et al., 2004; Kattenstroth et al., 2018; Ross et al., 2022), or found no change (Gibson et al., 2009; Rocchi et al., 2017; Saito et al., 2018; Timm & Kuehn, 2020). The discrepancy in the results in the GOT could possibly be explained by methodological differences in the number of trials and sessions as well as in threshold computations. One of these studies additionally used both the standard GOT and a modified version of it (discriminating a grooved from a smooth surface) which requires less detailed spatial resolution than the traditional GOT (Gibson et al., 2009). While they found no effect of RSS on the standard GOT, they reported an improvement in the modified GOT in the same participants, suggesting that RSS would affect the less demanding task (i.e. requiring only to detect the presence of gratings instead of discriminating their orientation). Additionally, they

tested and found no effect on the performance in the 3DT (three-dot task; Gibson et al., 2009). Overall, showing different effects of RSS across tasks, these results tend to indicate that the tasks are not equally sensitive to RSS-induced somatosensory plasticity. However, given that most studies only used one or two tasks in the same individuals, no definitive conclusion can be drawn on this matter.

Interestingly, the effect of RSS on tactile acuity at the stimulated finger was found to be modulated by the synchrony in RSS simultaneously applied on other fingers of the same hand. Indeed, when all fingers of the right hand were stimulated synchronously, the performance in the 2PDT was found to improve at each finger, whereas when they were stimulated asynchronously, no change in 2PDT thresholds was observed in any of the fingers (Kalisch et al., 2007). This suggests that for RSS to induce perceptual improvements, synchrony should not only occur within the finger stimulated (Dinse et al., 2005), but also between the fingers co-stimulated (when multiple fingers are stimulated).

Similarly to the previously reported cortical changes, RSS-induced improvements in tactile acuity were found to be transient, with a return to baseline within 8 hours (Godde et al., 2000). The time to return to baseline performance can be delayed by applying multiple sessions over consecutive days (Godde et al., 2000), or by increasing the frequency of the stimulation (Ragert et al., 2008). Importantly, the changes in tactile acuity were found to vary with the cortical changes. Indeed, changes in tactile acuity were correlated with the amount of enlargement of cortical representation in SI (Pleger et al., 2001; Dinse et al., 2003; Hodzic et al., 2004; Pleger et al., 2003), changes in cortical excitability (Höffken et al., 2007; Saito et al., 2018), and the gray matter volume changes in the insula (Schmidt-Wilcke et al., 2018). In addition, the tactile acuity performance (2PDT) after RSS was correlated with the intrinsic functional connectivity within SI (Heba et al., 2017). Taken together, these findings provide evidence of a link between RSS-induced cortical and perceptual changes.

While tactile spatial discrimination was repeatedly found to improve following RSS, results on tactile temporal discrimination are less consistent, with some authors reporting an improvement (Reuter et al., 2014; Erro et al., 2016; Rocchi et al., 2017), while others reported a decline (Hodzic et al., 2004). In contrast to discriminative touch, no effects on absolute touch thresholds (i.e. tactile detection) were observed (Kalisch et al., 2007; Kowalewski et al., 2012). The differential effect of RSS on tactile detection and spatial and temporal discrimination may reflect their reliance on distinct processes.

As outlined in Chapter III, enhanced tactile input can lead to improvements through either active training (training-dependent learning) or passive exposure to stimuli (training-independent learning). Since RSS is a passive intervention, the tactile learning it induces is classified as training-independent.

### **III- Transfer of tactile learning to unstimulated body parts**

Studies applying RSS to a finger consistently reported no improvement in tactile acuity in the homologous finger (e.g., Godde et al., 2000; Pleger et al., 2001; Hodzic et al., 2004), with one study also reporting no change in the adjacent finger (Godde et al., 2000). On this basis, scholars inferred that the effects were only local, i.e. limited to the stimulated finger. However, recent evidence emerged challenging this view showing tactile learning to spread to other unstimulated body parts.

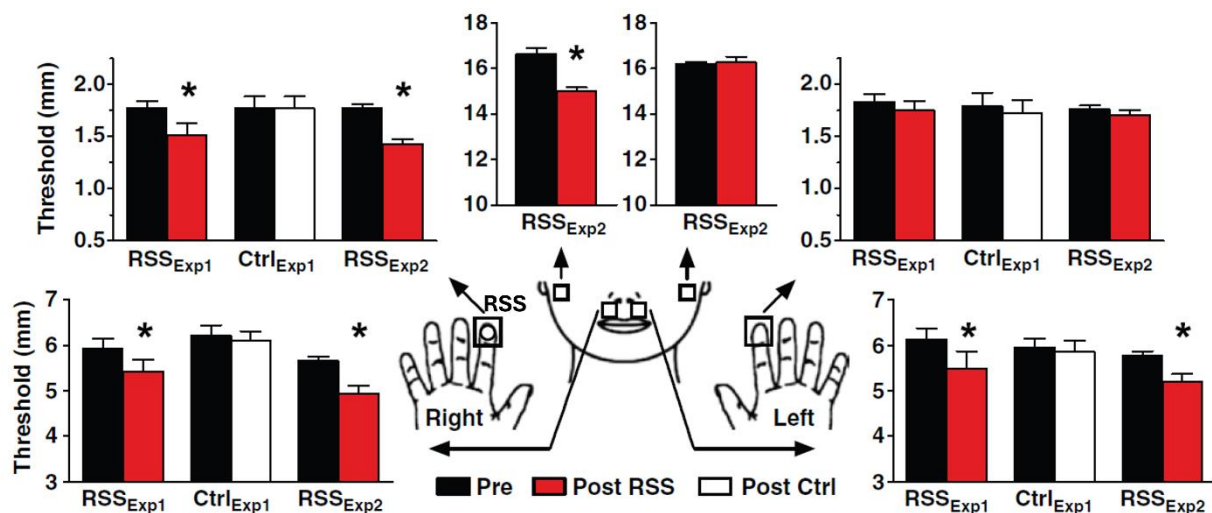
#### **1) Hand to face transfer of tactile learning**

Initially motivated by the knowledge about cortical plasticity between adjacent body parts representations, such as the hand and the face (see Chapter III, section I), studies from our group explored the potential transfer of tactile learning across these body parts. Following RSS at the right index fingertip, Muret et al. (2014) found that tactile acuity (2PDT) was improved at the stimulated finger, as well as at the right cheek and bilateral upper lips (the lips being bilaterally represented). These findings were consistent with the previously reported enlargement and shift of the representation of the stimulated index finger towards the representation of the face (Pleger et al., 2001). In addition, measuring dipole sources through MEG, Muret et al. (2016) found that RSS triggered a shift in the SI cortical representations of the stimulated finger and both upper lips. These findings were quite coherent with the previously reported enlargement of the cortical representation of the stimulated finger (Pleger et al., 2003).

Showing for the first time that RSS-induced cortical changes spread to distant regions and even to the other hemisphere, the authors hypothesized that such plasticity could be supported by either long-range corticocortical connections across body part representations, bilateral thalamocortical projections and/or transcallosal connections. To further investigate whether this transfer was driven by cortical proximity, they investigated whether a similar transfer occurred at the forearm, whose representation is at similar distance, but opposite to that of the face. While replicating once again the tactile acuity improvements at the stimulated index finger and both lips, Muret et al. (2018) found unaltered tactile acuity at the right forearm. This suggests that the face and hand may share a specific functional relationship. Even more intriguingly, the

transfer of improvement from the hand to the face was revealed to be bidirectional, as stimulating the upper lip improved tactile acuity at the right index finger (Macchione, 2018). This further strengthens the hypothesis of a functional bond facilitating the transfer between these body parts.

Overall, contrary to what was long thought, RSS training-independent tactile learning is not specific to the stimulated body part, but rather transfers to the face, with perceptual and cortical changes observable in both hemispheres (Figure 16).



**Figure 16. RSS-induced improvement of tactile acuity transfers from the finger to the face.** [Extracted from Muret et al., 2014] Mean two-point discrimination threshold pre (black) and post the procedure applied to the right-D2 (RSS: red; Control: white), assessed at right/left-D2, right/left-Lip and right/left-Cheek (mean  $\pm$  SEM). Repeated measures ANOVAs on data from the fingers, lips, and cheeks followed by Bonferroni-corrected post-hoc tests revealed significant threshold decreases ( $*P_{\text{Bonf}} < 0.05$ ) at right-D2, both sides of the upper-lip, and right-Cheek in the RSS groups only.

## 2) Hand to hand transfer of tactile learning

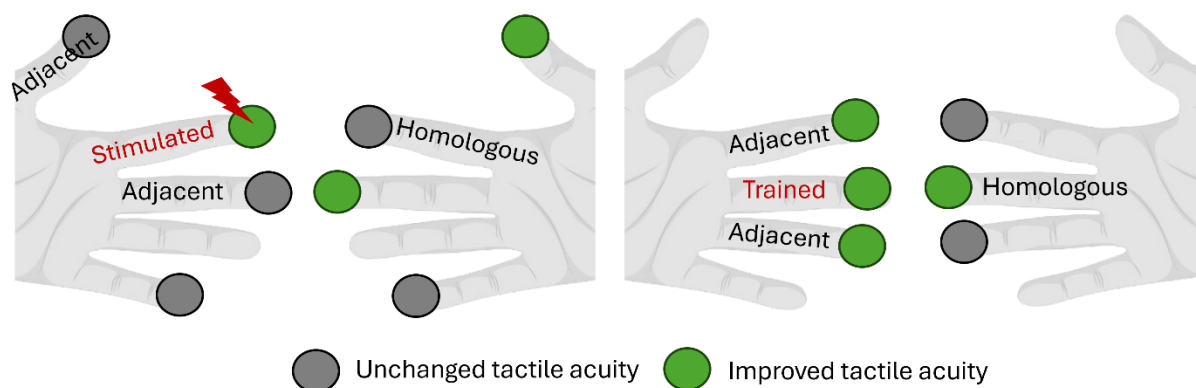
Since the earliest studies investigating the effects of RSS applied on the right index finger, no tactile acuity (2PDT) changes were reported on the homologous left index finger (e.g., Godde et al., 2000; Pleger et al., 2001, 2003; Muret et al., 2016), nor at the neighboring right middle finger (Godde et al., 2000; Muret et al., 2024) and thumb (Pleger et al., 2001; Rocchi et al., 2017; Muret et al., 2024). Besides, no change in tactile acuity was found on the more distant fingers of the right hand (ring finger: Timm & Kuehn, 2020; little finger: Muret et al., 2016) and the little finger of the left hand (Muret et al., 2016). These perceptual findings are coherent with neuroimaging reports showing no change in cortical representations of the left index finger, right thumb and both little fingers after RSS on the right index finger (Pleger et al., 2001,

2003; Dinse et al., 2003; Godde et al., 2003; Hodzic et al., 2004; Höffken et al., 2007; Muret et al., 2016).

Noteworthy though, recent findings from our group revealed tactile acuity improvements at the unstimulated left hand. More precisely, RSS on the right index finger improved tactile acuity at both the left thumb and middle fingers, while the right thumb and right middle finger remained unaffected (Muret et al., 2024). Furthermore, both the left thumb and middle finger were improved by the same magnitude as the stimulated finger ( $\approx 10\%$ ), suggesting a complete transfer of tactile acuity benefit. Interestingly, this pattern of transfer observed following training-independent tactile learning contrasts with the pattern of transfer typically observed following training-dependent learning, where tactile acuity improvements are usually reported at the trained finger and the adjacent and homologous fingers without extending to other fingers (Harris et al., 2001; Harrar et al., 2014; Dempsey-Jones et al., 2016).

Given that the major difference between these types of tactile learning is the involvement of attentional processes (present in training-dependent, but absent in RSS, training-independent learning), the authors proposed that the mechanisms underlying them could be different. While in training-dependent tactile learning, the pattern of transfer could arise from top-down modulation of SI tuning properties (Burton et al., 1999; Puckett et al., 2017), attention-independent RSS effects are more likely to arise from bottom-up processes. They further suggested that RSS could have induced a homeostatic modulation of inhibition within the somatosensory network, both on the intra-hemispheric lateral inhibition (Friedman et al., 2008; Severens et al., 2010) and the interhemispheric inhibition (Hoechstetter et al., 2001; Lipton et al., 2010). Such modulations would be mediated by intracortical horizontal connections between finger representations for the former and by callosal connections for the latter. Testing this hypothesis was part of my thesis work (see Experimental contributions, Study 3).

**A Training-independent tactile learning (2PDT)**    **B Training-dependent tactile learning (GOT)**



**Figure 17. Tactile improvement patterns following training-independent (RSS) and training-dependent tactile learning.** (A) When the index finger was stimulated through RSS, this finger along with the middle finger and thumb of the other hand displayed an improved tactile acuity as assessed through the 2PDT, while tactile acuity on the adjacent fingers (Muret et al., 2024) and little fingers was unchanged (Muret et al., 2016). (B) When the middle finger was trained on the GOT, both adjacent fingers showed improvement, along with the trained finger and its homologous fingers, while tactile acuity on the index and ring fingers of the other hand was unchanged (Dempsey-Jones et al., 2016).

#### **IV- Relevance of RSS in research and clinical rehabilitation**

The somatosensory cortex was the first cortical area where adult neuroplasticity was observed (Merzenich et al., 1984). Following this discovery, the somatosensory system prompted extensive research into the limits and mechanisms underlying adult plastic changes within the somatosensory system. Since its development in 1996, RSS was repeatedly used as a tool to induce somatosensory plasticity and probe its consequences at the behavioral level (e.g., Schlieper & Dinse, 2012; Kuehn et al., 2017; Brickwedde et al., 2019). The flexibility in adjusting the timing, frequency, and intensity and nature of stimulation of RSS protocols makes it a valuable tool for exploring somatosensory plasticity and its implications. Moreover, its non-invasive nature and simplicity in administration position RSS as an ideal method to investigate the connection between plasticity and perception in humans (see Parianen Leseman et al., 2015; Dinse & Tegenthoff, 2019 for reviews).

Besides, RSS also finds applications in the clinical field of tactile and motor rehabilitation. Tactile, and more specifically tactile acuity deficits, are found in many clinical conditions such as complex regional pain syndrome (e.g., Pleger et al., 2005), peripheral neuropathy (e.g., Wang et al., 2018), and stroke (e.g., Liu et al., 2023). Even more frequent is the case of tactile acuity deficits in healthy aging (e.g., Tremblay et al., 2003; Deflorio et al., 2023). Regardless of the cause, deficits in somatosensory function alters daily life activities (e.g., Patel et al., 2000; Birznieks et al., 2012) and independence (e.g., Tyson et al., 2008), and hinders motor rehabilitation (e.g., Celnik et al., 2007). As an example, tactile acuity deficits affect manual dexterity (Tremblay et al., 2003) and cause falls (Melzer et al., 2004) in the elderly. Besides, it is highly important for the motor function (Tremblay et al., 2003; Meyer et al., 2014). For these reasons, rehabilitation of tactile acuity is crucial for improving both somatosensory and motor functions. Studies investigating the effects of RSS on elderly and clinical populations brought promising results in this matter. Repeated sessions of RSS over several weeks, led to significant improvements in tactile acuity, absolute tactile detection threshold and motor performance in the elderly (Dinse et al., 2006; Kalisch et al., 2010) and stroke patients (Smith et al., 2009;



Kattenstroth et al., 2018; Chatterjee et al., 2019). Further research is needed to enable the implementation of training-independent RSS in clinical practice.

Because of its non-invasiveness, ease of use, flexibility and passive training-independent nature, RSS is used in research to investigate the link between somatosensory plasticity and tactile perception. Moreover, it shows significant potential for developing clinical strategies aimed at rehabilitating tactile and motor functions.

---

To conclude, the literature reviewed in this chapter shows that transient training-independent somatosensory plasticity can be efficiently induced through RSS, most likely via Hebbian LTP-like processes. Given that these plastic changes are accompanied by improvements in tactile perception, RSS serves as an effective tool for exploring the connection between somatosensory plasticity and tactile perception, as well as a promising tool for tactile rehabilitation. Although RSS has been extensively studied, the mechanisms underlying its physiological and perceptual effects - especially the remote ones - remain unclear and require additional investigation. Part of my thesis work was to bring a contribution to this matter (see Experimental contributions, Study 3).

## SUMMARY & AIMS

In these introductory chapters, I provided an overview of fundamental concepts related to somatosensation, from peripheral mechanisms to higher-level cognitive processes. I began by outlining the somatosensory system at multiple levels, highlighted recent insights into determinants of tactile acuity and presented the working models of mental body representations (MBRs) on which my doctoral work builds upon. I then described current knowledge on tactile learning and the underlying mechanisms of somatosensory plasticity. To explore the somatosensory system through behavioral approaches, the most common measures include tactile acuity tasks and tasks assessing MBRs. Tactile acuity, directly linked to the primary somatosensory cortex (SI), is often assessed and seen to reflect low-level somatosensory processing. In contrast, MBRs, which arise from multisensory integration with the contributions of associative areas, provide insight into higher-level cognitive processing within the somatosensory system. Together, these measures offer a comprehensive view of both basic and complex somatosensory functions.

At a higher cognitive level, while it is well-established that somatosensory processes play a role in constructing and maintaining MBRs, their specific contributions to each type of MBR remains unclear. As such, whether different MBRs are equally or differentially fed by tactile processing remains an open question, which has both theoretical and practical relevance. Understanding how tactile inputs influence different MBRs is essential for refining theoretical models and deepening our knowledge on the relationship between MBRs. Additionally, this knowledge could lead to new approaches for diagnosing and treating conditions in which MBRs are altered.

At a lower level, understanding how tactile acuity works is crucial for comprehending its interaction with other features of touch and its role in motor control. However, despite the widespread use of tactile acuity tasks in both clinical practice and research, little is known about the various features contributing to this acuity and the relative sensitivity of each task, and how these tasks are related. Assessing similarities and differences between three predominantly used tactile acuity tasks is essential as multiple tasks are regularly employed to diagnose conditions, evaluate rehabilitation progress, and support research on restoring or artificially providing tactile sensations in prosthetics.

To address both these questions related to low- and high-level somatosensory processing, I leveraged repetitive somatosensory stimulation (RSS) to alter the somatosensory system through the induction of somatosensory plasticity. Indeed, as described in Chapter IV, RSS effectively induces training-independent somatosensory plasticity, likely through Hebbian LTP-like mechanisms. Since these plastic changes are associated with enhanced tactile perception, RSS provides an effective tool for behaviorally investigating its effects on both low-level tactile processing and higher cognitive functions related to somatosensation. Since RSS was used to induce plasticity in the somatosensory system for both studies, it is crucial to understand its mechanisms of action. While the local effect of RSS has been shown to be associated with cortical changes in the SI and SII representations of the stimulated finger, the physiological mechanisms responsible for its remote effects on the unstimulated hand have yet to be investigated. The third study of my thesis aimed to contribute to this area of research.

Throughout this thesis work, I conducted a first study aimed at investigating whether three MBRs are equally or differentially fed by tactile processing, specifically by evaluating whether temporarily modulating tactile information through RSS affects them similarly or differently. I then conducted a second study to assess whether three tactile acuity tasks measure the same aspects of tactile acuity. This was achieved through a threefold approach: directly comparing the thresholds, investigating their relations to physiological anatomical parameters in the skin, and assessing the effects of RSS-induced somatosensory plasticity on each task. My third study aimed at investigating the physiological mechanisms underlying the effects of RSS on unstimulated fingers, using electroencephalography (EEG). Finally, given that RSS is a non-invasive and passive intervention that offers a promising therapeutic approach for tactile rehabilitation, I briefly outlined a final study designed to explore the remote effects of RSS in a clinical population, which has recently started.

## **EXPERIMENTAL CONTRIBUTIONS**

## STUDY 1: COGNITIVE STUDY

### **Repetitive somatosensory stimulation shrinks the body image**

Malika Azaroual-Sentucq<sup>1\*</sup>, Silvia Macchione<sup>1</sup>, Luke E. Miller<sup>2</sup>, Eric Koun<sup>1</sup>, Romeo Salemmé<sup>1</sup>,  
Matthew R. Longo<sup>3</sup>, Dollyane Muret<sup>4,5#</sup> & Alessandro Farnè<sup>1,6#</sup>

<sup>1</sup> Integrative Multisensory Perception Action & Cognition Team of the Lyon Neuroscience Research Center INSERM U1028 CNRS UMR5292 University UCBL Lyon 1, Lyon, France

<sup>2</sup> Donders Centre for Cognition of Radboud University in Nijmegen, Netherlands

<sup>3</sup> School of Psychological Sciences, Birkbeck, University of London, London, United Kingdom

<sup>4</sup> NeuroDiderot, Inserm, Université Paris Cité, Paris 75019, France

<sup>5</sup> NeuroSpin-UNIACT, CEA, Université Paris-Saclay, Gif-sur-Yvette 91191, France

<sup>6</sup> Neuro-Immersion Lab, Lyon, France

\* corresponding author(s)

# equal contribution

## Abstract

Current models of mental body representations (MBRs) indicate that tactile inputs feed several of them for different functions, implying that altering tactile inputs may affect MBRs differently. Here we tested this hypothesis by leveraging Repetitive Somatosensory Stimulation (RSS), known to improve tactile perception by modulating primary somatosensory cortex (SI) activity, and measured its effects over the *body image*, the *body model* and the *superficial schema* in a randomized sham-controlled, double-blind cross-over study. Results show that RSS affected the *body image*, participants perceiving their finger size as being smaller after RSS. While previous work showed increase of finger size perception after tactile anesthesia (Gandevia & Phegan 1999), these findings reveal that tactile inputs can diametrically modulate the body image. In contrast, RSS did not alter the *body model* or *superficial schema*. In addition, we report a novel mislocalization pattern, with a bias towards the middle finger in the distal phalanges that reverses towards the thumb in the proximal phalanx, enriching the known distortions of the *superficial schema*. Overall, these findings provide novel insights into the functional organization of MBRs and their relationships with somatosensory information. Reducing the perceived body size through RSS could be useful in helping treat body image disturbance.

Keywords: Mental body representations; Tactile localization; Somatosensory plasticity; Touch

## Introduction

Mental body representations (MBRs) are critical for several, fundamental sensory abilities, such as localizing touches on our body surface and estimating body part's size, as well as maintaining a coherent sense of bodily self. Indeed, tactile judgements are made by relating tactile inputs to MBRs, revealing a body-referencing of tactile perception (Serino & Haggard, 2010; Longo et al., 2010; De Haan & Dijkerman, 2020). The existence of different MBRs, related to specific sensorimotor functions, has been advocated by several models of MBRs. According to Serino & Haggard's (2010) multilevel model of somatosensory perception and body representation, MBRs housed in posterior parietal areas are continuously updated by the activity of the primary somatosensory cortex (SI). Importantly, this model accounts for the well-established finding that MBRs do not reflect the morphology of body parts accurately, but - to some extent - their distorted SI representations (Tamè et al., 2021, Tamè & Longo, 2023). Longo & Haggard's MBR model (Longo et al. 2010, 2015) also considers the involvement of specific MBRs in somatosensory processing, namely the *body model*, the *superficial schema* and the *body image*, and similarly proposes that they serve distinct purposes.

The *body model* is thought to be involved in perceiving metric properties of tactile stimuli like the tactile distance perceived between two points (Longo & Haggard, 2011), while the *superficial schema* is used for locating somatic stimuli on the body surface (Longo et al., 2015, Medina & Coslett, 2016). Whether inherent to the representations or a product of near-optimal Bayesian integration of somatosensory inputs (Peviani et al., 2024), perceptual distortions are consistently observed when assessing these MBRs. Indeed, Longo & Haggard (2010, 2011) observed that the hand is perceived wider and the fingers shorter when using indirect measures of hand size (e.g., the tactile distance perception and landmark localization tasks) indicating that the *body model* retains part of SI homuncular distortions. Similarly, using a tactile localization task on the hand's dorsum, Mancini et al. (2011) reported distal biases towards fingertips and thumb, indicating that the *superficial schema* is also distorted. In contrast, the *body image* corresponds to a conscious and relatively accurate representation allowing for instance to estimate one's hand's shape and size accurately, as typically assessed through a template matching task (Longo & Haggard, 2010; 2011). All three MBRs were found to rely on the parietal cortex (Castellini et al., 2013; Klautke et al., 2023; Porro et al., 2007; Spitoni et al., 2010), though some findings suggest the *body image* additionally involves extra-parietal regions (Miyake et al., 2010; Castellini et al., 2013; Dary et al., 2023).

While it is widely accepted that somatosensory processes contribute to building and maintaining MBRs, their exact contribution to each remains unclear. Considering the different functions of MBRs, current models imply that different somatosensory processes may underlie different MBRs. As such, whether different MBRs are equally or differentially fed by tactile processing remains an open question. Answering this question has both theoretical and practical implications. Clarifying to which extent tactile inputs contribute to each MBR is crucial to refine current theoretical models and will allow a deeper understanding of MBRs' interrelationship. In addition, this may open new avenues for the diagnosis and treatment of clinical conditions whereby MBRs are altered. To shed light on this issue, here we posit that if the three representations are similarly sustained by somatosensory activity, altering such activity would similarly affect them all. Alternatively, if they bear different relationships with somatosensory processes, some body representations could be affected differently.

One way to address this question consists in evaluating whether temporary modulating tactile information affects the different MBRs. Some pioneering studies investigated the effects of such modulation on a single MBR. For instance, seminal work by Gandevia & Phegan (1999) on the *body image* revealed that the body parts whose tactile inputs were temporarily reduced by anesthesia were perceived as bigger. More recently, Giurgola et al. (2019) showed that interfering with the activity of SI hand representation via repetitive Transcranial Magnetic Stimulation (rTMS) resulted in an overestimation of hand size. Thus, perception of body parts' size via the *body image* seems to be modified when tactile inputs are severely reduced, or somatosensory processing altered. Moreover, TMS over the SI hand representation impairs tactile identification of stimulated fingers (Seyal, Siddiqui & Hundal, 1997), suggesting that interfering with SI function is also detrimental to the *superficial schema*.

While these studies indicate a tight link between somatosensory processes and MBRs, they typically investigated only one, or two MBRs. To gain deeper insights into the relationship between touch and MBRs, we assessed the impact of increasing tactile inputs on the three MBRs. To this aim, we leveraged the properties of repetitive somatosensory stimulation (RSS), known to temporarily improve tactile perception by modulating SI activity (Beste & Dinse, 2013). RSS consists in the passive stimulation of a given body part (typically the right index fingertip) for a prolonged period, to induce synchronized neuronal activations in the corresponding SI representation, resulting in its transient enlargement and in improved tactile perception (see Beste & Dinse, 2013 and Parianen Lesemann et al., 2015 for reviews). Here we used RSS as a tool to temporarily increase tactile inputs and investigate its effect on the three



aforementioned MBRs, as assessed through three well-established paradigms: (i) the Template Matching Task (TMT) measuring the perceived size of the finger (involving the *body image*; Gandevia et al., 1999; Longo & Haggard, 2010; 2012a), (ii) the Tactile Distance Judgement Task (TDJT) assessing the distance between two tactile stimuli (involving the *body model*; Longo & Haggard, 2011; Tamè et al., 2021), and (iii) the Tactile Localization Task (TLT) measuring the localization of tactile stimuli (involving the *superficial schema*; Mancini et al., 2011).

We found that RSS alters participants' *body image* (TMT) without modifying the other MBRs/tasks, thus revealing that MBRs are not to be considered as equally dependent on somatosensory processes. Moreover, we found that increased tactile inputs (RSS) to the finger *reduces* the perceived finger size. This result, opposite to Gandevia and Phegan's original report (1999) obtained following reduction of tactile inputs (anesthesia), suggests that the *body image* is sensitive to somatosensory modulation in both directions.

## Methods

### *Participants*

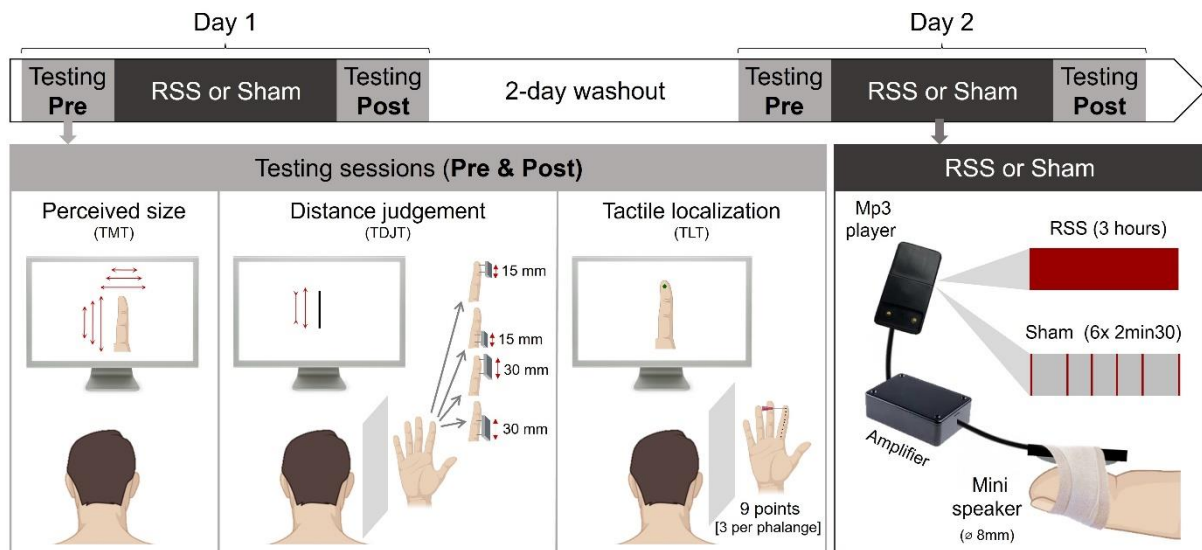
We included 33 healthy adults (27 women and 6 men; mean age  $\pm$  SD:  $22.8 \pm 3.4$  years). The sample size was determined by a power analysis using G\*Power 3.1 (Faul et al., 2007) based on the available work on TMT (Ambron & Coslett, 2023) and TDJT (Taylor-Clarke et al., 2004; de Vignemont & Haggard, 2005; Tajadura-Jimenez et al., 2015), although the interventions in the TDJT studies were mainly visual and auditory. Their effect sizes were between medium (computed Cohen's  $d = 0.5$ ) and large ( $d = 0.8$ ), their sample sizes ranging between 8 and 20. Our calculation showed that a sample size of 16 to 34 was required to detect a large to medium effect with 80% power using repeated measures ANOVAs.

Participants were right-handed (Edinburgh handedness inventory (Oldfield, 1971), average score  $\pm$  SD:  $85.2 \pm 15.6$ ), without any neurological nor psychiatric disease, and with no history of injuries at the right index finger. They gave their written informed consent before participating and received compensation at the end of the study. Procedures were approved by the French ethics committee (CPP SUD EST IV n. ID RCB: 2010-A01180-39).

### *Experimental timeline*

A randomized, double-blind, sham-controlled design was used (Figure 1). All participants received the RSS and Sham interventions on the right index fingertip on two different days separated by a two-day washout period, since RSS effects on tactile perception are known to

last up to 6 hours (Godde et al., 2000). Half of the participants received RSS first and the other half received Sham first, each participant being randomly assigned to either group. The effects of these interventions (RSS/Sham) on right index MBRs were investigated through Pre and Post testing sessions, including the TMT, the TDJT and the TLT delivered in a counterbalanced order. To verify RSS efficacy, tactile discrimination was also assessed before and after interventions through the 2PDT. More details about experimental procedures are available in Supplementary materials.



**Figure 1. Experimental timeline and depiction of the tasks and interventions used.** Participants received Sham and RSS on two different days (counter-balanced order). Before and after each intervention, perceived finger size, tactile distance judgement and tactile localization were assessed through the Template matching task (TMT), the Tactile Distance Judgement task (TDJT) and the Tactile localization task (TLT) respectively, in addition to the 2-point discrimination task (2PDT, not illustrated here).

Before the experiment, the participants' right index finger was high-resolution color scanned, and the image was resized to match the real size of their finger using Photoshop<sup>®</sup>, before being used in the TMT and TLT. The three tasks were implemented using MATLAB (MathWorks<sup>®</sup>, version 2015b).

### *Interventions (RSS & Sham)*

The intervention protocols consisted in a 3-hour task-free mechanical stimulation on the right index finger. A small (8 mm diameter) mini loudspeaker (LSM-S20K, Ekulit) controlled by a mp3 player (Lenco Xemio-240 4GB) was taped to the right index fingertip (Figure 1). In the RSS protocol, this mini loudspeaker delivered brief (10ms) supra threshold tactile stimuli for 3 hours, with inter-stimulus intervals ranging from 100 to 3000ms and following a Poisson distribution (average stimulation frequency of 1Hz). The Sham protocol consisted in 15 minutes of tactile stimulation distributed across the 3 hours (i.e., 6 blocks of 2.5min each). Within each

block, the mini loudspeaker delivered tactile stimuli with the same frequency and distribution as during RSS.

#### *Two-point Discrimination Task (2PDT)*

Tactile acuity on the right index fingertip was assessed using the two-point discrimination task (2PDT) with a well-established procedure (Godde et al., 2000; Muret et al., 2014, 2016). Eight probes were presented on the volar surface of the fingertip: one with a single tip and seven with two tips separated by various distances (0.7, 1, 1.3, 1.6, 1.9, 2.2 and 2.5 mm). Each probe was tested 8 times in pseudo-randomized order, resulting in 64 trials per session. Tips were presented aligned to the longitudinal axis of the finger. Participants were blindfolded and asked to indicate whether they perceived “one” or “two” tips at each trial with the specific instruction of saying “two” only when the tips were clearly distinguishable. They did not receive feedback about their performance and had no time constraint to answer.

For each participant, the average of the verbal responses (“one” or “two”) was computed and the percentage of “two” responses was plotted as a function of the distance between the probes. The psychometric function was fitted with a binary logistic regression. From these fitted data, the PSE was determined for each session (Pre & Post) and intervention (Sham & RSS) (Figure 2A).

#### *Template Matching Task (TMT)*

Participants were seated in front of a computer screen (at a distance of 55 cm), tilted at 30° above the horizontal plane, with their left hand on a keyboard and their right hand hidden under the table, open with their palm facing upwards. At each trial, an image of their real index finger (real size, larger, or smaller) was displayed on the screen, and they were asked to judge whether this finger was smaller or larger than the actual size of their finger by pressing the corresponding keyboard buttons (+ or -). They were instructed to focus on their right index finger and to try to be as accurate as possible, without receiving feedback about their performance and without time constraints.

The stimuli presented to the participant were as follows: four enlarged, four reduced (with uniform area distortions of  $\pm 3\%$ ,  $\pm 6\%$ ,  $\pm 9\%$ ,  $\pm 12\%$  relative to their actual finger size), and one real-sized image of their finger. Each stimulus was presented 12 times in randomized order for a total of 108 trials. For each participant, the percentage of responses corresponding to “image perceived larger” was plotted as a function of finger image distortion, and a psychometric function was fitted with a binary logistic regression (Statistica™ Tibco®, version 13.3). From these fitted data, the point of subjective equality (PSE), at which they perceived the image as

big as their finger, was determined as the distortion threshold at which participants were at chance level (Figure 2A).

#### *Tactile Distance Judgement Task (TDJT)*

Participants were seated in front of a computer screen (at a distance of 55 cm), with their unseen right hand lying supine on the table behind an occluding board. The experimenter touched the volar surface of their right index finger with 2 wooden rods simultaneously applied along the longitudinal axis, either within a single phalanx (i.e., rods spaced by 15 mm) or across two adjacent phalanges (i.e., rods spaced by 30 mm). For each distance, the rods were applied (for approximately 1 s) starting from 2 different locations: the base or the tip of the finger (Figure 1, middle lower panel). Each of the four conditions was repeated 10 times in a pseudo-randomized order, for a total of 40 trials. Participants were instructed to assess the tactile distance between the two rods by adjusting the length of a bar on the screen (pressing + and – buttons) to match the perceived distance between the two rods. They were instructed to focus on their right index finger sensation and to try to be as accurate as possible without any time constraint, and they did not receive feedback about their performance. The length of the bar as reproduced by participants was recorded and averaged for each session (Pre, Post), intervention (Sham, RSS), and position (base, tip).

#### *Tactile Localization Task (TLT)*

Participants were seated in front of a computer screen, in the same configuration as in the TDJT. The experimenter touched the volar surface of their right index finger with a plastic von Frey monofilament of 5 g, at one of 9 different locations on the longitudinal midline of the finger, with 3 positions per phalanx:  $\frac{1}{4}$ ,  $\frac{1}{2}$  and  $\frac{3}{4}$  of the length of each phalanx. The locations were numbered from 1 to 9 with the 1<sup>st</sup> location being the most proximal and the 9<sup>th</sup> the most distal. Each location was touched 10 times in a pseudo-randomized order, for a total of 90 trials. The real-sized image of their own finger was displayed on a black screen in front of them, and they were asked to report on the image the exact location where they perceived the touch. To do so, participants moved with their left hand a green cursor on the screen to the desired location and validated their choice by pressing a button. They were instructed to focus on their right index finger sensation, and to try to be as accurate as possible without any time constraint. They did not receive feedback about their performance.

Both the judged (J) and real (R) locations were recorded as x and y coordinates of the picture displayed on the screen. The origin of the coordinate system was centered on each of the real locations, with the y-axis representing the longitudinal (proximo-distal) axis of the finger and

the x-axis the bottom medio-lateral (ulnar-radial) axis of the finger. After normalizing the coordinates to each participant's finger length, three measures were calculated for each of the 9 locations (see Supplementary Figure S1): (i) the Euclidean distance between the J and R locations was computed using the following formula:  $\Delta_{JR} = \sqrt{(x_J - x_R)^2 + (y_J - y_R)^2}$ , (ii) the polar angle between the JR vector and the x-axis at the R location was computed as:  $\Theta_{JR} = \text{atan2}(y_J - y_R / x_J - x_R)$ , (iii) 95% confidence ellipses of the judged locations (with the mean judged location  $(\bar{x}_J, \bar{y}_J)$  being the center of the ellipse) were computed. The mean J-R distance and the mean J-R angle were used as a measure of constant error of tactile localization, while the mean area of the confidence ellipse was considered a measure of the variable error.

### *Statistical analysis*

Data were collected through Matlab (MathWorks<sup>®</sup>, version 2015b). Data were missing for two participants in the TLT (for technical reasons), and two participants were removed from the analysis of the TMT given the impossibility of fitting the data with a binary logistic regression. In total, the number of participants included in each task are the following: n=33 in the 2PDT and TDJT, n=32 in the variable error of TLT and n=31 in the constant error of TLT and in the TMT, with 30 participants common to the 4 tasks. Outliers were defined as falling outside 3SD around the average. First, in tasks containing single trials (TDJT & TLT), outlier trials were identified (intra subjects). No outlier trials were found in either task. In the TLT, a few missed trials were removed, representing 0.03, 0.21, 0.35 and 0.14% of the data in Pre Sham, Post Sham, Pre RSS and Post RSS, respectively. After trials removal, a minimum of 7 trials out of 10 were left for each condition. Then, in all tasks, outliers were identified at the group level (inter subjects). When present, statistical analyses are reported in the results section both including and excluding these outliers, as this did not change the findings. Results in the text are expressed as mean  $\pm$  SEM.

After verification of the normality (Shapiro-Wilk test), homoscedasticity (Levene's test), and sphericity (Mauchly's test) assumptions, repeated-measures ANOVAs (rmANOVAs) were conducted. When significant main effects or interactions were found, two-tailed t-tests were conducted with alpha levels Bonferroni-corrected for the number of tests performed ( $\alpha_{\text{Bonf}}$ ). Effect sizes were computed using Cohen's d (Cohen, 1988). When normality and/or homoscedasticity assumptions were not met, Friedman tests were conducted.

In the 2PDT and TMT, two-way rmANOVAs with the factors Intervention (Sham/RSS) and Session (Pre/Post) were used.

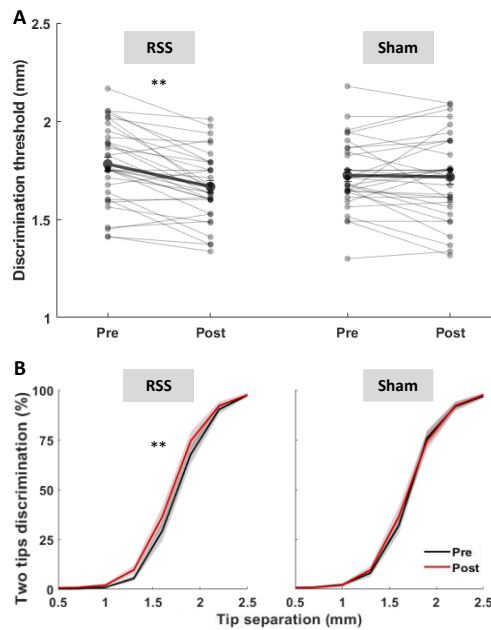
In the TDJT and TLT analyses, four-way rmANOVAs were used, with the common factors Intervention (Sham/RSS) and Session (Pre/Post); Position (Tip or Base of the finger) and Distance (15 mm or 30 mm) were also included for the TDJT analysis, and Position (n°1, n°2 or n°3 at each phalanx) and Phalanx (Proximal, Middle, Distal) for the TLT. Additionally, the difference between the real and the judged distances in the TDJT data was analyzed through two one-sample two-tailed paired t-tests (one for the 15 mm condition and the other for the 30 mm condition) and a two-tailed paired t-test to compare the two conditions. Finally, to determine the localization biases in the ulnar-radial (x) and proximo-distal (y) axes in the TLT data, the x and y components of the  $\Delta_{JR}$  vector were compared to zero (null bias) using one-sample two-tailed t-tests.

Except when specified otherwise, the threshold for statistical significance was set at  $p \leq 0.05$ . Statistical analyses were performed through Jamovi (version 2.2.5). Complementary Bayesian t-tests (Pre vs. Post) are reported in Supplementary Table S1.

## Results

### *Affecting tactile processes through RSS improves tactile perception*

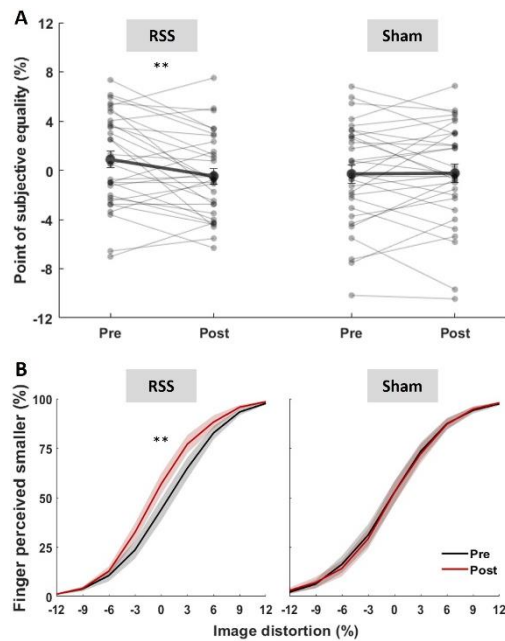
To assess whether RSS was successful in affecting somatosensory processing, we evaluated its impact on right D2's 2PDT threshold. A two-way rmANOVA revealed a significant Intervention\*Session interaction ( $F_{(1,64)} = 10.40$ ,  $p = 0.002$ ,  $\eta^2 = 0.02$ ) arising from a significant decrease in perceptual thresholds after RSS ( $t_{(32)} = 5.14$ ,  $p < 0.001$ ,  $\alpha_{Bonf} = 0.025$ ,  $d = 0.89$ , 95% CI [0.49, 1.30]), while they remained stable after Sham ( $t_{(32)} = 0.19$ ,  $p = 0.85$ ,  $d = 0.03$ ; Figure 2A). No significant difference was observed on the slopes of the psychometric curves as checked through a Friedman test ( $X^2_{(3)} = 0.34$ ,  $p = 0.953$ ; Figure 2B).



**Figure 2. RSS successfully improved 2PDT threshold.** (A) Individual (thin lines) and average (thick lines,  $\pm$  SEM) discrimination thresholds obtained Pre and Post RSS or Sham interventions. (B) Mean psychometric curves of the 2PDT Pre (black) and Post (red) RSS or Sham interventions (mean  $\pm$  SEM). \*\*  $p < 0.01$  (paired t-tests on the discrimination threshold,  $\alpha_{\text{Bonf}} = 0.025$ ).

*RSS impacts the body image: the stimulated finger is perceived as smaller*

We then assessed whether RSS had an impact on the finger size perception (i.e., *body image*) of the stimulated finger with the Template Matching Task (TMT). A two-way rmANOVA revealed a significant Intervention\*Session interaction ( $F_{(1,60)} = 4.49$ ,  $p = 0.038$ ,  $\eta^2 = 0.01$ ). Post-hoc paired t-tests showed that PSEs – expressed as the percentage of image distortion – were significantly smaller after RSS ( $t_{(30)} = 2.78$ ,  $p = 0.009$ ;  $\alpha_{\text{Bonf}} = 0.025$ ;  $d = 0.50$ , 95% CI [0.12, 0.87]; Figure 3A). On average, participants perceived their finger as  $-7.4 \pm 4.1$  % (mean  $\pm$  SEM) smaller than it was before RSS. In contrast, no significant change was observed after the Sham intervention ( $t_{(30)} = -0.12$ ,  $p = 0.909$ ). As in the 2PDT, no significant difference in psychometric curves' slopes was found across conditions ( $X^2_{(3)} = 2.27$ ,  $p = 0.518$ ; Figure 3B).



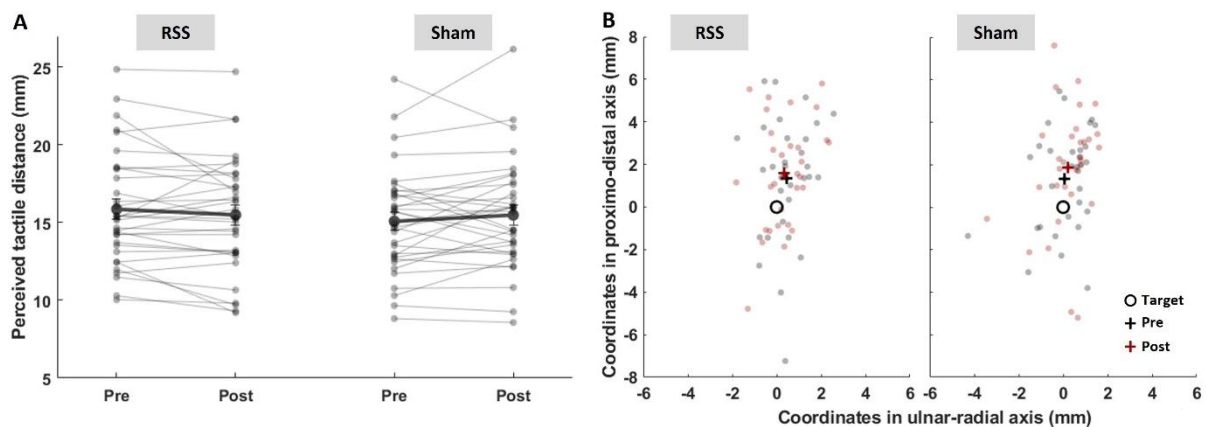
**Figure 3. The stimulated finger is perceived as smaller after RSS but not after Sham.** (A) Individual (thin lines) and average (thick lines,  $\pm$  SEM) PSEs obtained Pre and Post RSS or Sham interventions. (B) Mean psychometric curves of the TMT Pre (black) and Post (red) RSS or Sham interventions (mean  $\pm$  SEM). \*\*  $p < 0.01$  (paired t-tests on the PSE,  $\alpha_{\text{Bonf}} = 0.025$ ).

*RSS does not affect the body model and superficial schema of the stimulated finger*

The Tactile Distance Judgment Task (TDJT) was used to assess any effect of RSS on the *body model* and the *superficial schema*. A four-way rmANOVA showed no significant interaction between Interventions and Sessions ( $F_{(1,64)} = 3.35$ ,  $p = 0.072$ ,  $\eta^2 = 0.001$ ), with no further interaction with the Distance and Position (both  $F_{(1,64)} \leq 1.07$ , all  $p \geq 0.35$ ,  $\eta^2 = 0.001$ ; see Figure 4A). Besides, distances were underestimated both in the within phalanx (15 mm) and the across phalanges (30 mm) conditions as revealed through two-tailed one sample t-tests comparing the perceived distances to the real distance (both  $t \geq -11.30$ , both  $p$  values  $< 0.001$ , both  $d \geq -1.96$ ). No difference in underestimation between the two conditions was found through a two-tailed paired t-test ( $t_{(32)} = 0.96$ ,  $p = 0.346$ ). Finally, as expected from the higher density of mechanoreceptors (Johansson & Vallbo, 1979), distances (both 15 and 30 mm) were perceived significantly bigger (i.e., closer to the actual distance) at the tip than at the base of the finger ( $F_{(1,64)} = 53.16$ ,  $p < 0.001$ ,  $\eta^2 = 0.02$ ). Similar results were obtained without outliers ( $n = 31$ ; Supplementary Table S2).



The Tactile Localization Task (TLT) was used to assess the *superficial schema*. Localization performance was compared to the actual target position for each of the 9 locations along the finger. Their x and y coordinates were used to compute two localization error estimates: the constant error and the variable error. While the constant error consists in the length (error magnitude) and orientation (angle relative to x axis; error direction) of a vector connecting the real and the averaged judged locations, the variable error is the dispersion of the judged locations measured as the area of the 95% confidence ellipse computed from the judged locations. Four-way rmANOVAs revealed no significant main effects nor interactions involving the factors Intervention (Sham/RSS) and Session (Pre/Post) for either the constant error measures (i.e., error magnitude and direction; all  $F \leq 1.67$ , all  $p \geq 0.199$ ) nor the variable error measure quantified at each of the 9 locations (all  $F \leq 2.21$ , all  $p \geq 0.143$ ; Figure 4B; detailed statistics in Supplementary Table S2). Similar results were obtained without outliers ( $n=26, 28$  and  $23$  for error magnitude, direction and variable error respectively; Supplementary Table S2).



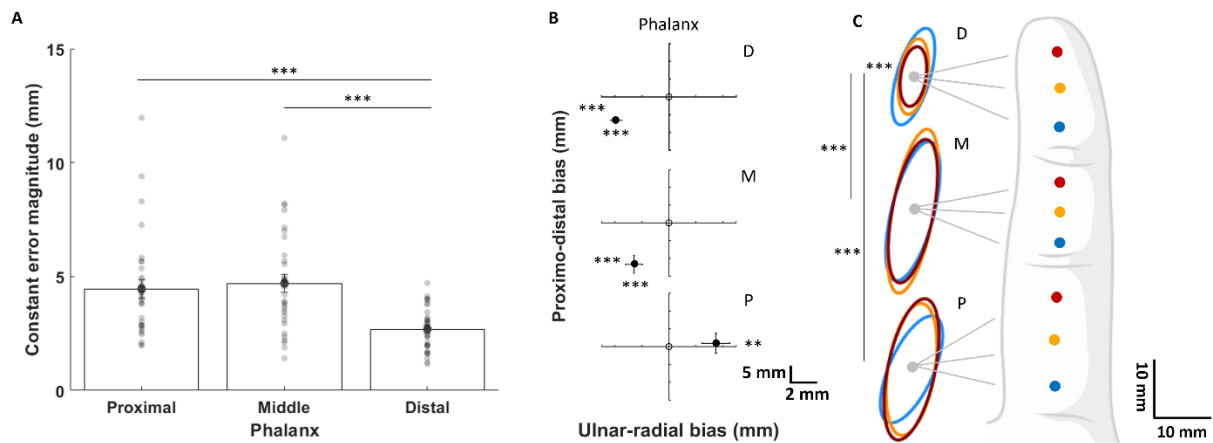
**Figure 4. RSS does not alter the perceived tactile distance nor tactile localization.** (A) Individual (thin lines) and average (thick lines,  $\pm$  SEM) perceived tactile distances obtained Pre and Post RSS or Sham interventions. The data represented is averaged across the two positions (tip & base) and distances (15 & 30 mm). (B) Individual (dots) and average (crosses) judged positions relative to the target point (circle) Pre (black) and Post (red) RSS or Sham interventions. The data represented is averaged across the 9 points.

Overall, the results showed that RSS, which was effective in reducing the 2PDT threshold at the stimulated finger, significantly affected only one of the three measures we assessed, namely that considered to tap into the *body image*. No significant correlation was found between changes in TMT thresholds and changes in 2PDT thresholds ( $r = 0.16$ ,  $p = 0.396$ ).

### *A systematic pattern of localization bias along the finger*

Besides the effects of RSS, the rmANOVA ran on error magnitudes also revealed a significant difference between phalanges ( $F_{(2,120)} = 18.25$ ,  $p < 0.001$ ,  $\eta^2 = 0.10$ ), arising from significantly shorter error magnitudes in the distal phalanx than in middle ( $t_{(30)} = 4.74$ ,  $p < 0.001$ ,  $\alpha_{\text{Bonf}} = 0.017$ ,  $d = 0.85$ ) and proximal ( $t_{(30)} = 3.93$ ,  $p < 0.001$ ,  $\alpha_{\text{Bonf}} = 0.017$ ,  $d = 0.71$ ) phalanges (Figure 5A). To further explore the pattern of these errors of localization per phalanx, we then compared the x and y coordinates of participants' mean localization relative to the target (defined as the origin of the coordinate system). One-sample two-tailed t-tests comparing the x component (i.e., lateral error) to zero revealed a significant ulnar bias for the distal and middle phalanges (both  $t_{(30)} \geq -4.18$ , both  $p < 0.001$ ,  $\alpha_{\text{Bonf}} = 0.017$ , both  $d \leq -0.75$ ; Figure 5B upper and middle panels), as well as a significant radial bias for the proximal phalanx ( $t_{(30)} = 3.34$ ,  $p = 0.002$ ,  $\alpha_{\text{Bonf}} = 0.017$ ,  $d = 0.60$ ; Figure 5B lower panel). In the proximo-distal axis, one-sample two-tailed t-tests comparing the y component to zero revealed a significant proximal bias for the distal and middle phalanges (both  $t_{(30)} \geq 4.68$ , both  $p < 0.001$ ,  $\alpha_{\text{Bonf}} = 0.017$ , both  $d \geq 1.306$ ; Figure 5B upper and middle panels). These results reveal a consistent bias in localization, with errors at the distal and middle phalanges directed towards the middle finger and the palm (proximo-ulnar bias), while errors at the proximal phalanx were directed towards the thumb (radial bias).

Similarly to the constant error, the rmANOVA ran on the variable error revealed a significant main effect of Phalanx ( $F_{(2,124)} = 81.28$ ,  $p < 0.001$ ,  $\eta^2 = 0.15$ ) arising from the areas of ellipses being significantly smaller at the distal than at the proximal ( $t_{(31)} = 8.39$ ,  $p < 0.001$ ,  $\alpha_{\text{Bonf}} = 0.017$ ,  $d = 1.48$ ) or middle ( $t_{(31)} = 9.10$ ,  $p < 0.001$ ,  $\alpha_{\text{Bonf}} = 0.017$ ,  $d = 1.61$ ) phalanges. A significant Phalanx\*Point interaction was also observed ( $F_{(4,248)} = 8.31$ ,  $p < 0.001$ ,  $\eta^2 = 0.015$ ), with a notable additional gradient observed within the distal phalanx (Supplementary Table S3 for additional post-hoc comparisons, mostly replicating the main effect of Phalanges). Indeed, the most distal ellipse (red dot on phalanx D in Figure 5C) was significantly smaller than the middle (yellow dot on phalanx D:  $t_{(31)} = 3.94$ ,  $p < 0.001$ ,  $\alpha_{\text{Bonf}} = 0.0014$ ,  $d = 0.70$ ), itself significantly smaller than the proximal one (blue dot on phalanx D:  $t_{(31)} = 4.45$ ,  $p < 0.001$ ,  $\alpha_{\text{Bonf}} = 0.0014$ ,  $d = 0.79$ ). Similar results were obtained without outliers ( $n=26$  and  $23$  for error magnitude and variable error respectively; Supplementary Table S2).



**Figure 5. The TLT uncovered a pattern of perceptual bias along the finger.** (A) Mean ( $\pm$  SEM) constant error magnitudes (length of error vectors) in the three phalanges. Errors were averaged across the 3 locations within each phalanx as they did not differ significantly (all  $F_{(2,120)} \leq 1.19$ , all  $p \geq 0.31$ ). \*\*\*  $p < 0.001$  (paired t-tests,  $\alpha_{\text{Bonf}} = 0.017$ ). (B) Mean ( $\pm$  SEM) difference between judged and target locations in ulnar-radial (x) and proximo-distal axis (y) for the proximal (P), middle (M) and distal (D) phalanges. \*\*\*  $p < 0.001$ ; \*\*  $p < 0.01$  (one-sample t-tests against zero,  $\alpha_{\text{Bonf}} = 0.017$ ). (C) Ellipses corresponding to the variable error for the blue, yellow and red target points within each of the three phalanges (proximal: P, middle: M, distal: D). Data is averaged across interventions (RSS and Sham) and sessions (Pre and Post) since those were not different (see main text). \*\*\*  $p < 0.001$  (paired t-tests,  $\alpha_{\text{Bonf}} = 0.0014$ ).

## Discussion

The present study aimed to elucidate the link between MBRs and their supposedly shared somatosensory basis. To this aim, we investigated the effect of increasing tactile inputs via RSS – known to reduce the 2PDT thresholds of the stimulated finger by modulating SI activity (Pleger et al., 2001, 2003) – on three MBRs of the same finger. Following either RSS or Sham intervention on the index finger, we assessed the *body image*, as probed through a Template Matching Task, the *body model*, as probed through a Tactile Distance Judgement Task, and the *superficial schema*, as probed through a Tactile Localization Task. We first ascertained RSS efficacy by replicating the expected finding of improved 2PDT performance at the index finger (Godde et al., 2000; Pleger et al., 2001, 2003, Muret et al., 2014, 2016). We then reported a reduction of perceived finger size following RSS and no change in tactile distance judgement or tactile localization. These results suggest that increasing somatosensory inputs alters the *body image*. Instead, RSS did not alter the *body model* or the *superficial schema* in either direction.

### *Increasing tactile inputs alters the body image*

The *body image* is known to be quite accurate (Longo & Haggard, 2010; Longo et al., 2010, 2015). Our findings corroborate this notion, as we found a baseline distortion of only 0.3% (0% = real size). After RSS, whose efficacy was confirmed by the tactile improvement in the 2PDT, participants perceived their finger as being smaller than before. This suggests that increasing inputs through RSS altered the *body image*. This finding is consistent with the results of

Gandevia & Phegan (1999) and Ambron & Coslett (2023) where the opposite modulation of inputs (i.e., reduction of inputs through anesthesia) increased the perceived size of the anesthetized body part. Altering tactile inputs thus seems to directly and bidirectionally impact the *body image*. One possible mechanism underlying the reduced body image of the finger may relate to the well-established effects of RSS on SI. By co-activating several skin receptive fields on the fingertip repeatedly for a protracted period of time, RSS has been shown to induce an enlargement of the stimulated finger's representation in SI – increasing the neuronal resources available to process inputs – through long-term potentiation-like plasticity (Godde et al., 1996; 2000; Pleger et al., 2001, 2003). The *RSS-induced reduction of body image* through an increase of SI finger area activity is coherent with the *anesthesia-induced increase of body image* (Gandevia & Phegan, 1999; Ambron & Coslett, 2023) possibly through an attenuation of SI finger area activity. Indeed, it has been reported that anesthetizing the index finger through pharmacological nerve block attenuates the activity of the SI finger area, as observed in fMRI (Wesselink et al., 2022).

### ***Increasing tactile inputs does not modify the body model and the superficial schema***

Unlike the *body image*, the *body model* and *superficial schema* are known to be distorted. Previous work reported an underestimation of the length of the fingers, together with a widening of the hand's width (Longo & Haggard, 2010; Mancini et al., 2011; Coelho et al., 2017). Our results are in agreement with these distortions as we found an underestimation of tactile distances, as well as a proximal bias in tactile localization for both the distal and middle phalanges and no proximo-distal bias in the proximal phalanx. Besides, our findings are in keeping with well-established characteristics related to variations in mechanoreceptors density along the finger. Indeed, mechanoreceptors density follow a gradient along the finger (Johansson & Vallbo, 1979; Ciano & Beatty, 2022) with the higher density at the fingertip being associated with higher spatial discrimination (Johansson & Vallbo, 1979), resulting in distances being perceived as bigger (Weber, 1996) and tactile localization being more accurate (Yoshioka et al., 2013). Besides replicating the distances perceived bigger at the fingertip, localization performance showed also smaller constant and variable errors in the distal phalanx (with an additional gradient of variability within the distal phalanx) indicating higher localization accuracy and precision.

When it comes to RSS effects, in contrast to the *body image*, RSS did not alter either the *body model* or the *superficial schema*. One should consider that the tasks underlying these MBRs might be less sensitive to the increase in tactile inputs induced by RSS. The fact that the *body*

*image* and the *body model/superficial schema* may be differentially affected is consistent with the results of Mergen et al.'s study (2018), whereby patients suffering from anorexia nervosa – known to overestimate their body size, especially on the abdomen region (Keizer et al., 2012) – displayed preserved tactile localization ability on the abdomen. This converges with our findings in indicating that the *body image* can be affected selectively with respect to the *superficial schema*.

Other sensory manipulations have been previously reported to alter the *body model*. Taylor-Clarke et al. (2004) found that visually magnifying the forearm and minifying the hand (i.e., changing their visual size) for 1h, decreased the well-established bias resulting in a bigger perceived distance on the finger than on the forearm. In other words, when the hand looks smaller, tactile distance is also perceived smaller as compared to when the hand appearance is veridical. Similarly, increased perceived tactile distance was observed when illusorily elongating the finger or the arm using either tendon stimulation (de Vignemont & Haggard, 2005) or a multisensory audio-tactile task (Tajadura-Jiménez et al. (2015)). Overall, these findings concur in showing that altering the perceived size of a body part (but not necessarily its *body image*) can affect the perceived distance between two points applied on this body part. However, it is worth noting that these manipulations consisted essentially in visual, proprioceptive and auditory illusions, making them less comparable to alterations of tactile inputs as implemented in the present work or following anesthesia. Together with our results, and knowing that MBRs are built based on both somatosensory (tactile and proprioceptive) and visual information (Bremner, 2016; De Klerk et al., 2021), we suggest that the *body model* and *superficial schema* may be less vulnerable to tactile manipulations than the *body image*. This may reflect either their relative ‘immunity’ to changes in tactile inputs, or their higher susceptibility to sensory correction: e.g., the altered tactile information could be compensated for by the intact proprioceptive and visual information.

Indeed, the *body model* and the *superficial schema* may generally be more rigid (i.e., their distortions seem less susceptible to change) than the *body image*. As shown by Longo & Haggard (2010, 2011) and Mancini et al. (2011), the distortions of the *body model* and *superficial schema* – as assessed through tactile size perception, landmark localization, and tactile localization tasks – are still found in different finger postures and hand orientations. Additionally, recent works (Bassolino & Becchio, 2023; Longo, 2023; Coelho & Gonzalez, 2024) seem to indicate that localizing tactile stimuli on the skin could require a correction factor. In this respect, the RSS-induced change in SI information received by the *superficial schema* and *body model* might have been corrected by this factor. This factor might apply only to body

representations that are distorted and more action control-related (Bassolino & Becchio, 2023; Longo, 2023; Coelho & Gonzalez, 2024) and not (or less so) to body representations that are accurate and more perception-related such as the *body image* (Dijkerman & De Haan, 2007).

### ***Changes in body image are not linked to changes in perceptual thresholds***

Regarding the potential relationship between the *body image* and 2PDT threshold changes, the lack of correlation suggests that these changes are not linearly related. The concomitant reduction of 2PDT threshold and *body image* size is coherent with the higher 2PDT thresholds found in patients exhibiting a bigger body image size (i.e., anorexia nervosa and chronic regional pain syndrome patients; Gadsby, 2017; Moseley et al., 2005, Keizer et al., 2012; Pleger et al., 2006), as compared to healthy populations. Yet, some studies reported an inverse relationship between such changes, with (i) a reduction of 2PDT thresholds and an increase of body image size following anesthesia (Ambron & Coslett, 2023), or (ii) an increase of 2PDT thresholds and a reduction of body image size following tendon vibration illusion (D'amour et al., 2015). Thus, the direction of change of 2PDT threshold does not seem to depend on the direction of change of the *body image* size.

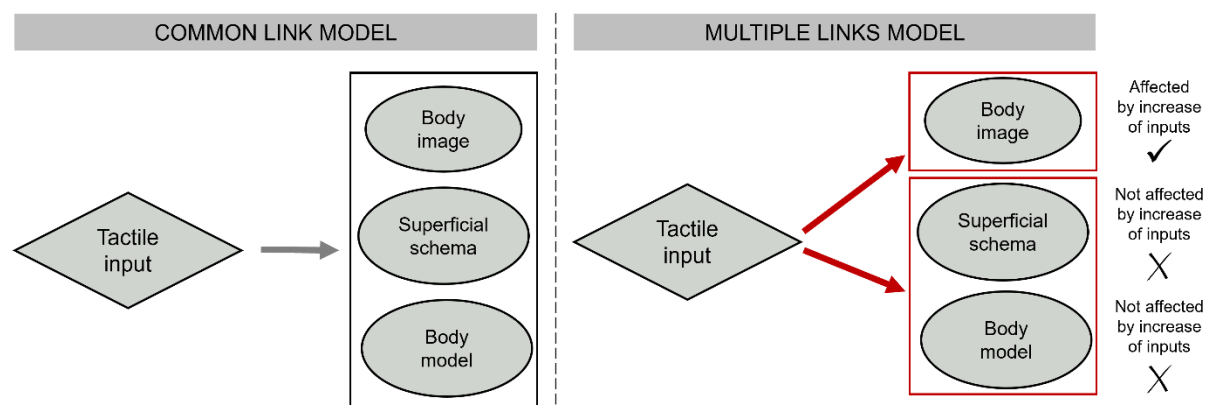
### ***A novel pattern of localization bias along the finger***

Besides replicating known distortions in MBRs and providing evidence for their differential sensitivity to modulation and reliance on tactile inputs, our results also bring new insights regarding MBRs. Intriguingly, we observed a specific pattern of ulnar-radial localization bias across phalanges, with the localization biased towards the thumb in the proximal phalanx and towards the middle finger in the more distal phalanges. Although localization within a single finger has rarely been investigated (Miller et al., 2022), studies assessing landmark (Longo et al., 2012b) and tactile (Dupin et al., 2022) localization at the whole hand scale, targeting the tips and bases of fingers on the dorsal (Dupin et al., 2022) and palmar (Longo et al., 2012b) surface, did not report such an ulnar-radial bias. This discrepancy may arise from the fact that they targeted the fingertip and the skin crease at the base of the finger, that can be considered as “landmarks”, while we targeted points away from creases/joints, equally distributed along the finger. It could also be due to postural differences as in our study, the hand was in a “natural” posture with fingers not splayed (abducted) nor pressed together (adducted), while in previous studies fingers were maintained abducted. A postural effect on tactile localization has been observed with localization on splayed fingers resulting in a wider hand representation than adducted fingers (Longo, 2015). Nevertheless, the radial bias of the proximal phalanx we newly report here seems in keeping with the radial bias found on the palm (Culver, 1970). Altogether,

our findings may reflect a bias towards adjacent fingers, at locations where informative tactile (co-)stimulation across fingertips is more likely to occur due to postural and movement synergies. Indeed, in a natural hand posture, the proximal phalanx of the index finger contacts both the middle finger and the thumb while the other two phalanges contact only the middle finger. This finding raises new questions about the role of tactile “synergies” in the distortions observed at the level of the *superficial schema*.

### ***Updating the theoretical framework of MBRs***

These findings help revising the model of MBRs, in particular with respect to their relationships with the tactile inputs (Figure 6). Indeed, the relationship between tactile inputs and the *body image* appears different from those linking them to the *superficial schema* and *body model*. While RSS is known to affect SI – nourishing all MBRs housed in the parietal cortex – this effect alone cannot account for the whole pattern of results observed in this study. The way SI exerts its modulatory effects differently on MBRs may either depend upon different sub-regions underpinning the *body image* and the other two MBRs, and/or upon the MBRs being linked to SI in a different way. Alternatively, beyond the parietal cortex, RSS-induced effects might spread to other areas exclusively involved in the *body image*. Indeed, the *body image* has been shown to involve also occipital, temporal and frontal areas (Miyake et al., 2010; Castellini et al., 2013; Dary et al., 2023) that have not been identified in the other two MBRs, predominantly relying on parietal cortex (Klautke et al., 2023; Porro et al., 2007; Spitoni et al., 2010). While future work will help disentangling these alternatives, our study provides novel evidence on the neglected link between MBRs and somatosensory processes, and paves the way to novel clinical applications for treatment of pathological MBR conditions.



**Figure 6. Update of the model of MBRs-tactile input relationship.** With regard to the relationship between tactile inputs and MBRs, there was no known distinction between the three MBRs. Following our results showing that RSS affects selectively the *body image*, we propose a model revision that splits the tactile input – MBRs relationship into (at least) two distinct relationships: (i) tactile input – *body image* and (ii) tactile input – *superficial schema/body model*.

## **Conclusion**

We provide evidence that converge with previous work in indicating that the *body image* is bi-directionally susceptible to changes following a temporary modulation of tactile inputs. Our findings also indicate that MBRs, even if all nourished by tactile afferents through SI, are not affected in the same way by increasing tactile information. We suggest that the *body model* and *superficial schema* may be more rigid and less affected by modulation of tactile inputs. Importantly, this study provides a proof of concept that a simple non-invasive and effortless tactile stimulation can alter the *body image* in the direction of a reduction of the perceived body size, which could translate into rehabilitative strategies to help treat *body image* disturbance, frequently occurring in eating disorders (anorexia nervosa, bulimia).

## **Acknowledgments**

This work was supported by the Agence Nationale de la Recherche (ANR-19-CE37-0005) BLIND\_TOUCH to AF and LEM, the Paul Bennetot Foundation (DL/VH 2018206) to AF, the Fondation pour la Recherche Médicale Doctoral Fellowship ECO202006011658 to MA-S, the Neurodis Foundation to AF and MA-S & the Federation pour la Recherche sur le Cerveau to AF and DM. We thank Frederic Volland for his help constructing the experimental setup, Valeria Ravenda and Isabella Bertoncini for helping with data collection, and Sonia Alouche, Sandra Chinel, Florence Leger and Celia Farge for administrative support.

## **Authors contributions**

MA-S, SM, LEM, MRL, DM and AF conceived the study and designed the experiment. L.E.M wrote some scripts for the experimental tasks. EK and RS designed the Sham stimulation protocol. MA-S and SM collected and analyzed the data. MA-S, DM and AF wrote the manuscript with inputs from all co-authors. All authors approved of the final submission.



## References

- Ambron, E. & Coslett, H. B. (2023). Apparent increase in lip size influences two-point discrimination. *Scientific Reports*, 13(1), 3082.
- Bassolino, M. & Becchio, C. (2023). The ‘hand paradox’: distorted representations guide optimal actions. *Trends in Cognitive Sciences*, 27(1), 7-8.
- Beste, C. & Dinse, H. R. (2013). Learning without Training. *Current Biology*, 23(11), R489-R499.
- Bremner, A. J. (2016). Developing body representations in early life: combining somatosensation and vision to perceive the interface between the body and the world. *Developmental Medicine and Child Neurology*, 58, 12-16.
- Castellini, G., Polito, C., Bolognesi, E., D’Argenio, A., Ginestroni, A., Mascalchi, M., Pellicanò, G., Mazzoni, L. N., Rotella, F., Faravelli, C., Pupi, A., & Ricca, V. (2013). Looking at my body. Similarities and differences between anorexia nervosa patients and controls in body image visual processing. *European Psychiatry*, 28(7), 427-435.
- Ciano, J. & Beatty, B. L. (2022). Regional variation in the density of Meissner’s corpuscles in human fingers. *Annals of Anatomy – Anatomischer Anzeiger*, 243, 151946.
- Coelho, L. A., Zaninelli, G., Gonzalez, C. L. R. (2017). A kinematic examination of hand perception. *Psychological Research*, 81(6), 1224-1231.
- Coelho, L. A., & Gonzalez, C. L. R. (2024). Perception, action, and the body model. *Neuropsychologia*, 196, 108853.
- Cohen, J. (1988). *Statistical Power Analysis for the Behavioral Sciences*. New York, NY: Routledge Academic.
- Culver, C. M. (1970). Errors in tactile localization. *American Journal of Psychology*, 83(3), 420-427.
- D’Amour, S., Pritchett, L. M., Harris, L. R. (2015). Bodily illusions disrupt tactile sensations. *Journal of Experimental Psychology: Human Perception and Performance*, 41(1), 42-49.
- Dary, Z., Lenggenhager, B., Lagarde, S., Medina Villalon, S., Bartolomei, F., & Lopez, C. (2023). Neural bases of the bodily self as revealed by electrical brain stimulation: A systematic review. *Human Brain Mapping*, 44(7), 2936-2959.
- De Haan, E. H. F. & Dijkerman H. C. (2020). Somatosensation in the Brain: A Theoretical Re-evaluation and a New Model. *Trends in Cognitive Sciences*, 24(7), 529-541.
- De Klerk, C. C. J. M., Filippetti, M. L., Rigato, S. (2021). The development of body representations: an associative learning account. *Proceedings of the Royal Society B-biological sciences*, 288(1949), 20210070.
- De Vignemont, F., Ehrsson, H. H., Haggard, P. (2005). Bodily Illusions Modulate Tactile Perception. *Current Biology*, 15(14), 1286-1290.
- Dijkerman, H. C., De Haan, E. H. F. (2007). Somatosensory processes subserving perception and action. *Behavioral and Brain Sciences*, 30(2), 189-239.
- Faul, F., Erdfelder, E., Lang, A.-G., Buchner, A. (2007). G\*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods*, 39, 175-191.
- Gadsby, S. (2017). Distorted body representations in anorexia nervosa. *Consciousness and Cognition*, 51, 17-33.
- Gandevia, S. C., Phegan C. M. L. (1999). Perceptual distortions of the human body image produced by local anaesthesia, pain and cutaneous stimulation. *The Journal of Physiology*, 514(Pt 2), 609-616.
- Giurgola, S., Pisoni, A., Maravita, A., Vallar, G., Bolognini, N. (2019). Somatosensory cortical representation of the body size. *Human Brain Mapping*, 40(12), 3534-3547.
- Godde, B., Spengler, F., Dinse, H. R. (1996). Associative pairing of tactile stimulation induces somatosensory cortical reorganization in rats and humans. *NeuroReport*, 8(1), 281-285.
- Godde, B., Stauffenberg, B., Spengler, F., Dinse, H. R. (2000). Tactile Coactivation-Induced Changes in Spatial Discrimination Performance. *The Journal of Neuroscience*, 20(4), 1597-1604.
- Hodzic, A., Veit, R., Karim, A. A., Erb, M., & Godde, B. (2004). Improvement and Decline in Tactile Discrimination Behavior after Cortical Plasticity Induced by Passive Tactile Coactivation. *The Journal of Neuroscience*, 24(2), 442-446.
- Johansson, R.S. & Vallbo, A.B. (1979). Tactile sensibility in the human hand: relative and absolute densities of four types of mechanoreceptive units in glabrous skin. *The Journal of Physiology*, 286, 283-300.
- Keizer, A., Smeets M. A. M., Dijkerman, H. C., van Elburg A., Postma, A. (2012). Aberrant somatosensory perception in Anorexia Nervosa. *Psychiatry Research*, 200(2-3), 530-537.

- Klautke, J., Foster, C., Medendorp, W. P., & Heed, T. (2023). Dynamic spatial coding in parietal cortex mediates tactile-motor transformation, *14*(1), 4532.
- Le Cornu Knight, F., Longo, M. R., Bremner, A. J. (2014). Categorical perception of tactile distance. *Cognition*, *131*(2), 254-262.
- Longo, M.R. (2023). Motor adaptation and distorted body representations. *Trends in Cognitive Sciences*, *27*(1), 241-254.
- Longo, M. R. (2015). Posture modulates implicit hand maps. *Consciousness and Cognition*, *36*, 96-102.
- Longo, M. R. & Haggard, P. (2010). An implicit body representation underlying human position sense. *Proceedings of the National Academy of Sciences*, *107*(26), 11727-11732.
- Longo, M. R. & Haggard, P. (2011). Weber's Illusion and Body Shape: Anisotropy of Tactile Size Perception. *Journal of Experimental Psychology*, *37*(3), 720-726.
- Longo, M. R., & Haggard, P. (2012a). Implicit body representations and the conscious body image. *Acta Psychologica*, *141*(2), 164-168.
- Longo, M. R., & Haggard, P. (2012b). A 2.5-D Representation of the Human Hand. *Journal of Experimental Psychology: Human Perception and Performance*, *38*(1), 9-13.
- Longo, M. R., Azanón E., Haggard, P. (2010). More than skin deep: Body representation beyond primary somatosensory cortex. *Neuropsychologia*, *48*(3), 655-668.
- Longo, M. R., Mancini, F., Haggard, P. (2015). Implicit body representations and tactile spatial remapping. *Acta Psychologica*, *160*, 77-87.
- Mancini, F., Longo M. R., Iannetti G. D., Haggard P. (2011). A supramodal representation of the body surface. *Neuropsychologia*, *49*(5), 1194-1201.
- Medina, J., & Coslett, H. B. (2016). Understanding body representations. *Cognitive Neuropsychology*, *33*(1-2), 1-4.
- Mergen, J., Keizer, A., Koelkebeck, K., van den Heuvel M. R. C., Wagner, H. (2018). Women with Anorexia Nervosa do not show altered tactile localization compared to healthy controls, *Psychiatry Research*, *267*, 446-454.
- Miller, L. E., Fabio, C., Azaroual, M., Muret, D., van Beers, R. J. Farnè, A., Medendorp, W. P. (2022). A neural surveyor to map touch on the body. *Proceedings of the National Academy of Sciences*, *119*(1), e2102233118.
- Miyake, Y., Okamoto, Y., Onoda, K., Kurosaki, M., Shirao, N., Okamoto, Y., & Yamawaki, S. (2010). Brain activation during the perception of distorted body images in eating disorders. *Psychiatry Research: Neuroimaging*, *181*(3), 183-192.
- Moseley, G. L. (2005). Distorted body image in complex regional pain syndrome. *Neurology*, *65*(5), 773-773.
- Muret, D., Dinse, H. R., Macchione, S., Urquizar, C., Farnè, A., & Reilly, K. T. (2014). Touch improvement at the hand transfers to the face. *Current Biology*, *24*(16), R736-R737.
- Muret, D., Daligault, S., Dinse, H. R., Delpuech, C., Mattout, J., Reilly, K. T., & Farnè, A. (2016). Neuromagnetic correlates of adaptive plasticity across the hand-face border in human primary somatosensory cortex. *Journal of Neurophysiology*, *115*(4), 2095-2104.
- Oldfield, R. C. (1971). The assessment and analysis of handedness : The Edinburgh inventory. *Neuropsychologia*, *9*(1), 97-113.
- Parianen Lesemann, F. H., Reuter, E.-M., & Godde, B. (2015). Tactile stimulation interventions : Influence of stimulation parameters on sensorimotor behavior and neurophysiological correlates in healthy and clinical samples. *Neuroscience & Biobehavioral Reviews*, *51*, 126-137.
- Pleger, B., Dinse, H. R., Ragert, P., Schwenkreis, P., Malin, J. P., Tegenthoff, M. (2001). Shifts in cortical representations predict human discrimination improvement. *Proceedings of the National Academy of Sciences*, *98*(21), 12255-12260.
- Pleger, B., Foerster, A.-F., Ragert, P., Dinse, H. R., Schwenkreis, P., Malin, J.-P., ... Tegenthoff, M. (2003). Functional Imaging of Perceptual Learning in Human Primary and Secondary Somatosensory Cortex. *Neuron*, *40*(3), 643-653.
- Pleger, B., Ragert, P., Schwenkreis, P., Förster, A.-F., Wilimzig, C., Dinse, H., Nicolas, V., Maier, C., & Tegenthoff, M. (2006). Patterns of cortical reorganization parallel impaired tactile discrimination and pain intensity in complex regional pain syndrome. *NeuroImage*, *32*(2), 503-510.

- Porro, C., Martinig, M., Facchin, P., Maieron, M., Jones, A., & Fadiga, L. (2007). Parietal cortex involvement in the localization of tactile and noxious mechanical stimuli : A transcranial magnetic stimulation study. *Behavioural Brain Research*, 178(2), 183-189.
- Serino, A. & Haggard, P. (2010). Touch and the body. *Neuroscience & Biobehavioral Reviews*, 34(2), 224-236.
- Seyal, M., Siddiqui, I., Hundal, N. S. (1997). Suppression of spatial localization of a cutaneous stimulus following transcranial magnetic pulse stimulation of the sensorimotor cortex. *Electroencephalography and Clinical Neurophysiology*, 105(1), 24-28.
- Spitoni, G. F., Galati, G., Antonucci, G., Haggard, P., & Pizzamiglio, L. (2010). Two forms of touch perception in the human brain. *Experimental Brain Research*, 207(3-4), 185-195
- Tajadura-Jiménez, A., Tsakiris, M., Marquardt, T., and Bianchi-Berthouze, N. (2015). Action sounds update the mental representation of arm dimension : contributions of kinaesthesia and agency. *Frontiers in Psychology*, 6(689).
- Tamè, L., Longo, M. R. (2023). Emerging principles in functional representations of touch. *Nature Reviews Psychology*, 2, 459-471.
- Tamè, L., Tucciarelli, R., Sadibolova, R., Sereno, M. I., Longo, M. R. (2021). Reconstructing neural representations of tactile space. *NeuroImage*, 229, 117730.
- Taylor-Clarke, M., Jacobsen, P., Haggard, P. (2004). Keeping the world a constant size: object constancy in human touch. *Nature Neuroscience*, 7(3), 219-220.
- The jamovi project (2021). jamovi (Version 1.6) [Computer Software]. Retrieved from <https://www.jamovi.org>
- Weber, E.H. (1996). De subtilitate tactus. In: *E.H. Weber on the Tactile Senses*. 2nd ed. Academic Press, London, 21-128 (Original work published 1834).
- Wesselink, D. B., Sanders, Z., Edmondson, L. R., Dempsey-Jones, H., Kieliba, P., Kikkert, S., Themistocleous, A. C., Emir, U. E., Diedrichsen, J., Saal, H. P., & Makin, T. R. (2022). Malleability of the cortical hand map following a finger nerve block. *Science Advances*, 8(16), eabk2393.
- Yoshioka, T., Dillon, M. R., Beck, G. C., Rapp, B., & Landau, B. (2013). Tactile Localization on Digits and Hand : Structure and Development. *Psychological Science*, 24(9), 1653-1663.

## SUPPLEMENTARY MATERIALS for

### **Repetitive Somatosensory Stimulation Shrinks The Body Image**

Malika Azaroual-Sentucq, Silvia Macchione, Luke E. Miller, Eric Koun, Romeo Salemme,  
Matthew R. Longo, Dollyane Muret & Alessandro Farnè

#### **Experimental procedures:**

To ensure the same skin locations were tested in Pre and Post sessions for the TDJT and TLT, while preventing participants from seeing the marks on their finger, the locations were drawn on the skin with invisible ink which was made visible when lighted with UV light (during the experimental sessions only, hidden from the participant's sight). In order to make the ink clearly visible to the experimenter, both tasks were conducted in a darkened room. The TMT was also conducted in darkness to have a similar experimental environment.

#### Instructions during RSS & Sham stimulations:

During both RSS and Sham stimulations, participants were instructed not to attend to the stimulation and to continue with their daily activities, but to avoid intensive use of their fingers (e.g., typing on a keyboard) to avoid major concomitant sensorimotor activity.

#### **Details about the tasks:**

##### 2PDT:

Each probe was tested 8 times in pseudo-randomized order, resulting in 64 trials per session. To prevent desensitization of the skin area under assessment due to repeated indentation, short breaks were allowed every 20-30 trials. After allowing the participant to feel the extreme distances (i.e., 0 and 2.5 mm) a familiarization phase was performed (in which each probe was tested 4 times in pseudo-randomized order, for a total of 32 trials). Then, in order to try to achieve a stable baseline performance, two sessions (S1 & S2) separated by a 20-minute break were conducted, as performed in previous studies (Muret et al., 2014; 2016).

Thresholds obtained at S1 and S2 were statistically analyzed for stability with a rmANOVA with the factors Intervention (Sham/RSS) and Time (S1/S2). No main Time effect ( $F(1,62) = 0.26$ ,  $p = 0.609$ ,  $\eta^2 = 0.001$ ) nor interaction ( $F(1,62) = 0.02$ ,  $p = 0.883$ ,  $\eta^2 = 0.000$ ) were found, indicating that discrimination thresholds were stable at baseline. The data of S2 were considered as the Pre session data.

##### TMT:

Each stimulus was presented 12 times in randomized order for a total of 108 trials. A familiarization session consisting in 9 trials (each stimulus presented once) was conducted before starting the experiment.

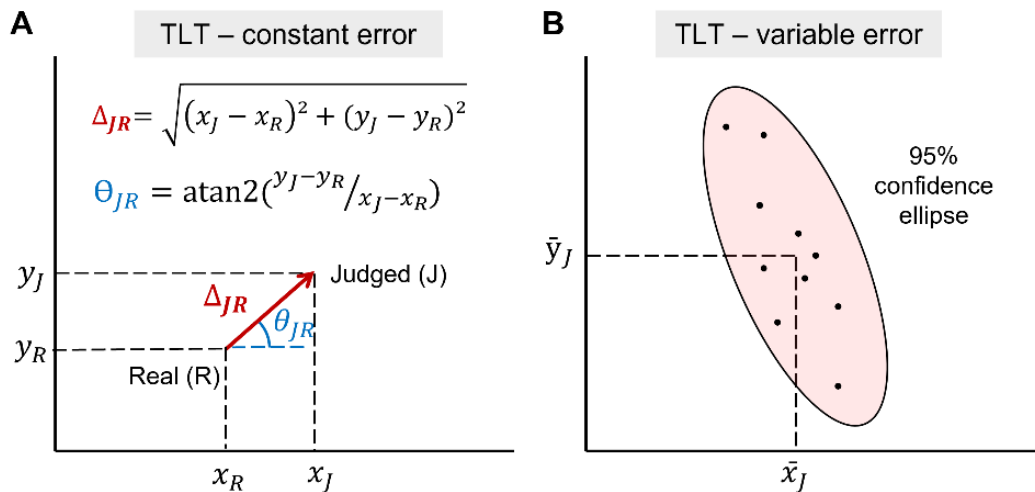
## TDJT:

The location at the base of the finger was placed at a distance of ¼th of the length of the proximal phalanx from the crease separating the finger from the palm, while the location at the tip of the finger was placed at a distance of ¼th of the length of the distal phalanx from the tip of the finger. Each of the four possible conditions (i.e., 15mm-base, 15mm-tip, 30mm-base, 30mm-tip) was repeated 10 times in a pseudo-randomized order, for a total of 40 trials.

On the screen, the initial size of the bar was either of 1 mm or 45 mm in a pseudo-randomized order.

## TLT:

Each of the 9 locations along the finger was touched 10 times in a pseudo-randomized order, for a total of 90 trials. From these, the constant and variable localization errors were computed at each point as described in Figure S1.



**Figure S1. Representation of the outcome measures of interest computed at the individual level in the TLT task.** (A) To determine the constant error, the difference between the judged (J) and real (R) locations as well as the angle between the JR vector and the x-axis at the R location were computed from their x and y coordinates. (B) To determine the variable error, the 95% confidence ellipses were computed from the judged locations (black dots), and their area was extracted (colored in pink here).

## **Supplementary Table S1. Results of Bayesian paired sample t-tests ( $BF_{incl}$ )**

Task	Sham Pre vs Sham Post	RSS Pre vs RSS Post
2PDT	0.189	1608.864
TMT	0.193	4.759
TDJT	0.386	0.419
TLT – constant error magnitude	0.418	0.213
TLT – constant error direction	1.773	0.432
TLT – variable error	1.247	0.198

## Supplementary Table S2. Results of statistical analyses with and without the inter subjects outliers

Task	Variable	Test	Effect	All subjects included				Without outliers			
				Statistic (F or t)	df	p	$\eta^2$ or d	Statistic (F or t)	df	p	$\eta^2$ or d
TDJT	Judged distance (n=33)	rmANOVA	Group*Session	3.35	1; 64	0.072	0.001	3.151	1; 60	0.081	0.001
			Group*Session*Position	1.065	1; 64	0.306	0.000	1.891	1; 60	0.174	0.000
			Group*Session*Distance	0.902	1; 64	0.346	0.000	1.072	1; 60	0.305	0.000
			Position	53.16	1; 64	<0.001	0.02	72.137	1; 60	<0.001	0.02
		One-sample t-test (judged vs real)	Judged vs real 15mm cond	-10.7	32	<0.001	-1.86	-14.2	30	<0.001	-2.55
	Judged vs real 30mm cond		-11.3	32	<0.001	-1.96	-13.7	30	<0.001	-2.46	
Real-Judged difference (n=33)	Paired t-tests	15 vs 30 mm	0.96	32	0.346	0.167	1.51	31	0.141	0.267	
TLT	Constant error magnitude (n=31)	rmANOVA	Group*Session	1.671	1; 60	0.201	0.001	0.262	1; 50	0.611	0.000
			Group*Session*Phalanx	1.238	2; 120	0.294	0.001	1.336	2; 100	0.268	0.001
			Group*Session*Point	0.018	2; 120	0.982	0.000	0.030	2; 100	0.971	0.000
			Phalanx	18.251	2; 120	<0.001	0.102	15.799	2; 100	<0.001	0.097
		Post-hoc t-test (Phalanx) **	Distal vs Middle	4.735	30	<0.001	0.850	3.782	25	<0.001	0.742
	Distal vs Proximal		3.934	30	<0.001	0.707	4.201	25	<0.001	0.824	
	Constant error direction (n=31)	rmANOVA	Group*Session	0.443	1; 60	0.508	0.000	1.328	1; 54	0.254	0.001
			Group*Session*Phalanx	1.638	2; 120	0.199	0.001	2.300	2; 108	0.105	0.002
			Group*Session*Point	1.533	2; 120	0.220	0.001	0.876	2; 108	0.419	0.001
	Variable error (n=32)	rmANOVA	Group*Session	2.205	1; 62	0.143	0.001	0.306	1; 44	0.583	0.000
			Group*Session*Phalanx	0.218	2; 124	0.804	0.000	1.989	2; 88	0.143	0.002
			Group*Session*Point	0.369	2; 124	0.693	0.000	0.936	2; 88	0.396	0.001
			Phalanx	81.281	2; 124	<0.001	0.152	64.656	2; 88	<0.001	0.183
		Post-hoc t-test (Phalanx) **	Phalanx*Point	8.310	4; 248	<0.001	0.015	9.658	4; 176	<0.001	0.030
			Distal vs Middle	9.102	31	<0.001	1.609	9.646	22	<0.001	2.011
Post-hoc t-test (Point*Phalanx) ***		Distal vs Proximal	8.385	31	<0.001	1.482	9.156	22	<0.001	1.909	
	Within distal : D vs M	3.936	31	<0.001	0.696	3.079	22	0.005	0.642		
	Within distal : M vs P	4.448	31	<0.001	0.786	3.087	22	0.005	0.644		

\* Without outliers: Judged distance (n=31); Real-Judged difference (n=32); Constant error magnitude (n=26); Constant error direction (n=28); Variable error (n=23)

\*\*  $\alpha_{\text{Bonf}} = 0.017$ \*\*\*  $\alpha_{\text{Bonf}} = 0.006$

## Supplementary Table S3. Post-hoc tests following the significant Phalanx\*Point interaction in the variable localization error with and without the inter subjects outliers

Phalanx	Point 1	Point 2	All subjects included (n=32)				Without outliers (n=23)			
			Statistic (t)	df	p*	d	Statistic (t)	df	p*	d
Proximal	Proximal	Middle	-1.662	31	0.107	-0.294	-2.807	22	0.010	-0.585
	Proximal	Distal	-1.753	31	0.089	-0.310	-3.005	22	0.007	-0.627
	Middle	Distal	-0.997	31	0.326	-0.176	-0.993	22	0.331	-0.207
Middle	Proximal	Middle	-1.094	31	0.282	-0.193	-2.041	22	0.053	-0.425
	Proximal	Distal	-0.209	31	0.836	-0.037	-1.131	22	0.270	-0.236
	Middle	Distal	1.023	31	0.314	0.181	0.656	22	0.519	0.137
Distal	Proximal	Middle	4.448	31	<0.001	0.786	3.087	22	0.005	0.644
	Proximal	Distal	5.287	31	<0.001	0.935	3.897	22	<0.001	0.813
	Middle	Distal	3.936	31	<0.001	0.696	3.079	22	0.005	0.642

\*  $\alpha_{\text{Bonf}} = 0.006$

## **STUDY 2: PERCEPTUAL STUDY**

### **Understanding measures of spatial discrimination: a comparative study of three tactile acuity tasks**

Malika Azaroual-Sentucq<sup>1,2\*</sup>, Frédéric Volland<sup>1</sup>, Alessandro Farnè<sup>1,2#</sup> & Dollyane Muret<sup>3,4#</sup>

<sup>1</sup> Integrative Multisensory Perception Action & Cognition Team of the Lyon Neuroscience Research Center INSERM U1028 CNRS UMR5292 University UCBL Lyon 1, Lyon, France

<sup>2</sup> Université UCBL Lyon 1, Université de Lyon, Lyon, France

<sup>3</sup> Université de Paris, NeuroDiderot, Inserm, Paris, France

<sup>4</sup> Université Paris-Saclay, NeuroSpin-UNIACT, CEA, Gif-sur-Yvette, France

\* corresponding author(s)

# equal contribution

## **Abstract**

Tactile acuity is a fundamental aspect of human tactile perception as it is required for fine motor skills and object recognition. Despite the wide use of tactile acuity tasks in clinical settings and research, little is known about the various features that contribute to this acuity and the relative sensitivity of each task. The present study aimed at assessing similarities and differences between three predominantly used tactile acuity tasks, namely the two-point discrimination (2PDT), the two-point orientation (2POT) and the grating orientation (GOT) tasks, by comparing their thresholds and investigating their links to anatomical parameters. Moreover, owing to the interest in tracking tactile threshold changes for both research and clinical applications, we compared the modulation of the tasks by repetitive somatosensory stimulation (RSS), known to improve tactile acuity through cortical plasticity. RSS was applied on the right index finger of 29 healthy adults and its impact on the three tasks was assessed at the stimulated finger as well as at the left index finger (control) and left middle finger which has been recently found to display tactile acuity improvement following RSS. On the basis of their link to each other and to anatomical parameters, the most similar tasks are the GOT and 2POT as their thresholds correlated, displayed the same interindividual variability, and depended on the fingertip area. In this respect, they are likely to measure a same aspect of tactile acuity. However, the 2PDT as delivered here is more conservative (higher thresholds), presents no aberrant values and displays a lower interindividual variability. On the basis of their modulation by RSS, both the GOT and 2PDT showed a significant reduction in threshold on the stimulated finger, suggesting that they may capture a similar aspect of tactile acuity. In contrast, the 2PDT and 2POT may capture similar changes in acuity for the unstimulated fingers, whereas the GOT may be more sensitive in detecting impaired performance. Considering these similarities and differences among the tasks, we conclude that the aspects measured by each task are not entirely separate but rather partially overlapping. This highlights the complexity of tactile acuity and emphasizes the necessity of employing multiple tasks, while ensuring methodological consistency across tasks, to fully capture this complexity.

**Keywords:** Tactile spatial discrimination tasks; Repetitive somatosensory stimulation; Tactile acuity; Touch



## **Introduction**

The spatial resolution of touch - or tactile acuity - is a fundamental aspect of human tactile perception as it is required for fine motor skills and object recognition (Tremblay et al., 2003; Pruszynski et al., 2018; Bilaloglu et al., 2016). Although understanding how tactile acuity works is crucial for grasping its interaction with other features of touch and its role in motor control, little is known about the various features that contribute to this acuity and the most effective ways to measure it. This is essential because various tasks are routinely employed in clinical settings to diagnose conditions and assess rehabilitation benefits (Lundborg & Rosén, 2004; Van Nes et al., 2008), as well as in research attempting to restore or artificially provide tactile inputs in prosthetics (Pestell et al., 2022; Valette et al., 2023).

The original and most common tactile acuity task is the Two-Point Discrimination Task (2PDT). Consisting in discriminating between one or two points touching the skin, this task has been extensively used since Weber's landmark work (1978) and is still used nowadays, not only in fundamental research (Muret et al., 2016; Schmidt-Wilcke et al., 2018; Sasaki et al., 2023), but also in clinical practice to diagnose deficits and assess recovery (Lundborg & Rosén, 2004; Van Boven & Johnson, 1994a; Van Nes et al., 2008). However, several concerns have long been raised about this task, particularly when used with subjective methods whereby participants receive only two- point stimulations (at different separations), but also when including single point stimulation (i.e., objective methods, see Johnson et al., 1994; Johnson & Phillips, 1981). In essence, to solve the subjective version of the 2PDT, participants may rely on a criterion (i.e. splitting their sensation continuum into "one" vs. "two" categories) and this is thought to increase variability among participants; in the objective version, the single and double stimuli differ in perceived intensity (one pin is felt more intense than two pins) and this may provide a non-spatial cue to solve the task. Thus, some participants may answer "two" even when there is no distance between the two points (Johnson & Phillips, 1981; Tawney, 1895; Craig & Johnson, 2000). As put forward by Lundborg and Rosén (2004) another major problem with 2PDT is the lack of standardized testing procedures, which may account for several of these concerns.

The most prominent alternative method to assess tactile acuity is the Grating Orientation Task (GOT), which consists in discriminating between gratings (carved in a plastic dome) touching the skin along and across the proximo-distal axis of the finger (Johnson & Phillips, 1981). This task is considered more reliable than the 2PDT (Holmes & Tamè, 2023) since it is immune to intensity cues as both the along and across stimuli have comparable perceived intensity. Yet,

Bensmaia's group reported that afferent fibers exhibit greater sensitivity, with stronger and more modulated responses, to gratings presented along the skin ridges (i.e. vertical; which corresponds to along the axis of the finger for the monkeys) compared to gratings presented across the skin ridges (Bensmaia et al., 2006). Similarly, Phillips & Johnson (1981) reported that the afferent fibers represented the spatial details more effectively when gratings were presented along the skin ridges than across. Both these findings showing a greater sensitivity to one orientation compared to the other suggests that the two orientations do not elicit the same response from afferent fibers. Behaviorally, this is likely involved (at least partly) in the perceptual anisotropy that have been reported in this task, with better performance observed for the horizontal (which corresponds to along the skin ridges in humans) compared to the vertical orientations (Wheat & Goodwin, 2000; Vega-Bermudez & Johnson, 2004). In addition, solving the GOT has been shown to involve visual cortical processing (Sathian & Zangaladze, 2002) in contrast to the 2PDT, considered to involve purely somatosensory processing. As for the criterion issue identified in the 2PDT, it is still unsolved in this task as tactile orientations are also represented as a continuum which should be split into two categories to solve the task.

Half-way between the 2PDT and the GOT lies the Two-Point Orientation Task (2POT), more recently proposed by Tong et al. (2013) - but first used by Stevens & Patterson (1995) - where participants have to discriminate the orientation of two points touching the skin along or across the proximo-distal axis of the finger. This task, which combines elements of both the 2PDT and GOT, has the benefit of eliminating non-spatial intensity cues. However, like the GOT, it does not address the issue of response criteria and has been used less frequently than the 2PDT and GOT, leaving its relationship to these tasks unclear.

At the peripheral level, although recent findings suggest a shared contribution of a wide range of mechanoreceptors (Cataldo et al, 2023; Saal & Bensmaia, 2014; Hayward et al., 2014), tactile acuity is thought to involve predominantly slowly-adapting type 1 (SAI) afferent fibers terminating in Merkel cells, and to a lesser extent, rapidly-adapting type 1 (RAI) afferent fibers terminating in Meissner corpuscles (Phillips & Johnson, 1981; see Johnson & Hsiao, 1992 for a review). As such, one would expect appropriate measures of tactile acuity to be somehow related to the density of these mechanoreceptors at the tested skin area. In line with this and despite their limitations, the ratio of the 2PDT threshold measured on the distal phalanx of the index finger to those on the two more proximal phalanges (2.31/1; Vallbo & Johansson, 1978) has been found to match the ratio of Merkel cells density at these locations (2.37/1; Johansson & Vallbo, 1979). Moreover, Meissner corpuscles and Merkel cells are more densely distributed

in the fingertips (Johansson & Vallbo, 1979) shown to have smaller 2PDT (Vallbo & Johansson, 1978) and GOT thresholds (Craig, 1999) - i.e. higher acuity - as compared to the rest of the fingers and palm. Additionally, the GOT threshold at the index fingertip has been shown to correlate with fingertip area which itself correlates with sweat pores density (Peters et al., 2009) – used as a proxy of Merkel cells density (Yamada et al., 1996). Finally, the 2PDT and 2POT thresholds measured at the index fingertip, finger base, palm and forearm were found to correlate with the estimated receptive field (RF) spacing of the SAI afferents (ending with Merkel cells) of these skin regions (Tong et al., 2013). Considering these findings, these three tasks seem all to reflect tactile acuity.

However, since no study directly compared the three tasks in the same subjects and with similar methods, it remains unknown how they relate to each other and whether they actually capture similar aspects of tactile perception. Only three studies compared them two by two and showed that the index finger's 2PDT thresholds were comparable to respectively GOT (Bruns et al., 2014) and 2POT (Tong et al., 2013) thresholds. But 2PDT and GOT thresholds were either correlated (Härtner et al., 2021) or not (Bruns et al., 2014) and, unlike the 2POT performance, the 2PDT performance at zero tip separation was above chance level (Tong et al., 2013; as in Johnson & Phillips, 1981). However, the use of different methodologies for each task makes it impossible to draw any definitive conclusion about what they measure.

Here we fill this gap leveraging a threefold approach. First, we directly compared tactile acuity thresholds as obtained by measuring 2PDT, 2POT and GOT within the same participants and with similar methodologies. Second, to deepen our understanding of what they measure, we investigate whether (and how) they are affected by a procedure known to improve tactile acuity, namely Repetitive Somatosensory Stimulation (RSS; see Beste & Dinse, 2013 for a review). RSS consists in an either mechanical or electrocutaneous (Ragert et al., 2005) stimulation that was found to increase tactile acuity at the stimulated area, predominantly documented using the 2PDT (Godde et al., 1996, 2000; Pleger et al., 2001, 2003; Kalisch et al., 2007; Ragert et al., 2008), while findings related to the GOT have been inconsistent (Hodzic et al., 2004; Kattenstroth et al., 2018; Ross et al., 2022; Gibson et al., 2009; Timm & Kuehn, 2020; Rocchi et al., 2017). Recent work also reported remote tactile improvement at the unstimulated hand (Muret et al., 2024) but only one task (2PDT) was tested. Third, we relate the outcome measures of the three tasks at baseline to each other and to sweat pores density and ridges width at baseline, which provide an indirect estimation of Merkel cells and Meissner corpuscles densities respectively (i.e., Merkel cells are found aggregated around sweat ducts (Cauna, 1954)

and Meissner corpuscles density is negatively correlated with the width of the skin ridges (Dillon et al., 2001).

We posit that if the three tasks measure similar aspects of tactile acuity, they should display similar differences across fingers, similar relationships with physiological measures and should be similarly affected by RSS.

## **Methods**

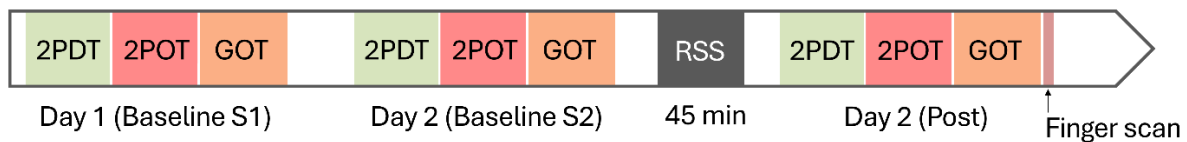
### *Participants*

We included 29 healthy adults (15 females; mean age  $\pm$  SD:  $22.8 \pm 3.2$  years). The sample size was determined by a power analysis using G\*Power 3.1 (Faul et al., 2007) with  $\alpha = 0.05$ . Effect sizes for local improvements in 2PDT (Schlieper & Dinse, 2012) and GOT (Kattenstroth et al., 2018) thresholds following electrical RSS have been computed as Cohen's  $d = 0.63$  and  $0.61$  respectively. Additionally, the effect size for the remote effect of mechanical RSS on the left middle finger 2PDT threshold (Muret et al., 2024) is  $d = 1.05$ . Our calculation thus showed that a sample size of 24 was required to detect an effect with 80% power using repeated measures ANOVAs.

Participants were right-handed (assessed through the Edinburgh handedness inventory (Oldfield, 1971), average score  $\pm$  SD:  $82.7 \pm 16.8$ ), without any neurological or psychiatric disease, and with no history of injuries at the hands. All participants gave their written informed consent before participating and received compensation at the end of the study. Procedures were approved by the Inserm ethics committee (IRB00003888).

### *Experimental timeline*

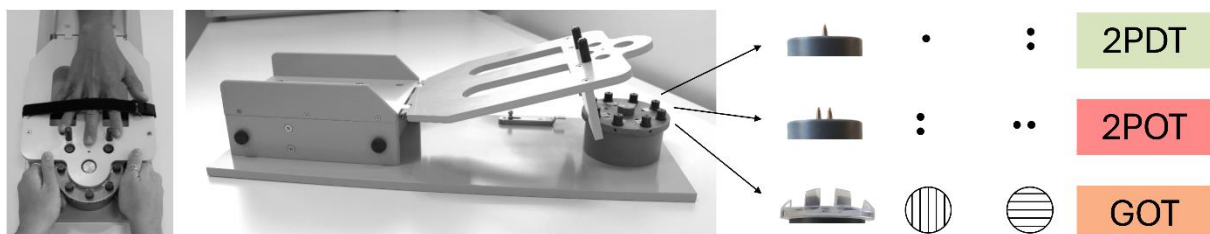
All participants performed the three tasks (in a counter-balanced order) on both index (rD2 & lD2) and left middle (lD3) fingers before and after receiving the RSS stimulation on the right index fingertip. After a familiarization session, two baseline sessions were performed on two consecutive days (S1 & S2) to avoid fatigue and assess the stability of the baseline performance. On the second day, participants then received 45min of RSS on rD2 before a last session (Post) of the three tasks was performed after a 10min break (Figure 1). At the end of the experiment, the participants' three fingertips were scanned for distal phalanx area, sweat pores, and skin ridges measurements. The three tasks required unspeeded 2 alternative-forced choice responses (2AFC) procedures (without feedback) and were implemented using MATLAB (MathWorks<sup>®</sup>, version 2015b).



**Figure 1. Experimental timeline.** Participants performed the 2-point discrimination (2PDT), 2-point orientation (2POT) and grating orientation (GOT) tasks on three fingers (rD2, ID2, ID3) before and after receiving RSS on their right index finger (rD2). At the end of the experiment, the participants' three fingertips were scanned for distal phalanx area, sweat pores, and skin ridges measurements.

### *Experimental setup and device*

To maximize tasks comparability, participants' posture and the setup was common across the three tasks. Participants were blindfolded and seated comfortably with their forearm resting on a device minimizing the difference in pressure applied across trials (Figure 2) inspired from the one described in detail in Godde et al. (2000). Briefly, the hand was positioned on a plate above a rotatable disk on which stimuli were mounted, and the tested fingertip was secured above a hole through which stimuli were presented. The experimenter moved the plate down to passively apply stimuli to the volar surface of the tested finger with similar pressure across stimuli and fingers, consistent from one trial to another. Because tactile orientation is best detected when the head is aligned with the body midline (French et al., 2022), participants' heads were held facing straight ahead using a chinrest. To make sure the positions of the chair, chinrest and device were consistent across the two days, they were marked on the floor and table.



**Figure 2. Experimental device used for the three tasks.** The device was common to the three tasks, only the probes differed: one or two tips oriented either in the longitudinal axis of the finger (2PDT), in both longitudinal and transversal axes (2POT) and grating domes in both orientations (GOT).

### *Two-Point Discrimination Task (2PDT)*

The 2PDT was applied with a well-established procedure (Godde et al., 2000; Pleger et al., 2001, 2003; (Muret et al., 2014, 2016). Eight probes were presented at the fingertip: one with a single tip (distance 0) and seven with two tips separated by various distances (D2: 0.7, 1, 1.3, 1.6, 1.9, 2.2 and 2.5 mm; D3: 1, 1.4, 1.8, 2.2, 2.6, 3.2, 4 mm). Tips were presented aligned to the longitudinal axis of the finger. Participants were asked to indicate whether they perceived

“one” or “two” tips at each trial with the specific instruction of saying “two” only when the tips were clearly distinguishable.

#### *Two-Point Orientation Task (2POT)*

The same probes as in the 2PDT (including the single tip) were presented at the fingertip either in the longitudinal or the transversal axis of the finger. At each trial, participants were asked to indicate whether they perceived the pins as oriented in the longitudinal axis (answer “vertical”) or in the transversal axis (“horizontal”) of their finger.

#### *Grating Orientation Task (GOT)*

Johnson-van Boven-Phillips (JVP) domes (Van Boven & Johnson, 1994b) were presented at the fingertip either in the longitudinal or the transversal axis of the finger. The domes are carved with grooves and ridges of varying widths (0.35, 0.5, 0.75, 1.0, 1.25, 1.5, 2.0, 3.0 mm). At each trial, participants were asked to indicate whether they perceived the gratings oriented in the longitudinal axis (answer “vertical”) or in the transversal axis (“horizontal”) of their finger.

#### *Thresholds computation*

To allow for rigorous comparison, the number of trials, of sessions and the threshold computation method were made identical across the tasks. First, we allowed the participants to feel the extreme distances in the 2PDT and the two orientations (with the largest distance and grating width) in the 2POT and GOT. Then they underwent a familiarization phase, in which each probe was tested 4 times in pseudo-randomized order, for a total of 32 trials. In the following baseline (S1 & S2) and Post-RSS sessions, each probe was tested 8 times in pseudo-randomized order, resulting in 64 trials per session. To prevent desensitization of the skin area under assessment due to repeated indentation, short breaks were allowed every 20-30 trials.

In the 2PDT, the average of the verbal responses (“one” or “two”) was computed and the percentage of “two” responses was plotted as a function of the distance between the probes. In the 2POT and GOT, the “vertical” and “horizontal” verbal responses were first labeled as “correct” or “incorrect”, then the average of the correct and incorrect responses was computed and the percentage of “correct” responses was plotted as a function of the distance between the probes.

The data of S2 were considered as the Pre-RSS session. In all tasks, the psychometric function was fitted with a binary logistic regression. From these fitted data, the point of subjective equality (PSE) - corresponding to 50% for the 2PDT (because here “answer two” is plotted

instead of “correct answer”) and 75% for the 2POT and GOT (chance performance is 50%) - was determined for each session (S1, S2 & Post).

For representational purposes, the effects of RSS were shown as a Post-Pre change percentage (Figure 7). Since the baseline thresholds of the three tasks differ significantly (see Results section), Post-Pre changes expressed as percentages of Pre thresholds would be biased by their baseline value, biasing the visual comparison between the three tasks. To overcome this (for data representation only), Pre thresholds were equalized to an arbitrary value and Post-Pre threshold changes were computed on this basis.

### *RSS stimulation*

The stimulation consists in a 45-min task-free electrocutaneous stimulation on the rD2 delivered by a constant current stimulator (Digitimer DS7A) controlled by a Matlab program (MathWorks<sup>®</sup>, version 2021b). Two adhesive electrodes (4.8 x 3 cm; Ambu<sup>®</sup> Neuroline 714) were taped on the proximal (cathode) and distal (anode) phalanges of the right index fingertip of the participant. Trains of 20 Hz (single pulses of 0.2 ms) were sent for 1s with an intertrain interval of 5s (Erro et al., 2016; Kalisch et al., 2010). Stimulation intensity was set at the maximal tolerated intensity (mean  $\pm$  SD = 5.24  $\pm$  2.43 mA), as it has been shown to induce the largest improvement on 2PDT thresholds (Schlieper & Dinse, 2012). Participants were instructed not to attend to the stimulation and to continue with their daily activities, but to avoid intensive use of their fingers (e.g., typing on a keyboard) to avoid major concomitant sensorimotor activity.

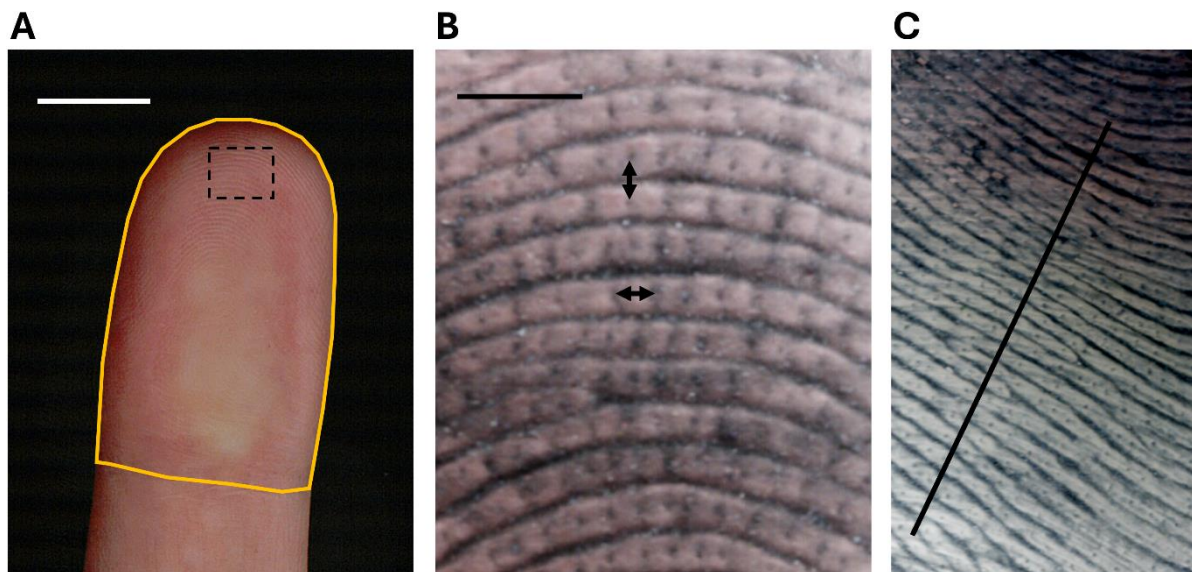
### *Fingertip scanning and anatomical measurements*

To measure the distal phalanx surface area, both hands were scanned at 600 dpi (Toshiba e-STUDIO 3525AC). The distal phalanx of each finger of interest (rD2, lD2 & lD3) was detoured and the corresponding area was measured in ImageJ (version 1.54g; Figure 3A).

To measure sweat pores density (proxy of Merkel cells density) at the fingertips, the distal part of the distal phalanges (fingertip tilted to mimic their position during the tasks) were scanned following the procedure established by Peters et al. (2009). The distal phalanges of the fingers of interest were coated with a dark gray washable finger paint (Crayola) and scanned through a high-resolution scanner (Epson Perfection V39II) at 3200 dpi. Using ImageJ, the distances between pores both within and between ridges were measured (Figure 3B). Following Peters et al.'s method (2009), twenty within-ridge (w) and twenty between-ridges (b) pore-to-pore

distances were measured (Figure 3B), averaged and used to compute the global pore density in the fingertip:  $\text{density (pore/mm}^2\text{)} = 1/(\bar{w} * \bar{b})$  (with  $\bar{w}$  the average of  $w$  and  $\bar{b}$  the average of  $b$ ). Additionally, to separately calculate density of sweat pores in the longitudinal (vertical) and transversal (horizontal) axis of the finger, we used  $\bar{w}$  and  $\bar{b}$  as measures of the pore-to-pore distances in the transversal and longitudinal orientation respectively (most of the  $w$  and  $b$  distances are indeed oriented transversally and longitudinally, respectively). To measure ridges width (proxy of Meissner corpuscles density) at the fingertips, the number of ridges that cross a 10 mm long line perpendicular to the ridges was counted (Figure 3C). The ridge width corresponds to 10 divided by this number (Dillon et al., 2001).

The measurements of the distal phalanx area and the sweat pores density were made by two independent observers, while the measurements of the ridges width were made by one observer. The interobserver reliability was assessed through intraclass correlation coefficients (ICC; Portney & Watkins, 2009). Interobserver agreement was good for the distal phalanx area (ICC = 0.79) and poor for sweat pores density (ICC = 0.41). Measures of the two observers were averaged for subsequent analysis.



**Figure 3. Measures of anatomical parameters.** (A) Scan from fingertip traced for area measurement (scale bar, 1 cm). (B) High resolution (3200 dpi) scan from stained fingertip for pore-to-pore measurements. Horizontal arrow: within-ridge; Vertical arrow: between-ridges (scale bar, 1 mm). (C) High resolution (3200 dpi) scan from stained fingertip for ridge width measurements. The ridge width corresponds to 10 divided by the number of ridges crossing the 10 mm long line.



### *Statistical analysis*

The data from all tasks were collected through Matlab (MathWorks®, version 2021b) and statistical analyses were performed with Jamovi (version 2.2.5). Outliers, defined as falling outside 3SD around the average per participant per condition, were not included in the analyses. Two subjects (1 male and 1 female) were outliers for S1-S2 stability (one in GOT rD2, and the other in GOT ID3). For material availability reasons, high resolution scans were available for 19 out of the remaining 27 participants.

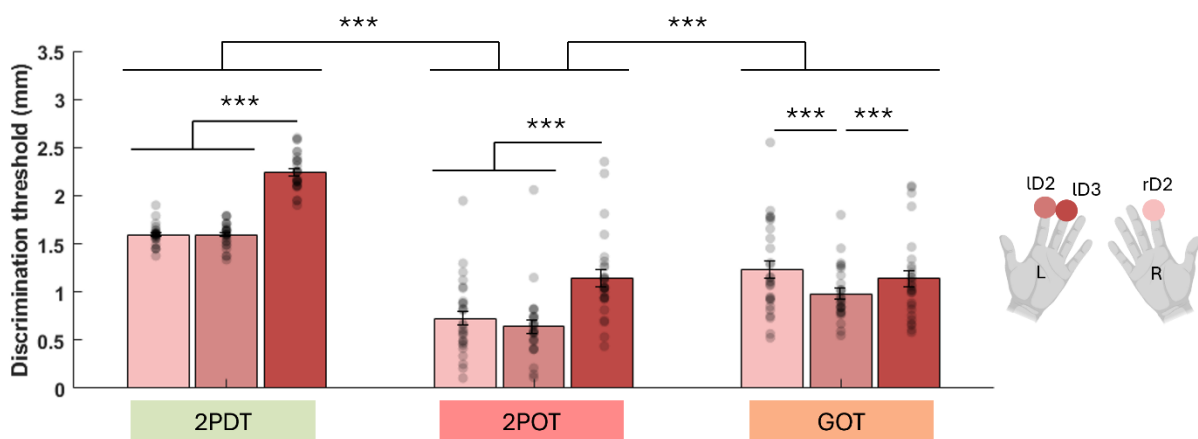
After verification of the normality (Shapiro-Wilk test), homoscedasticity (Levene's test), and sphericity (Mauchly's test) assumptions, repeated-measures ANOVAs (rmANOVAs) were conducted. In all tasks, two-way rmANOVAs with the factors Finger (rD2/ID2/ID3) and Session (Pre/Post) were used. When significant main effects or interactions were found, two-tailed t-tests were conducted with alpha levels Bonferroni-corrected for the number of tests performed ( $\alpha_{\text{Bonf}}$ ). Effect sizes were computed using Cohen's  $d$  (Cohen, 1988), and based on benchmarks suggested by Cohen, a large effect size was defined as greater than 0.8. When homoscedasticity assumptions were not met, Mann-Whitney tests were conducted, and effect sizes were computed as  $r_{\text{tb}}$  using rank biserial correlations. Pearson's correlations and Levene's tests (interindividual variability) were performed to compare the three tasks. Except when specified otherwise, the alpha level was set at  $\alpha = 0.05$ . Bayesian t-tests were conducted, with a Cauchy prior width set to .707 (default). We reported the corresponding Bayes Factors ( $\text{BF}_{10}$ ), showing the relative support for the alternative hypothesis, using the threshold of  $\text{BF}_{10} < 1/3$  as sufficient evidence in support of the null hypothesis (Dienes, 2014).

Thresholds obtained at S1 and S2 (before RSS) were statistically analyzed for stability with a rmANOVA with the factors Task (2PDT/2POT/GOT), Finger (rD2/ID2/ID3) and Time (S1/S2). No significant main effect of Time ( $F_{(1,26)} = 3.84$ ,  $p = 0.061$ ,  $\eta^2 = 0.002$ ,  $\text{BF}_{10} = 0.82$ ), but a significant Time\*Finger interaction ( $F_{(2,52)} = 4.22$ ,  $p = 0.020$ ,  $\eta^2 = 0.002$ ,  $\text{BF}_{10} = 0.09$ ) were found. Post-hoc tests revealed a significant reduction of threshold from S1 to S2 in ID2 ( $t_{(26)} = 3.47$ ,  $p = 0.002$ ,  $\alpha_{\text{Bonf}} = 0.017$ ,  $d = 0.67$ , 95% CI [0.24, 1.08],  $\text{BF}_{10} = 20.06$ ) and a stable threshold for rD2 and ID3 (both  $t_{(26)} \leq 0.67$ ,  $p \geq 0.507$ ,  $\alpha_{\text{Bonf}} = 0.017$ ,  $d \leq 0.13$ ,  $\text{BF}_{10} \leq 0.25$ ). Thus, S2 was taken as the baseline performance.

## Results

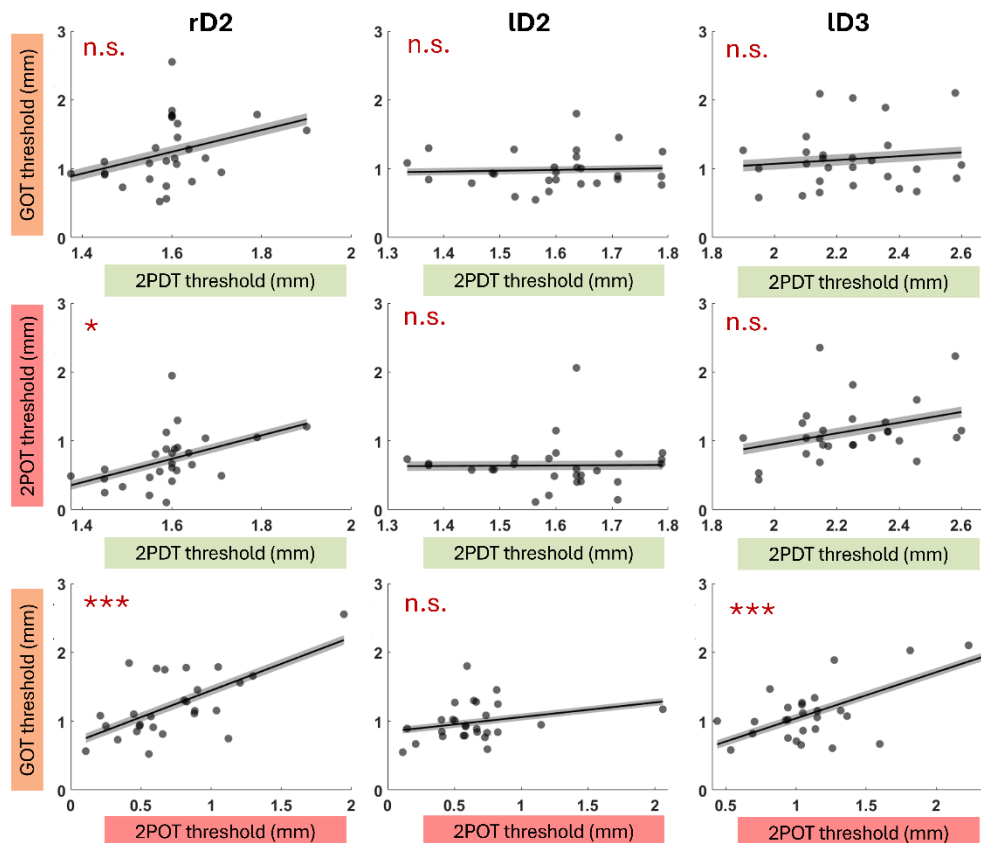
### *Tactile acuity thresholds across tasks*

To first investigate whether the three tasks converge towards similar thresholds across fingers, baseline thresholds were compared across tasks and fingers through a two-way rmANOVA. The test revealed a significant main effect of Task ( $F_{(2,52)} = 141.0$ ,  $p < 0.001$ ,  $\eta^2 = 0.51$ ,  $BF_{10} > 100$ ) arising from 2PDT thresholds being higher than GOT thresholds ( $t_{(26)} = 10.39$ ,  $p < 0.001$ ,  $\alpha_{Bonf} = 0.017$ ,  $d = 2.0$ , 95% CI [1.33, 2.65],  $BF_{10} > 100$ ), themselves higher than 2POT thresholds ( $t_{(32)} = -5.82$ ,  $p < 0.001$ ,  $\alpha_{Bonf} = 0.017$ ,  $d = -1.12$ , 95% CI [-1.60, -0.63],  $BF_{10} > 100$ ; Figure 4). The rmANOVA also revealed a significant main effect of Finger ( $F_{(2,52)} = 69.90$ ,  $p < 0.001$ ,  $\eta^2 = 0.10$ ,  $BF_{10} > 100$ ), as well as a significant Task\*Finger interaction ( $F_{(4,104)} = 24.60$ ,  $p < 0.001$ ,  $\eta^2 = 0.05$ ,  $BF_{10} > 100$ ). Post-hoc tests showed higher thresholds on ID3 than on the other fingers in both 2PDT and 2POT (all  $t_{(26)} \geq -17.94$ , all  $p < 0.001$ ,  $\alpha_{Bonf} = 0.006$ , all  $d \geq -1.15$ , all  $BF_{10} > 100$ ), and lower threshold on ID2 than on the other fingers in GOT ( $t_{(26)} = 3.89$ ,  $p < 0.001$ ,  $\alpha_{Bonf} = 0.006$ ,  $d = 0.75$ , 95% CI [0.32, 1.17],  $BF_{10} = 51.9$ ). Interestingly, the 2POT thresholds approached values near zero (as shown in Figure 4), with some even falling into negative ranges (indicating exceptionally high performance at very small distances) during Session 1 (Session 1 not represented in the Figure 4, see Supplementary figure S1). The GOT also displayed a few aberrant very low thresholds labeled as outliers (removed). Moreover, the interindividual variability was significantly smaller in 2PDT ( $\sigma = 0.01$  mm) than in 2POT ( $\sigma = 0.11$  mm;  $F_{(1,52)} = 7.91$ ,  $p = 0.007$ ) and GOT ( $\sigma = 0.13$  mm;  $F_{(1,52)} = 19.80$ ,  $p < 0.001$ ), while it was not significantly different between 2POT and GOT ( $F_{(1,52)} = 0.81$ ,  $p = 0.372$ ).



**Figure 4. Fingers thresholds across the three tasks at baseline.** Individual (dots) and average (bars,  $\pm$  SEM) thresholds obtained at rD2 (light pink), ID2 (dark pink) and ID3 (red) in 2PDT, 2POT and GOT. \*\*\*  $p < 0.001$  (paired t-tests,  $\alpha_{Bonf} = 0.017$ ).

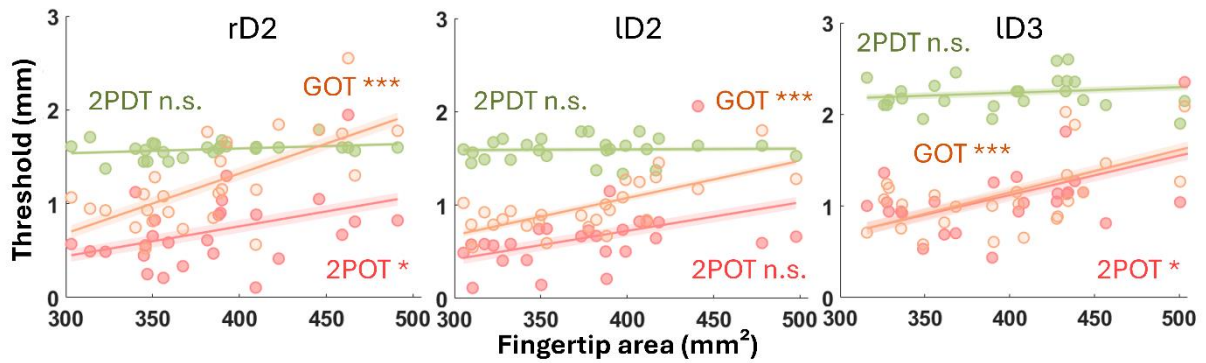
Then the three tasks were compared through correlation tests. On the rD2, the 2POT thresholds correlated with both the 2PDT ( $r = 0.46$ ,  $p = 0.017$ ,  $\alpha_{\text{Bonf}} = 0.017$ ,  $\text{BF}_{10} = 3.56$ ) and GOT thresholds ( $r = 0.64$ ,  $p < 0.001$ ,  $\alpha_{\text{Bonf}} = 0.017$ ,  $\text{BF}_{10} > 100$ ). On the ID3, only 2POT and GOT thresholds were correlated ( $r = 0.67$ ,  $p < 0.001$ ,  $\alpha_{\text{Bonf}} = 0.017$ ,  $\text{BF}_{10} > 100$ ), the correlations between the other tasks being non-significant (both  $r \leq 0.33$ ,  $p \geq 0.088$ ,  $\alpha_{\text{Bonf}} = 0.017$ ,  $\text{BF}_{10} \leq 0.95$ ). Finally, correlations between tasks were not significant on the ID2 (all  $r \leq 0.28$ ,  $p \geq 0.163$ ,  $\alpha_{\text{Bonf}} = 0.017$ ,  $\text{BF}_{10} \leq 0.60$ ; Figure 5).



**Figure 5. Fingers thresholds correlations across tasks.** Scatterplots of individual thresholds obtained in the three tasks, represented two-by-two, and regression lines  $\pm$  SEM (shaded area). Thresholds are represented averaged across fingers (first column: red) and at each finger (other columns: black). \*  $p < 0.05$ , \*\*\*  $p < 0.001$  (correlation tests,  $\alpha_{\text{Bonf}} = 0.017$ ).

#### *Tasks thresholds relation with fingertip area*

To investigate the effect of fingertip area on thresholds, we conducted Pearson's correlation tests. These tests revealed that GOT thresholds correlated with areas at all fingers (all  $r \geq 0.61$ ,  $p \leq 0.001$ ,  $\alpha_{\text{Bonf}} = 0.017$ ,  $\text{BF}_{10} \geq 40.40$ ) and 2POT thresholds correlated with areas at the rD2 and ID3 (both  $r \geq 0.48$ ,  $p \leq 0.012$ ,  $\alpha_{\text{Bonf}} = 0.017$ ,  $\text{BF}_{10} \geq 4.79$ ), but not at the ID2 ( $r = 0.44$ ,  $p = 0.025$ ,  $\alpha_{\text{Bonf}} = 0.017$ ,  $\text{BF}_{10} = 2.62$ ). No correlations were found in 2PDT (all  $r \leq 0.33$ ,  $p \geq 0.102$ ,  $\alpha_{\text{Bonf}} = 0.017$ ,  $0.25 \leq \text{BF}_{10} \leq 0.87$ ; Figure 6).



**Figure 6. Tasks thresholds variations with fingertip area.** Scatterplots of individual thresholds (○) obtained in the three tasks at each finger vs fingertip area. \*  $p < 0.05$ , \*\*\*  $p < 0.001$  (correlation tests,  $\alpha_{\text{Bonf}} = 0.017$ ).

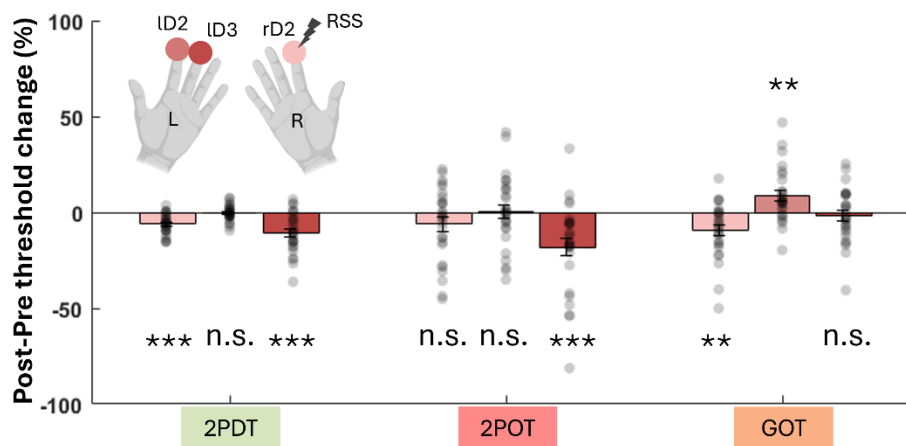
#### *Tasks thresholds relation with sweat pores density and ridge width*

To further investigate whether the thresholds depend on Merkel cells and Meissner corpuscles, we conducted correlation tests with sweat pores density (proxy of Merkel cells) and ridge width (proxy of Meissner corpuscles). No significant correlations were found with sweat pores density (all  $-0.39 \leq r \leq 0.39$ ,  $p \geq 0.111$ ,  $\alpha_{\text{Bonf}} = 0.017$ ,  $0.39 \leq \text{BF}_{10} \leq 0.95$ ) and ridge width (all  $-0.14 \leq r \leq 0.16$ ,  $p \geq 0.29$ ,  $\alpha_{\text{Bonf}} = 0.017$ ,  $0.29 \leq \text{BF}_{10} \leq 0.49$ ) for any of the tasks.

Since the 2PDT stimuli are unidimensional (vertically oriented), while both other tasks stimuli are bidimensional (vertical & horizontal), we additionally investigated the separate effects of within- (horizontal) and between- (vertical) ridges sweat pores distance on tasks performance in each orientation. For both orientations, no significant correlations between the thresholds and the pore-to-pore distances were found for any of the tasks at any of the fingers (Horizontal: all  $r \geq -0.23$ ,  $p \geq 0.361$ ,  $\alpha_{\text{Bonf}} = 0.025$ ,  $0.30 \leq \text{BF}_{10} \leq 0.43$ ; Vertical: all  $r \geq -0.40$ ,  $p \geq 0.097$ ,  $\alpha_{\text{Bonf}} = 0.017$ ,  $0.30 \leq \text{BF}_{10} \leq 1.05$ ). Besides, comparing the pore-to-pore distance in both orientations through a two-way rmANOVA revealed a significant Orientation main effect ( $F_{(1,17)} = 29.20$ ,  $p < 0.001$ ,  $\eta^2 = 0.11$ ,  $\text{BF}_{10} > 100$ ) indicating that vertical distances (between-ridges) are significantly bigger than horizontal distances (within-ridges) in all fingers as revealed through two-tailed paired t-tests (all  $t_{(17)} \geq -4.73$ , all  $p \leq 0.002$ ,  $\alpha_{\text{Bonf}} = 0.017$ , all  $d \geq -1.11$ , all  $\text{BF}_{10} \geq 19.70$ ). Similarly, comparing the performance in both orientations through a three-way rmANOVA revealed a significant Task\*Orientation interaction ( $F_{(1,52)} = 15.74$ ,  $p < 0.001$ ,  $\eta^2 = 0.08$ ,  $\text{BF}_{10} > 100$ ), indicating higher performance in the vertical than in the horizontal orientation in 2POT ( $t_{(26)} = 5.98$ ,  $p < 0.001$ ,  $\alpha_{\text{Bonf}} = 0.025$ ,  $d = 1.15$ , 95% CI [0.66, 1.63],  $\text{BF}_{10} > 100$ ), but similar performance between orientations in GOT ( $t_{(26)} = -0.22$ ,  $p = 0.824$ ,  $\alpha_{\text{Bonf}} = 0.025$ ,  $d = -0.04$ , 95% CI [-0.42, 0.34],  $\text{BF}_{10} = 0.21$ ) as revealed through two-tailed paired t-tests (See Supplementary figure S2).

### Tasks thresholds variation following RSS

We then compared the effect of RSS applied on rD2 on the tactile thresholds as measured by the three tasks. A three-way rmANOVA revealed a significant Task\*Finger\*Session interaction ( $F_{(4,104)} = 3.04$ ,  $p = 0.02$ ,  $\eta^2 = 0.004$ ,  $BF_{10} = 15.08$ ), indicating that the effect of RSS on the thresholds differed across tasks. Post-hoc tests showed that after RSS, 2PDT thresholds were significantly reduced on rD2 and ID3 (both  $t_{(26)} \geq 5.29$ , both  $p < 0.001$ ,  $\alpha_{Bonf} = 0.006$ , both  $d \geq 1.02$ , both  $BF_{10} > 100$ ), but remained unchanged on ID2 ( $t_{(26)} = 0.43$ ,  $p = 0.674$ ,  $\alpha_{Bonf} = 0.006$ ,  $d = 0.08$ , 95% CI [-0.30, 0.46],  $BF_{10} = 0.22$ ). Similarly, 2POT thresholds were reduced on ID3 ( $t_{(26)} = 3.99$ ,  $p < 0.001$ ,  $\alpha_{Bonf} = 0.006$ ,  $d = 0.77$ , 95% CI [0.33, 1.19],  $BF_{10} = 65.64$ ), but remained unchanged on rD2 ( $t_{(26)} = 1.69$ ,  $p = 0.104$ ,  $\alpha_{Bonf} = 0.006$ ,  $d = 0.32$ , 95% CI [-0.07, 0.71],  $BF_{10} = 0.71$ ) - though with an inconclusive  $BF_{10}$  - and ID2 ( $t_{(26)} = -0.07$ ,  $p = 0.945$ ,  $\alpha_{Bonf} = 0.006$ ,  $d = -0.01$ , 95% CI [-0.39, 0.36],  $BF_{10} = 0.20$ ). Conversely, GOT thresholds were reduced after RSS on rD2 ( $t_{(26)} = 3.39$ ,  $p = 0.002$ ,  $\alpha_{Bonf} = 0.006$ ,  $d = 0.65$ , 95% CI [0.23, 1.06],  $BF_{10} = 16.67$ ), while they remained unchanged on ID3 ( $t_{(26)} = 0.64$ ,  $p = 0.53$ ,  $\alpha_{Bonf} = 0.006$ ,  $d = 0.12$ , 95% CI [-0.26, 0.50],  $BF_{10} = 0.25$ ), and significantly increased on ID2 ( $t_{(26)} = -3.15$ ,  $p = 0.004$ ,  $\alpha_{Bonf} = 0.006$ ,  $d = -0.61$ , 95% CI [-1.01, -0.19],  $BF_{10} = 10.00$ ; Figure 7), displaying a different pattern of changes on unstimulated fingers.



**Figure 7. Tasks thresholds changes following RSS.** Individual (dots) and average (bars,  $\pm$  SEM) Post-Pre threshold changes at rD2 (light pink), ID2 (dark pink) and ID3 (red) in 2PDT, 2POT and GOT. \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$  (paired t-tests (Post vs Pre),  $\alpha_{Bonf} = 0.006$ ).

### Discussion

The present study aimed at assessing similarities and differences among three predominantly used tactile acuity tasks, namely the 2PDT, 2POT and GOT, leveraging a threefold approach (i) comparing the thresholds, (ii) investigating their links to anatomical parameters (skin area and mechanoreceptors) and (iii) comparing their potential modulation by RSS. To this aim, we

measured tactile acuity with each of these tasks in the same participants at three different fingers - rD2, lD2, and lD3 - before and after applying RSS on rD2. We first observed that the three tasks give rise to different absolute thresholds, the highest being obtained with the 2PDT and the lowest with the 2POT. Then we observed that the 2POT and GOT are the most comparable regarding their correlation, interindividual variability and link to fingertip area. Finally, we showed that the three tasks were partially affected differently by RSS. These results suggest that, while each of these measures relates to tactile acuity, they do neither show the same relationships with physiological skin features, nor the same behavioral sensitivity to RSS intervention.

#### *The three tasks return different tactile acuity thresholds*

The thresholds we reported for each task are comparable to the thresholds reported in the literature (Vallbo & Johansson, 1978; Van Boven & Johnson, 1994b; Tong et al., 2013). Comparing the thresholds within the same individuals, our results showed that all tasks give rise to significantly different thresholds, with the 2PDT thresholds higher than the GOT thresholds, themselves higher than the 2POT thresholds.

Contrary to one of the main criticisms raised against the 2PDT (Johnson & Phillips, 1981; Tawney, 1895; Craig & Johnson, 2000), we never observed “zero” thresholds in the present study, but neither in previous ones from our (Muret et al., 2014, 2016, 2024; Muret & Dinse, 2018) and other groups using the same apparatus, instructions and procedures (Godde et al., 2000; Pleger et al., 2003; Bruns et al., 2014). While these results may underline the importance of standardizing the 2PDT methodology to get reliable thresholds, it also warns to not throw the baby out with the bathwater. Indeed, when care is taken in using the 2PDT objectively, the resulting threshold may be in line with what would be expected as a function of the stimulated body part. Indeed, 2PDT and 2POT show similar pattern across fingers. Knowing that the 2POT is thought to preserve the reliability of the GOT by using stimuli typically used for the 2PDT, their similar pattern is another piece of evidence in favor of the 2PDT as actually being a reliable measure of tactile acuity, at least when used with the present pain-taking procedures. These are likely the reasons we observed higher thresholds in the 2PDT (with our instruction to say “two” only when the tips are clearly distinguishable) compared to the 2POT and GOT (no specific instruction regarding the criterion to use).

The difference we found between 2PDT and GOT thresholds contrasts with the findings of Bruns et al. (2014), who did not report a significant difference between the two tasks. However,

they conducted a principal component analysis showing that both thresholds were distinct from each other, suggesting that they may not measure the same construct. As for the difference we observed between 2PDT and 2POT thresholds, it is consistent with the findings of Richardson & Wuillemin (1981) showing better performances in 2POT than 2PDT on the forearm. These authors hypothesized that these tasks may take advantage of different properties of the cutaneous RFs. They proposed that the perception of twoness depends on having a relatively inactive RF between the two points (Vallbo & Johansson, 1978), while orientation discrimination likely requires only the activation of distinct sets of RFs by the stimuli to be differentiated. In contrast, Tong et al. (2013) found no significant difference between thresholds of both tasks. However, this discrepancy could be attributed to their method of threshold computation as they used an adaptive Bayesian algorithm and they computed 95% thresholds as they were not able to find 75% thresholds in the 2PDT for all individuals (when the zero tip separation was already above 75% of correct response). Interestingly, our data revealed the opposite scenario, where exceptionally high performance (resulting in very low or negative thresholds) was observed in the 2POT, and on a few occasions in the GOT, while no excessively low or negative thresholds were found in the 2PDT (see Supplementary figure S1). Additionally to the computation method, the discrepancy between our findings and theirs may be explained by the difference in testing devices and instructions. While they used manual calipers to apply the two points and gave no specific instruction regarding the criterion to use, we used a device which minimizes the difference in pressure across trials and gave a quite conservative instruction for the 2PDT (asking to answer “two” only when the tips are clearly distinguishable). Regarding the comparison between the 2POT and GOT thresholds, no study investigated it to the best of our knowledge, making these findings a novel contribution to this matter.

Besides, our results showed that the 2PDT and 2POT thresholds were lower for the D2s compared to the D3s, while the GOT threshold on the 1D2 was lower than on the other two fingers. These findings are coherent with Kalisch et al. (2007), who reported an increasing gradient of 2PDT thresholds from the thumb to the little finger, as well as with Muret et al. (2016, 2018), who showed higher thresholds on the D2 compared to the D3. In contrast, findings related to the GOT are more variable, with some studies indicating better performance on the D2 than the D3 (Vega-Bermudez & Johnson, 2001), while others found no significant difference between the two (Sathian & Zangaldze, 1996). The lower GOT threshold on the 1D2 compared to the rD2 has however never been reported in the literature. Nonetheless, we cannot rule out the possibility that the differences we observed may be attributed to the larger tip

distances used for the D3s compared to the D2s in the 2PDT and 2POT, but not in the GOT (the grating widths were consistent across all fingers).

Comparing the interindividual variabilities across tasks, we found that the variability was higher in the 2POT and GOT than in the 2PDT. The lower variance we observed in the 2PDT compared to the GOT mirrors the reduced variability found in the 2PDT relative to the GOT, as calculated from Bruns et al. (2014)'s available data (Levene's test:  $F_{(1,34)} = 4.68$ ,  $p = 0.038$ ). The lower variability in the 2PDT could be attributed to the conservative instructions provided to participants, both in our study and in Bruns et al. (2014), potentially minimizing the differences in the response criteria adopted by each individual. Another possibility is that the variability difference may be related to the physiological properties of the skin. Indeed, skin compliance has been reported to affect the GOT thresholds, with more compliant skin resulting in lower thresholds (Vega-Bermudez & Johnson, 2004). While a potential effect of compliance could also apply to the 2PDT, it may have a more pronounced impact on orientation discrimination in the GOT due to the larger contact area between the stimuli and the skin. It may also have a greater impact on the 2POT than on the 2PDT because it is applied in both vertical and horizontal orientations, with the latter orientation being shown to be more influenced by compliance than the former (Vega-Bermudez & Johnson, 2004). Therefore, both the instructions and the variability in skin compliance may account for the differences in variability between the tasks.

Overall, instructions, setup and threshold computation matter and could lead to different outcome measures even when efforts are made to maintain consistency across tasks, as was done in this study. In the present study, the 2PDT, conducted in the manner we described, produced the most conservative thresholds without any aberrant values, whether excessively low or negative. The 2PDT and 2POT show similar patterns across fingers (possibly due to the setup), while the 2POT and GOT are the most similar in terms of interindividual variability (potentially due to the instruction).

#### *2POT and GOT thresholds are correlated*

Next, we investigated the correlations between the three tasks and found that only the GOT and 2POT thresholds were correlated for two of the three fingers tested (i.e. the rD2 and ID3). It remains unclear however why this correlation was not observed for the ID2, and the inconclusive BF ( $BF_{10} = 0.60$ ) suggests that the sample size for this finger may have been insufficient to detect such a correlation. The lack of correlation between the GOT and 2PDT



aligns with Bruns et al. (2014), who also found no significant correlation between these tasks, but contrasts with the findings of Härtner et al. (2021) who reported a significant correlation between both tasks. While these two studies used the same methodology for the GOT (manual application and gratings presented in a decreasing order), they used different methodologies for the 2PDT. Indeed, while Bruns et al. (2014) used a device to minimize inter-trial differences in pressure (the same as ours) and presented the distances in a randomized order, Härtner et al. (2021) applied the stimuli manually, in a decreasing order similarly to the GOT. Besides, for both tasks, these studies used different threshold computation methods. Our methods being closer to the ones of Bruns et al. (2014), it is coherent that we found similar correlations, and the discrepancy of both our results with Härtner et al.'s results likely arise from these methodological differences. Since only the two tasks that involve the same orientation component are correlated, we conclude that the similarity in task drives the correlation between tactile acuity tasks.

#### *Tasks thresholds relation with fingertip area*

Exploring the relationship between tactile acuity thresholds and fingertip area, we sought to gain a general understanding of their dependence on mechanoreceptor density. Our results showed that the GOT thresholds obtained on all three fingers correlated with the fingertip area. This is consistent with the findings of Peters et al. (2009) revealing such a correlation of the GOT on the area of the dominant D2 fingertip with a method similar to ours. This effect of fingertip area was attributed to its effect on mechanoreceptor density, as was observed by Peters et al. (2009) through a significant correlation between the area and the sweat pores density (around which Merkel cells are aggregated). Additionally, we found a significant correlation between the fingertip area and the 2POT thresholds obtained at two out of three fingers (rD2 and lD3), though the correlations were weaker than in the GOT. In contrast, the fingertip area did not correlate with the 2PDT thresholds at any finger. This may indicate that the 2PDT is not as much dependent on the mechanoreceptor density as the other two tasks. Alternatively, one possible reason for this difference of correlations across tasks may relate to the skin area stimulated during the task. Since the GOT engages a larger skin area than the other two tasks, it may be more influenced by fingertip area and the density of underlying receptors compared to the other tasks. This may be the reason why the 2POT displays a weaker and less consistent correlation with fingertip area, suggesting it may require greater statistical power to detect any relationship with fingertip area. In the 2PDT, the stimulated area is even smaller, as it is restricted to a single dimension, which would require even greater statistical power to identify

such a correlation. Therefore, an analysis accounting for the two dimensions may clarify these results (see next section).

#### *Tasks thresholds relation with sweat pores density and ridge width*

While in the previous section we investigated the link between thresholds and the fingertip areas as an indicator of overall mechanoreceptor density, in this section we aimed to further disentangle the dependencies related to Merkel cells (represented by sweat pores) and Meissner corpuscles (represented by ridge width). Given that Peters et al. (2009) identified a correlation between fingertip area and sweat pore density, we hypothesized that tactile acuity thresholds would similarly correlate with sweat pore density. Additionally, we explored the relationship with ridge width, as Meissner corpuscles may contribute to tactile acuity as well. However, our analyses found no correlation between any of the thresholds and these measures. While we had strong expectations to find correlations with Merkel cell density, the lack of correlations with Meissner corpuscle density is less surprising as they are considered to be less involved in tactile acuity than Merkel cells (Phillips & Johnson, 1981). The lack of correlation with both these measures separately may indicate that the performance on these tasks may not rely on a single type of mechanoreceptor but rather on the combination and interaction of mechanoreceptors present in the fingertip area (particularly for the GOT and 2POT, which correlated with fingertip area). Alternatively, the lack of correlation may be related to methodological aspects such as a lack of statistical power (as suggested by the inconclusive BFs) or a lack of consistency in measurements (as suggested by the poor ICC<sup>1</sup>).

Besides, we conducted separate analyses of sweat pore distances in the two orientations to account for the different stimulus orientations used in the tasks. However, this analysis revealed no correlation between the horizontal and vertical measurements and the thresholds. Consequently, this finding rules out the possibility of an orientation-specific effect of Merkel cell density which could have been overlooked with a global density measure. Interestingly, we found that the sweat pores distances are significantly larger in the vertical than in the horizontal orientation. This suggests that Merkel cell density may be lower in the vertical orientation, potentially resulting in a lower tactile acuity in this orientation. This is coherent with the findings of Bensmaia et al. (2006) and Phillips & Johnson (1981) in monkeys showing that the spatial details are represented more effectively and the afferent fibers exhibit greater sensitivity when gratings are parallel to the skin ridges (which are horizontal at the human fingertips). This

---

<sup>1</sup> The measures will be retaken by observers with more specific instructions.

may be a combined effect of higher skin compliance (Vega-Bermudez & Johnson, 2004) and the potentially higher density of Merkel cells indicated by our findings in this orientation.

To further investigate whether this anisotropy impacts perception, we explored the performance in the GOT and 2POT in both orientations. Surprisingly, contrary to our expectations based on the lower sweat pore density in the vertical orientation, we observed a higher 2POT performance in this orientation than in the horizontal orientation (See Supplementary figure S2). Showing in the same individuals a lower density in Merkel cells (through sweat pores) and a better 2POT performance in the vertical orientation, our results may be interpreted in two ways. On one side, they may indicate that the 2POT performance is not significantly influenced by Merkel cell density. However, this seems unlikely, considering our previous evidence indicating its dependence on fingertip area. Alternatively, it may illustrate that mechanoreceptor density is not the most determinant factor for tactile acuity. Indeed, beyond the receptor density and RFs spacing, the complex shapes of RFs (exhibiting multiple hotspots) were recently shown to account best for tactile acuity (Pruszynski et al., 2018; Jarocka et al., 2021). Additionally, the dependence of tactile acuity on central mechanisms (e.g., Haag et al., 2015; Härtner et al., 2021) may also weaken its link to peripheral parameters.

In contrast, we found no anisotropy in the GOT performance as both orientations yielded similar results. Showing higher Merkel cell density in one orientation and an anisotropy in the 2POT but not in the GOT, our results suggest that both tasks may not be modulated by Merkel cell density the same. The literature on anisotropy in performance in these tasks is mixed. Coherent with our results, some studies reported a better performance in the vertical orientation for the 2POT (Stevens & Patterson, 1995) and in a grating detection task (Essock et al., 1997), while others reported a better performance in the horizontal direction for the GOT (Vega-Bermudez & Johnson, 2004) and tactile discrimination of gaps (Wheat & Goodwin, 2000). The differences between these findings may be attributable to the potential difference in exact location of testing, as it has been shown that the vertical orientation is the most sensitive at the fingertip while the horizontal orientation is the most sensitive at other parts of the distal phalanx and finger (Gibson & Craig, 2005). Although the difference in location could offer an explanation - though not all of the studies mentioned above report their specific locations - no definitive answer has been reached on this issue, indicating a need for further investigation.

### *Tasks thresholds variation following RSS*

To further compare these three tasks through an interventional approach, we applied RSS to the rD2 and assessed its effect on the thresholds across the tasks on this finger. We found that following RSS, the 2PDT and GOT thresholds were significantly reduced, indicating a better performance on these tasks. This replicates the well-known effect of RSS on the 2PDT (e.g., Godde et al., 1996; Kalisch et al., 2007; Muret et al., 2016, 2024) and the less consistent effect reported on the GOT. Indeed, while some studies observed an improvement following RSS (Hodzic et al., 2004; Kattenstroth et al., 2018; Ross et al., 2022), some others reported no change (Gibson et al., 2009; Rocchi et al., 2017; Timm & Kuehn, 2020). Interestingly, when the effects of RSS on the GOT and 2PDT were investigated in the same participants, only the 2PDT was improved, while the GOT remained unchanged (Timm & Kuehn, 2020). In our study however, the performance in both tasks improved. This discrepancy might be explained by methodological differences between the studies. Indeed, while we kept the same method for computing the thresholds in both tasks (binary logistic regression), they used different methods for both tasks (binary logistic regression for the 2PDT; interpolation for the GOT). Our findings indicate that while RSS enhanced the thresholds in the GOT and 2PDT, it did not have the same effect on the 2POT. This suggests that the GOT and 2PDT may assess a similar aspect of tactile acuity, supposed to rely on changes in RF size (Pleger et al., 2001, 2003), that is not captured by the 2POT. Nevertheless, given the very low thresholds found in the 2POT and the inconclusive BF, a lack of improvement due to a floor effect or to a lack of statistical power cannot be ruled out.

Besides, we also investigated the effects of RSS at other unstimulated fingers and found that following RSS on the rD2, the 2PDT and 2POT thresholds were significantly reduced on the ID3 but unchanged on the ID2. This replicates our recent finding of a transfer of improvement from the stimulated rD2 to the ID3 (Muret et al., 2024). Interestingly, we also found that the GOT threshold was significantly increased on the ID2 but unchanged on the ID3. This is the first result reporting a RSS-induced worsening of tactile acuity on the homologous finger, as the threshold of the ID2 was consistently found stable across studies using the 2PDT and GOT (e.g., Godde et al., 2000; Pleger et al., 2003; Hodzic et al., 2004). Intriguingly, this finger displayed several distinctive characteristics throughout the analyses in this study. Indeed, it has the lowest baseline GOT threshold, and unlike the other fingers, its GOT threshold did not correlate with its 2POT threshold. We hypothesize that its low baseline threshold on the GOT may have allowed for greater potential for impairment compared to the other tasks.

Finally, the 2PDT and 2POT display a pattern of tactile acuity change on the unstimulated fingers that is opposite to the pattern displayed by GOT. This seems to indicate that the 2PDT and 2POT seem to capture a feature of acuity changes that is different from the ones that GOT captures. Additionally, the fact that RSS did not affect the same tasks on the stimulated finger and on the unstimulated finger suggests that mechanisms underlying both effects (local and remote) may be different. Indeed, while substantial evidence in the literature indicates that RF sizes enlarge in the area corresponding to the stimulated finger, we still lack understanding of the mechanisms underlying the remote effects of RSS on the unstimulated fingers. These results may indicate that the local and remote effects of RSS may (at least partly) rely on different mechanisms.

## Conclusion

The present study aimed at assessing similarities and differences between three predominantly used tactile acuity tasks, namely the 2PDT, 2POT and GOT, by comparing their thresholds, investigating their links to anatomical parameters and comparing their modulation by RSS. We conclude that the tasks capture similar aspects of tactile acuity in pairs, with the GOT and 2POT exhibiting comparable interindividual variability and associations with fingertip area, the GOT and 2PDT demonstrating similar sensitivity to RSS at the stimulated finger, and the 2PDT and 2POT showing similar sensitivity to RSS at the unstimulated finger. Considering these similarities and differences among the tasks, we conclude that the aspects measured by each task are not entirely separate but rather partially overlapping. This highlights the complexity of tactile acuity and emphasizes the necessity of employing multiple tasks, maintaining methodological consistency across tasks, to fully capture this complexity.

## References

- Beste, C., & Dinse, H. R. (2013). Learning without training. *Current Biology: CB*, 23(11), R489-499. <https://doi.org/10.1016/j.cub.2013.04.044>
- Bensmaia, S. J., Craig, J. C., Yoshioka, T., & Johnson, K. O. (2006). SA1 and RA Afferent Responses to Static and Vibrating Gratings. *Journal of Neurophysiology*, 95(3), 1771-1782. <https://doi.org/10.1152/jn.00877.2005>
- Bilaloglu, S., Lu, Y., Geller, D., Rizzo, J. R., Aluru, V., Gardner, E. P., & Raghavan, P. (2016). Effect of blocking tactile information from the fingertips on adaptation and execution of grip forces to friction at the grasping surface. *Journal of Neurophysiology*, 115(3), 1122-1131. <https://doi.org/10.1152/jn.00639.2015>
- Bruns, P., Camargo, C. J., Campanella, H., Esteve, J., Dinse, H. R., & Röder, B. (2014). Tactile Acuity Charts : A Reliable Measure of Spatial Acuity. *PLoS ONE*, 9(2), e87384. <https://doi.org/10.1371/journal.pone.0087384>
- Cataldo, A., Frier, W., & Haggard, P. (2023). Quantifying spatial acuity of frequency resolved midair ultrasound vibrotactile stimuli. *Scientific Reports*, 13(1), 21149. <https://doi.org/10.1038/s41598-023-48037-0>
- Cauna, N. (1954). Nature and functions of the papillary ridges of the digital skin. *The Anatomical Record*, 119(4), 449-468. <https://doi.org/10.1002/ar.1091190405>

- Craig, J. C. (1999). Grating orientation as a measure of tactile spatial acuity. *Somatosensory & Motor Research*, 16(3), 197-206. <https://doi.org/10.1080/08990229970456>
- Craig, J. C., & Johnson, K. O. (2000). The Two-Point Threshold : Not a Measure of Tactile Spatial Resolution. *Current Directions in Psychological Science*, 9(1), 29-32. <https://doi.org/10.1111/1467-8721.00054>
- Dienes, Z. (2014). Using Bayes to get the most out of non-significant results. *Frontiers in Psychology*, 5. <https://doi.org/10.3389/fpsyg.2014.00781>
- Dillon, Y. K., Haynes, J., & Henneberg, M. (2001). The relationship of the number of Meissner's corpuscles to dermatoglyphic characters and finger size. *Journal of Anatomy*, 199(5), 577-584. <https://doi.org/10.1046/j.1469-7580.2001.19950577.x>
- Dupin, L., Cuenca, M., Baron, J.-C., Maier, M. A., & Lindberg, P. G. (2022). Shrinking of spatial hand representation but not of objects across the lifespan. *Cortex*, 146, 173-185. <https://doi.org/10.1016/j.cortex.2021.10.009>
- Erro, R., Rocchi, L., Antelmi, E., Palladino, R., Tinazzi, M., Rothwell, J., & Bhatia, K. P. (2016). High frequency repetitive sensory stimulation improves temporal discrimination in healthy subjects. *Clinical Neurophysiology*, 127(1), 817-820. <https://doi.org/10.1016/j.clinph.2015.06.023>
- Essock, E. A., Krebs, W. K., & Prather, J. R. (s. d.). Superior Sensitivity for Tactile Stimuli Oriented Proximally-Distally on the Finger : Implications for Mixed Class 1 and Class 2 Anisotropies.
- Gibson, G. O., & Craig, J. C. (2005). Tactile spatial sensitivity and anisotropy. *Perception & Psychophysics*, 67(6), 1061-1079. <https://doi.org/10.3758/BF03193632>
- Gibson, G. O., Makinson, C. D., & Sathian, K. (2009). Tactile co-activation improves detection of afferent spatial modulation. *Experimental Brain Research*, 194(3), 409-417. <https://doi.org/10.1007/s00221-009-1717-5>
- Godde, B., Spengler, F., Dinse, H. R. (1996). Associative pairing of tactile stimulation induces somatosensory cortical reorganization in rats and humans. *NeuroReport*, 8(1), 281-285.
- Godde, B., Stauffenberg, B., Spengler, F., & Dinse, H. R. (2000). Tactile Coactivation-Induced Changes in Spatial Discrimination Performance. *The Journal of Neuroscience*, 20(4), 1597-1604. <https://doi.org/10.1523/JNEUROSCI.20-04-01597.2000>
- Faul, F., Erdfelder, E., Lang, A.-G., Buchner, A. (2007). G\*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods*, 39, 175-191. <https://doi.org/10.3758/BF03193146>
- French, B., Chiaro, N. V. D., & Holmes, N. P. (2022). Hand posture, but not vision of the hand, affects tactile spatial resolution in the grating orientation discrimination task. *Experimental Brain Research*. <https://doi.org/10.1007/s00221-022-06450-3>
- Haag, L. M., Heba, S., Lenz, M., Glaubitz, B., Höffken, O., Kalisch, T., Puts, N. A., Edden, R. A. E., Tegenthoff, M., Dinse, H., & Schmidt-Wilcke, T. (2015). Resting BOLD fluctuations in the primary somatosensory cortex correlate with tactile acuity. *Cortex*, 64, 20-28. <https://doi.org/10.1016/j.cortex.2014.09.018>
- Härtner, J., Strauss, S., Pfannmöller, J., & Lotze, M. (2021). Tactile acuity of fingertips and hand representation size in human Area 3b and Area 1 of the primary somatosensory cortex. *NeuroImage*, 232, 117912. <https://doi.org/10.1016/j.neuroimage.2021.117912>
- Hayward, V., Terekhov, A. V., Wong, S.-C., Geborek, P., Bengtsson, F., & Jörntell, H. (2014). Spatio-temporal skin strain distributions evoke low variability spike responses in cuneate neurons. *Journal of The Royal Society Interface*, 11(93), 20131015. <https://doi.org/10.1098/rsif.2013.1015>
- Hodzic, A., Veit, R., Karim, A. A., Erb, M., & Godde, B. (2004). Improvement and Decline in Tactile Discrimination Behavior after Cortical Plasticity Induced by Passive Tactile Coactivation. *The Journal of Neuroscience*, 24(2), 442-446. <https://doi.org/10.1523/JNEUROSCI.3731-03.2004>
- Holmes, N. P., & Tamè, L. (2023). Detection, Discrimination & Localization : The Psychophysics of Touch. In N. P. Holmes (Éd.), *Somatosensory Research Methods* (Vol. 196, p. 3-33). Springer US. [https://doi.org/10.1007/978-1-0716-3068-6\\_1](https://doi.org/10.1007/978-1-0716-3068-6_1)
- Jarocka, E., Pruszyński, J. A., & Johansson, R. S. (2021). Human Touch Receptors Are Sensitive to Spatial Details on the Scale of Single Fingerprint Ridges. *The Journal of Neuroscience*, 41(16), 3622-3634. <https://doi.org/10.1523/JNEUROSCI.1716-20.2021>
- Johansson, R. S., & Vallbo, A. B. (1979). Tactile sensibility in the human hand : Relative and absolute densities of four types of mechanoreceptive units in glabrous skin. *The Journal of Physiology*, 286(1), 283-300. <https://doi.org/10.1113/jphysiol.1979.sp012619>

- Johnson, K. O., & Hsiao, S. S. (1992). Tactual form and texture perception. *Annual Review of Neuroscience*, 15, 227-250.
- Johnson, K. O., & Phillips, J. R. (1981). Tactile spatial resolution. I. Two-point discrimination, gap detection, grating resolution, and letter recognition. *Journal of Neurophysiology*, 46(6), 1177-1192. <https://doi.org/10.1152/jn.1981.46.6.1177>
- Johnson, K.O., Van Boven, R.W., & Hsiao, S.S. (1994). The perception of two points is not the spatial resolution threshold. In J. Boivie, P. Hansson, & U. Lindblom (Eds.), *Touch, temperature, and pain in health and disease: Mechanisms and assessments* (pp. 389–404). Seattle, WA: IASP Press
- Kalisch, T., Tegenthoff, M., & Dinse, H. R. (2007). Differential effects of synchronous and asynchronous multifinger coactivation on human tactile performance. *BMC Neuroscience*, 8(1), 58. <https://doi.org/10.1186/1471-2202-8-58>
- Kalisch, T., Tegenthoff, M., & Dinse, H. R. (2010). Repetitive Electric Stimulation Elicits Enduring Improvement of Sensorimotor Performance in Seniors. *Neural Plasticity*, 2010, 1-11. <https://doi.org/10.1155/2010/690531>
- Kattenstroth, J. C., Kalisch, T., Sczesny-Kaiser, M., Greulich, W., Tegenthoff, M., & Dinse, H. R. (2018). Daily repetitive sensory stimulation of the paretic hand for the treatment of sensorimotor deficits in patients with subacute stroke: RESET, a randomized, sham-controlled trial. *BMC Neurology*, 18(1), 2. <https://doi.org/10.1186/s12883-017-1006-z>
- Lundborg, G., & Rosén, B. (2004). The Two-Point Discrimination Test – Time For a Re-Appraisal? *Journal of Hand Surgery*, 29(5), 418-422. <https://doi.org/10.1016/J.JHSB.2004.02.008>
- Muret, D., Daligault, S., Dinse, H. R., Delpuech, C., Mattout, J., Reilly, K. T., & Farnè, A. (2016). Neuromagnetic correlates of adaptive plasticity across the hand-face border in human primary somatosensory cortex. *Journal of Neurophysiology*, 115(4), 2095-2104. <https://doi.org/10.1152/jn.00628.2015>
- Muret, D., & Dinse, H. R. (2018). Tactile learning transfer from the hand to the face but not to the forearm implies a special hand-face relationship. *Scientific Reports*, 8(1), 11752. <https://doi.org/10.1038/s41598-018-30183-5>
- Muret, D., Dinse, H. R., Macchione, S., Urquizar, C., Farnè, A., & Reilly, K. T. (2014). Touch improvement at the hand transfers to the face. *Current Biology*, 24(16), R736-R737. <https://doi.org/10.1016/j.cub.2014.07.021>
- Muret, D., Macchione, S., Dinse, H. R., Koun, E., Salemme, R., Reilly, K., & Farne, A. (2024). Hand to Hand : A novel pattern of remote tactile improvement following training-independent learning. <https://doi.org/10.31234/osf.io/hbsya>
- Oldfield, R. C. (1971). The assessment and analysis of handedness : The Edinburgh inventory. *Neuropsychologia*, 9(1), 97-113
- Pestell, N., Griffith, T., & Lepora, N. F. (2022). Artificial SA-I and RA-I afferents for tactile sensing of ridges and gratings. *Journal of The Royal Society Interface*, 19(189), 20210822. <https://doi.org/10.1098/rsif.2021.082>
- Peters, R. M., Hackeman, E., & Goldreich, D. (2009). Diminutive Digits Discern Delicate Details : Fingertip Size and the Sex Difference in Tactile Spatial Acuity. *The Journal of Neuroscience*, 29(50), 15756-15761. <https://doi.org/10.1523/JNEUROSCI.3684-09.2009>
- Phillips, J. R., & Johnson, K. O. (1981). Tactile spatial resolution. II. Neural representation of Bars, edges, and gratings in monkey primary afferents. *Journal of Neurophysiology*, 46(6), 1192-1203. <https://doi.org/10.1152/jn.1981.46.6.1192>
- Pleger, B., Dinse, H. R., Ragert, P., Schwenkreis, P., Malin, J. P., & Tegenthoff, M. (2001). Shifts in cortical representations predict human discrimination improvement. *Proceedings of the National Academy of Sciences*, 98(21), 12255-12260. <https://doi.org/10.1073/pnas.191176298>
- Pleger, B., Foerster, A.-F., Ragert, P., Dinse, H. R., Schwenkreis, P., Malin, J.-P., Nicolas, V., & Tegenthoff, M. (2003). Functional Imaging of Perceptual Learning in Human Primary and Secondary Somatosensory Cortex. *Neuron*, 40(3), 643-653. [https://doi.org/10.1016/S0896-6273\(03\)00677-9](https://doi.org/10.1016/S0896-6273(03)00677-9)
- Portney L. G. & Watkins M. P. (2009). *Foundations of Clinical Research: Applications to Practice*, Pearson/Prentice Hall, Upper Saddle River, NJ, USA
- Pruszynski, J. A., Flanagan, J. R., & Johansson, R. S. (2018). Fast and accurate edge orientation processing during object manipulation. *eLife*, 7, e31200. <https://doi.org/10.7554/eLife.31200>

- Ragert, P., Kalisch, T., & Dinse, H. (2005). Perceptual changes in human tactile discrimination behavior induced by coactivation using LTP- and LTD-protocols. In H. Zimmermann & K. Kriegelstein (Eds.), *Proceedings of the 6th Meeting and the German Neurobiology Conference* (p. 60B). Göttingen: Thieme.
- Ragert, P., Kalisch, T., Bliem, B., Franzkowiak, S., & Dinse, H. R. (2008). Differential effects of tactile high- and low-frequency stimulation on tactile discrimination in human subjects. *BMC Neuroscience*, *9*(1), 9. <https://doi.org/10.1186/1471-2202-9-9>
- Richardson, B. L., & Wuillemin, D. B. (1981). Different orientations of sub-two-point threshold tactile stimuli can be discriminated. *Bulletin of the Psychonomic Society*, *18*(6), 311-314. <https://doi.org/10.3758/BF03333637>
- Rocchi, L., Erro, R., Antelmi, E., Berardelli, A., Tinazzi, M., Liguori, R., Bhatia, K., & Rothwell, J. (2017). High frequency somatosensory stimulation increases sensori-motor inhibition and leads to perceptual improvement in healthy subjects. *Clinical Neurophysiology*, *128*(6), 1015-1025. <https://doi.org/10.1016/j.clinph.2017.03.046>
- Ross, B., Dobri, S., Jamali, S., & Bartel, L. (2022). Entrainment of somatosensory beta and gamma oscillations accompany improvement in tactile acuity after periodic and aperiodic repetitive sensory stimulation. *International Journal of Psychophysiology*, *177*, 11-26. <https://doi.org/10.1016/j.ijpsycho.2022.04.007>
- Saal, H. P., & Bensmaia, S. J. (2014). Touch is a team effort : Interplay of submodalities in cutaneous sensibility. *Trends in Neurosciences*, *37*(12), 689-697. <https://doi.org/10.1016/j.tins.2014.08.012>
- Sasaki, R., Kojima, S., Otsuru, N., Yokota, H., Saito, K., Shirozu, H., & Onishi, H. (2023). Beta resting-state functional connectivity predicts tactile spatial acuity. *Cerebral Cortex*, *33*(16), 9514-9523. <https://doi.org/10.1093/cercor/bhad221>
- Sathian, K., & Zangaladze, A. (1996). Tactile spatial acuity at the human fingertip and lip : Bilateral symmetry and interdigit variability. *Neurology*, *46*(5), 1464-1464. <https://doi.org/10.1212/WNL.46.5.1464>
- Sathian, K., & Zangaladze, A. (2002). Feeling with the mind's eye : Contribution of visual cortex to tactile perception. *Behavioural Brain Research*, *135*(1-2), 127-132. [https://doi.org/10.1016/S0166-4328\(02\)00141-9](https://doi.org/10.1016/S0166-4328(02)00141-9)
- Schlieper, S., & Dinse, H. R. (2012). Perceptual improvement following repetitive sensory stimulation depends monotonically on stimulation intensity. *Brain Stimulation*, *5*(4), 647-651. <https://doi.org/10.1016/j.brs.2011.07.002>
- Schmidt-Wilcke, T., Wulms, N., Heba, S., Pleger, B., Puts, N. A., Glaubitz, B., Kalisch, T., Tegenthoff, M., & Dinse, H. R. (2018). Structural changes in brain morphology induced by brief periods of repetitive sensory stimulation. *NeuroImage*, *165*, 148-157. <https://doi.org/10.1016/j.neuroimage.2017.10.016>
- Stevens, J. C., & Patterson, M. Q. (1995). Dimensions of Spatial Acuity in the Touch Sense : Changes over the Life Span. *Somatosensory & Motor Research*, *12*(1), 29-47. <https://doi.org/10.3109/08990229509063140>
- Tawney, G. (1895). The perception of two points not the space-threshold. *Psychological Review*, *2*, 585-593.
- Timm, F., & Kuehn, E. (2020). A Mechanical Stimulation Glove to Induce Hebbian Plasticity at the Fingertip. *Frontiers in Human Neuroscience*, *14*, 177. <https://doi.org/10.3389/fnhum.2020.00177>
- Tong, J., Mao, O., & Goldreich, D. (2013). Two-Point Orientation Discrimination Versus the Traditional Two-Point Test for Tactile Spatial Acuity Assessment. *Frontiers in Human Neuroscience*, *7*. <https://doi.org/10.3389/fnhum.2013.00579>
- Tremblay, F., Wong, K., Sanderson, R., & Coté, L. (2003). Tactile spatial acuity in elderly persons : Assessment with grating domes and relationship with manual dexterity. *Somatosensory & Motor Research*, *20*(2), 127-132. <https://doi.org/10.1080/0899022031000105154>
- Valette, R., Gonzalez-Vargas, J., & Dosen, S. (2023). The impact of walking on the perception of multichannel electro tactile stimulation in individuals with lower-limb amputation and able-bodied participants. *Journal of NeuroEngineering and Rehabilitation*, *20*(1), 108. <https://doi.org/10.1186/s12984-023-01234-4>
- Vallbo, A. B., & Johansson, R. S. (1978). The tactile sensory innervation of the glabrous skin of the human hand. In: "Active Touch, the Mechanism of Recognition of Objects by Manipulation", Gordon, G. (ed.), Pergamon Press Ltd. (Oxford), 29-54.
- Van Boven, R. W., & Johnson, K. O. (1994a). A psychophysical study of the mechanisms of sensory recovery following nerve injury in humans. *Brain*, *117*(1), 149-167. <https://doi.org/10.1093/brain/117.1.149>

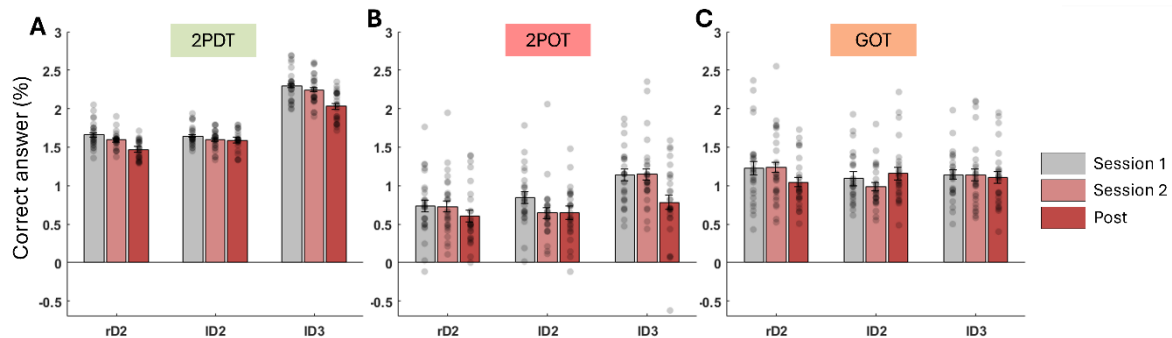


- Van Boven, R. W., & Johnson, K. O. (1994b). The limit of tactile spatial resolution in humans : Grating orientation discrimination at the lip, tongue, and finger. *Neurology*, *44*(12), 2361-2361. <https://doi.org/10.1212/WNL.44.12.2361>
- Van Nes, S. I., Faber, C. G., Hamers, R. M. T. P., Harschnitz, O., Bakkers, M., Hermans, M. C. E., Meijer, R. J., Van Doorn, P. A., Merkies, I. S. J., & on behalf of the PeriNomS Study Group. (2008). Revising two-point discrimination assessment in normal aging and in patients with polyneuropathies. *Journal of Neurology, Neurosurgery & Psychiatry*, *79*(7), 832-834. <https://doi.org/10.1136/jnnp.2007.139220>
- Vega-Bermudez, F., & Johnson, K. O. (2001). Differences in spatial acuity between digits. *Neurology*, *56*(10), 1389-1391. <https://doi.org/10.1212/WNL.56.10.1389>
- Vega-Bermudez, F., & Johnson, K. O. (2004). Fingertip skin conformance accounts, in part, for differences in tactile spatial acuity in young subjects, but not for the decline in spatial acuity with aging. *Perception & Psychophysics*, *66*(1), 60-67. <https://doi.org/10.3758/BF03194861>
- Weber, E. H. (1978). *The Sense of Touch*, Academic Press.
- Wheat, H. E., & Goodwin, A. W. (2000). Tactile Discrimination of Gaps by Slowly Adapting Afferents : Effects of Population Parameters and Anisotropy in the Fingerpad. *Journal of Neurophysiology*, *84*(3), 1430-1444. <https://doi.org/10.1152/jn.2000.84.3.1430>
- Yamada, N., Kashima, Y., & Inoué, T. (1996). Scanning Electron Microscopy of the Basal Surface of the Epidermis of Human Digits. *Cells Tissues Organs*, *155*(4), 242-248. <https://doi.org/10.1159/000147812>

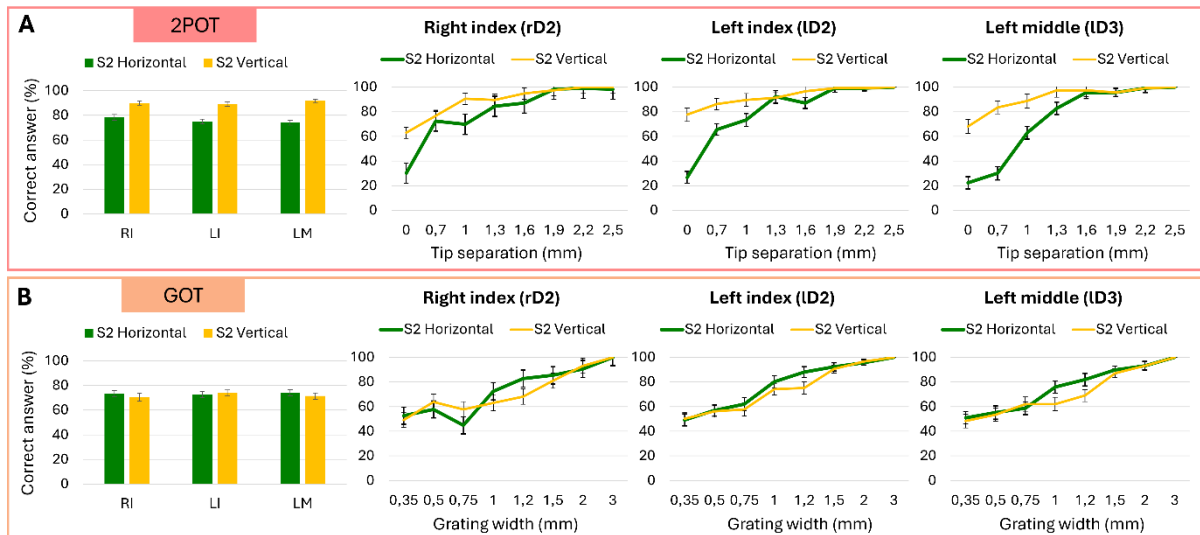
## SUPPLEMENTARY MATERIALS for

# Understanding measures of spatial discrimination: a comparative study of three tactile acuity tasks

Malika Azaroual-Sentucq, Frédéric Volland, Alessandro Farnè & Dollyane Muret



**Supplementary Figure S1. Tactile acuity thresholds in all sessions.** Individual (dots) and average (bars,  $\pm$  SEM) thresholds in the 2PDT (A), 2POT (B), and GOT (C) in the baseline sessions (Session 1 and Session 2) and after RSS (Post). Abnormally low and negative thresholds are visible in the 2POT.



**Supplementary Figure S2. 2POT (A) and GOT (B) performance in the horizontal and vertical orientations.** Left: Average (bars,  $\pm$  SEM) global percentage of correct answer in the horizontal (green) and vertical (yellow) directions regardless of the tip separation and grating width. Right: Average ( $\pm$  SEM) percentage of correct answer in the horizontal (green) and vertical (yellow) directions for each tip separation and grating width at each finger.

## STUDY 3: ELECTROPHYSIOLOGICAL STUDY

### Exploring the intra- and inter-hemispheric inhibitory interactions between fingers' representations

Malika Azaroual-Sentucq<sup>1,2\*</sup>, Luke E. Miller<sup>3</sup>, Eric Koun<sup>1,4</sup>, Romeo Salemme<sup>1,4</sup>,  
Alessandro Farnè<sup>1,2,4#</sup> & Dollyane Muret<sup>5,6#</sup>

<sup>1</sup> Integrative Multisensory Perception Action & Cognition Team of the Lyon Neuroscience Research Center INSERM U1028 CNRS UMR5292 University UCBL Lyon 1, Lyon, France

<sup>2</sup> Université UCBL Lyon 1, Université de Lyon, Lyon, France

<sup>3</sup> Donders Centre for Cognition of Radboud University in Nijmegen, Netherlands

<sup>4</sup> Neuro-Immersion Lab, Lyon, France

<sup>5</sup> Université de Paris, NeuroDiderot, Inserm, Paris, France

<sup>6</sup> Université Paris-Saclay, NeuroSpin-UNIACT, CEA, Gif-sur-Yvette, France

\* corresponding author(s)

# equal contribution

## **Abstract**

Throughout life, our somatosensory system has the ability to adapt to changing tactile environments through experience-dependent plasticity that can be reflected in perceptual changes. Some forms of passive tactile exposure has been repeatedly shown to induce cortical plasticity and enhance tactile performance. Among these, repetitive somatosensory stimulation (RSS) is known to induce Hebbian-like plasticity associated with tactile improvement not only at the stimulated index finger but also at the unstimulated thumb and middle finger of the other hand. But the neural mechanisms of such a pattern of transfer are still unknown. We hypothesized that this transfer could be mediated by the modulation of inhibitory processes between fingers' representations of the same hand (i.e., lateral inhibition) and between hands (i.e., inter-hemispheric inhibition). To test this hypothesis, we leveraged a well-established double stimulation paradigm in electroencephalography (EEG) to assess levels of inhibition between cortical representations of fingers in two sham-controlled double-blind experiments. Preliminary analyses conducted so far did not disclose any significant effect of RSS on either type of inhibition, nor on tactile perception. The lack of replication of the well-established perceptual effect of RSS on the stimulated finger is possibly due to methodological issues and we recommend interpreting these results as preliminary. An additional experiment is planned to address this concern and enable a more definitive conclusion regarding our hypothesis. Nevertheless, this study showed an RSS-unrelated difference in magnitude between lateral and inter-hemispheric inhibition, an increase of inhibition across sessions, as well as a specific pattern of correlations of inhibition between fingers pairs. Overall, although further investigation is needed to conclude on the effects of RSS on lateral and inter-hemispheric inhibition, this study brings some insights about the somatosensory inhibitory interactions between fingers of both hands.

**Keywords:** intracortical inhibition; inter-hemispheric inhibition; tactile learning; somatosensory plasticity; EEG; touch

## Introduction

Touch is one of the most fundamental senses, playing a vital role in human experience and interactions with the external world. Specifically at the hands, tactile acuity is involved in daily activities requiring highly skilled manual dexterity (Tremblay et al., 2003; Pruszynski et al., 2018). Throughout life, our somatosensory system has the ability to adapt to changing tactile environments through experience-dependent somatosensory plasticity that may result in subsequent perceptual changes (Braun et al., 2000; Beste & Dinse, 2013). For example, training monkeys to discriminate frequencies at a finger triggers somatosensory plasticity in the form of an enlargement of its contralateral cortical representation in the primary somatosensory cortex (SI) and a tactile improvement (Recanzone et al., 1992). Similarly to training-dependent plasticity, which requires attention, passive exposure to Hebbian-like tactile stimulations, such as Repetitive Somatosensory Stimulation (RSS), seemingly results in similar cortical and perceptual effects at the stimulated finger (Pleger et al., 2001, 2003; Dinse et al., 2003; Godde, Ehrhardt & Braun, 2003).

Importantly, in both cases, cortical changes and tactile improvement are not limited to the trained or stimulated finger, but they spread to “naive” fingers following topographic, yet almost reversed, patterns. While training-dependent learning transfers to the untrained adjacent fingers within the trained hand and to the homologous finger on the opposite hand (Harris et al., 2001; Harrar et al., 2014), RSS-induced learning transfers to non-homologous fingers of the opposite hand (Muret et al., 2024). Specifically, RSS applied at the right index finger (rD2) improved tactile acuity not only at the stimulated rD2 but also at the left middle finger (lD3) and thumb (lD1), while performance remained unchanged at the adjacent right middle finger (rD3) and thumb (rD1) and at the homologous left index finger (lD2). The differing patterns of improvement across fingers of both hands may reflect different underlying mechanisms. While the pattern of transfer of training-dependent tactile improvement could be dependent on top-down modulation of SI tuning properties (Burton et al., 1999; Iguchi et al., 2005), the attention-independent RSS effects could more likely result from bottom-up processes. Indeed, the cortical and perceptual effects of RSS are believed to result from Hebbian-like potentiation of the neural resources underlying a set of receptive fields spanning the stimulated fingertip area, strengthening their connectivity and temporarily increasing their synaptic efficiency (see Parianen Lesemann et al., 2015; Dinse & Tegenthoff, 2019 for reviews).

As for the transfer of tactile improvement, because Hebbian and homeostatic plasticity are tightly linked (Keck et al., 2017; Turrigiano, 2017), we hypothesized that the local potentiation

induced by RSS may result in homeostatic modulation of inhibitory processes (Keck et al., 2017; Zenke, Gerstner & Ganguli, 2017). More precisely, we advance the hypothesis that RSS may modulate intra-hemispheric lateral inhibition (between the fingers' representations of the same hand; Lipton et al., 2010; Severens et al., 2010) and the inter-hemispheric inhibition (between the fingers' representations of opposite hands; Hoechstetter et al., 2001; Simões et al., 2001). Several models of inhibitory processes modulation may indeed account for the transfer of learning to fingers of the other hand observed after RSS (see Supplementary Figure S1). To detail one of them, the enlarged and potentiated representation of the stimulated rD2 could increase both the lateral inhibition between rD2's representation (rD2-rep) and the representation of its adjacent fingers and the inter-hemispheric inhibition between rD2-rep and the representation of its homologous fingers. This increase in inhibition directed toward rD1-rep, rD3-rep and lD2-rep may prevent these fingers from benefiting from the potentiation of the neural resources underlying rD2-rep and the associated tactile improvement. By enhancing the inter-hemispheric inhibition exerted by rD2-rep on lD2-rep, RSS may in turn reduce lD2-rep's ability to laterally inhibit its neighboring cortical areas, lD1-rep and lD3-rep. Similarly, the strengthened lateral inhibition from rD2-rep towards rD1-rep and rD3-rep may in turn reduce the inter-hemispheric inhibition these areas exert on their homologues, lD1-rep and lD3-rep. These indirect reductions in inhibition could account for the improved tactile perception observed at these fingers. Alternative models of increase and decrease of lateral and inter-hemispheric inhibition could lead to the same pattern of perceptual improvements (Figure S1), involving heterotopic inter-hemispheric inhibitions between representations of non-homologous fingers (Krubitzer et al., 1998; DeCosta-Fortune et al., 2015). For instance, the lD1-rep and lD3-rep receiving less inhibition from the rD2-rep could account for the improved tactile perception at lD1 and lD3. The lD1-rep and lD3-rep could in turn enhance the inhibition they exert on their neighboring lD2-rep, accounting for the lack of improvement on lD2-rep (Figure S1, model D). Thus, if RSS alters the inhibition balance between lD2-rep and lD3-rep, this could explain the pattern of perceptual improvements. Because these models of modulation are equally likely to occur, we do not have specific predictions for each pair of fingers. Overall, we hypothesize that RSS improves tactile perception at the unstimulated lD1 and lD3, by modulating lateral inhibition between rD2 and its neighbors, and/or the inter-hemispheric inhibition between these three fingers (rD1/2/3) and their homologues.

To test this hypothesis, we assessed the effects of RSS applied to rD2 on lateral and inter-hemispheric inhibition between the following four pairs of fingers: rD2-lD2, rD3-lD3, rD2-

rD3, ID2-ID3. Due to methodological constraints, we chose to assess only the D2-D3 pairs, as we do not expect a different outcome for the D2-D1 pairs. We measured the level of inhibition within each pair leveraging a well-established double stimulation paradigm in electroencephalography (EEG), first developed by Gandevia et al. (1983). Stimulating two neighboring fingers simultaneously or individually while recording somatosensory evoked potentials, Gandevia et al. (1983) found that the potential evoked by the simultaneous stimulation was lower in amplitude than the arithmetic sum of the potentials evoked by individual stimulations, revealing the suppressive interaction between the afferent inputs from the two fingers. Since then, this paradigm has been repeatedly used to quantify somatosensory inhibitory process (e.g., Cardini et al., 2011; Arslanova et al., 2020).

We adapted and used this paradigm to assess both lateral and inter-hemispheric inhibition between fingers' representations of both hands. Because this study failed to replicate the well-established perceptual effect of RSS on the stimulated finger, possibly due to methodological issues, we consider these results as preliminary. A follow-up experiment is planned to address these issues and provide a more definitive conclusion regarding the hypothesis.

## **Methods**

### *Participants*

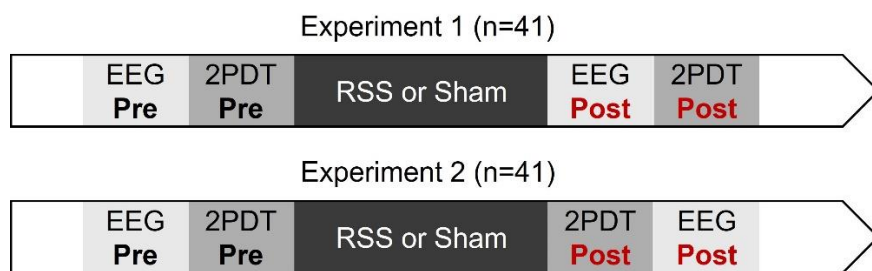
We included 41 healthy adults (33 females; mean age  $\pm$  SD:  $22.4 \pm 2.6$  years) in Experiment 1, and 41 healthy adults (28 females; mean age  $\pm$  SD:  $23.3 \pm 3.4$  years) in Experiment 2. For each Experiment, participants were randomly allocated to an intervention group (Experiment 1: 20 Sham; 21 RSS; Experiment 2: 21 Sham; 20 RSS). The group sample size was determined by a power analysis using G\*Power 3.1 (Faul et al., 2007) based on previous work assessing inhibition between fingers' representations with similar EEG paradigms (Cardini et al., 2011; Arslanova et al., 2020) and on RSS-induced cortical changes in MEG (Muret et al., 2016), although the intervention in Cardini et al. (2011) and the cortical changes measured in Muret et al. (2016) were different from ours. Their effect sizes were between medium (Cohen's  $d = 0.5$ ) and large ( $d = 0.8$ ), their sample sizes ranging from 15 to 21. Our calculation showed that a sample size of 14 to 24 was required to detect a large to medium effect with 80% power using repeated measures ANOVAs.

Participants were right-handed (assessed through the Edinburgh handedness inventory; Oldfield, 1971), without any neurological nor psychiatric disorder, and with no history of injuries at the hands. All participants gave their written informed consent before participating

and received compensation at the end of the study. Procedures were approved by the French ethics committee (CPP SUD EST IV n. ID RCB: 2010-A01180-39).

### *Experimental timeline*

A randomized, double-blind, sham-controlled design was used for both Experiments (Figure 1). In Experiment 1, before (Pre) and after (Post) receiving either the RSS or Sham intervention on the right index finger (rD2), participants underwent EEG and 2PDT assessments. Because we suspected a potential interference of the EEG's electrocutaneous stimulation with RSS effects (measured with 2PDT), the order of the Post tasks was reversed in the Experiment 2, with the participants performing the 2PDT before undergoing the EEG.



**Figure 1. Experimental timeline.** Participants underwent the EEG and the 2-point discrimination task (2PDT) before (Pre) and after (Post) receiving either RSS or Sham intervention on their right index finger (rD2). After the intervention, they either underwent the EEG and the 2PDT in the same order as in the Pre session (Experiment 1), or the converse (Experiment 2).

### *EEG experimental setup*

Electrophysiological recordings were performed following a well-established procedure (Cardini et al., 2011; Arslanova et al., 2020). Participants were seated in front of a computer screen (at a distance of 55 cm), with both hands palm down resting on a foam placed under their wrists, hidden under a wooden box. Electrocutaneous stimuli were delivered by a constant current stimulator (Digitimer DS7A, controlled by Matlab) on their right and left D2 and D3 through ring electrodes (Neurospec) placed on their distal phalanx (cathode 1 cm proximal to the anode). Each stimulation consisted in a square-wave pulse current lasting 0.2 ms and delivered at an intensity 1.4 times higher than the individual's detection threshold (mean intensity  $\pm$  SD Exp1 =  $2.43 \pm 0.89$  mA; Exp2 =  $2.83 \pm 0.78$  mA). D2 and D3 of each hand were separated by foam to prevent contact between the electrodes. The detection threshold was defined as the intensity at which 50% of the stimuli were perceived, and measured through a staircase procedure. The four fingers were stimulated either individually or by pairs according to eight conditions: four conditions of single-finger stimulation (rD2, lD2, rD3, lD3) and four conditions of double-finger synchronous co-stimulation (rD2-lD2, rD3-lD3, rD2-rD3, lD2-lD3), with 450 stimuli per condition. These were delivered in four separate blocks, each



containing 900 stimuli (either 112 or 113 per condition in a randomized order). To prevent habituation, the inter-stimulus intervals (ISIs) varied between 350 and 550 ms (by steps of 50 ms, randomized), for an average of 450 ms between stimuli.

Participants were instructed to maintain gaze at a fixation cross in the middle of the screen. Blinking periods (3 seconds) during which no stimuli were delivered were allowed every 30 trials, and indicated as a change of color of the cross.

#### *EEG data recording and pre-processing*

EEG data was recorded through BrainAMP amplifiers system and BrainVision Recorder software (v. 1.25.0001 2022) using fourteen scalp electrodes (FP1, FP2, C1, C2, C3, C4, C5, C6, CP1, CP2, CP3, CP4, CP5, CP6) according to the 10-20 System. The left and right mastoids were also recorded for offline re-referencing. The reference electrode was AFz and the ground electrode was placed on the nose (right side). Electrode impedances were kept below 30 K $\Omega$ . Horizontal electrooculogram (EOG) was recorded from an electrode placed on the outer canthi of the left eye, and vertical EOG was recorded from an electrode placed below the right eye. The position of seven electrodes (three at each side of the head and the reference) was recorded before the Pre session using a neuronavigation system (Brainsight v. 2.4.11) in order to reposition them exactly at the same position in the Post session. EEG signals were amplified and digitized at 1 KHz.

EEG data pre-processing was performed using EEGLAB v2021.1 (Delorme & Makeig, 2004). Data were re-referenced to the average of the mastoids. Epochs of 350 ms were extracted from the raw EEG data from 150 ms before each stimulus to 200 ms after stimulus onset, and baseline correction was performed using the window from -150 to 0 ms. Data were high-pass filtered at 0.5 Hz and low-pass filtered at 40 Hz. Trials with eyeblinks (any of FP1, FP2, HEOG and VEOG exceeding  $\pm 80$   $\mu$ V) or with voltage exceeding  $\pm 120$   $\mu$ V at any channel between -150 and 200 ms were eliminated. The signal was then visually inspected for additional removal of potential visible artefacts. The mean ( $\pm$ SD) percentage of trials rejected was 2.6 % ( $\pm$  2.2 %) for Experiment 1, and 3.1 % ( $\pm$  3.1 %) for Experiment 2.

#### *EEG data processing*

To extract the somatosensory evoked potential (SEP) for each condition, epochs were averaged across trials and across the appropriate channels. For conditions of individual and double stimulations on the same hand, the epochs were averaged across the sensorimotor channels (C1 to CP6) from the contralateral hemisphere. For double stimulation conditions involving one left

and one right finger, epochs were averaged across all sensorimotor channels from both hemispheres. The amplitude of the P50 component, which was shown to originate from the entry of the signal in the contralateral SI (Hämäläinen et al., 1990), was measured as the maximal signal value in the 30-70 ms window. As pioneered by Gandevia et al. (1983), the suppression between fingers is defined as the difference in amplitude between the arithmetic sum of potentials evoked by two individually stimulated fingers and the potentials evoked by simultaneous stimulation of the two fingers. Using our amplitudes at the P50, the suppression can be computed through a somatosensory suppression index (SSI) following the equation:  $SSI = \text{Finger 1} + \text{Finger 2} - \text{Fingers 1 \& 2 co-stimulated}$ .

The SSI was computed for each of the four fingers pairs, and for each session (Pre and Post).

#### *Interventions (RSS & Sham)*

The intervention protocols consisted in a 3-hour passive mechanical stimulation of the right index finger. A small (8 mm diameter) mini loudspeaker (LSM-S20K, Ekulit) controlled by a mp3 player (Lenco Xemio-240 4GB) was taped to the right index fingertip. In the RSS protocol, this mini loudspeaker delivered brief (10ms) supra threshold tactile stimuli for 3 hours, with ISIs ranging from 100 to 3000ms and following a Poisson distribution (average stimulation frequency of 1Hz). The Sham protocol consisted in 15 minutes of similar tactile stimulation distributed across the 3 hours (i.e., 6 blocks of 2.5 min each). Within each block, the mini loudspeaker delivered tactile stimuli with the same frequency and distribution as during RSS.

#### *Two-point Discrimination Task (2PDT)*

Tactile acuity was assessed on the right and left index (D2) and middle (D3) fingertips through the two-point discrimination task (2PDT) with a well-established procedure (Godde et al., 2000; Muret et al., 2014, 2016). Eight probes were presented on the volar surface of the fingertip: one with a single tip and seven with two tips separated by various distances (D2: 0.7, 1, 1.3, 1.6, 1.9, 2.2 and 2.5 mm; D3: 1, 1.4, 1.8, 2.2, 2.6, 3.2, 4 mm).

After allowing the participant to feel the extreme distances, a familiarization phase was performed in which each probe was tested 4 times in pseudo-randomized order, for a total of 32 trials. Two baseline sessions (S1 & S2) were then performed. In these sessions and in the Post-intervention session, each probe was tested 8 times in pseudo-randomized order, resulting in 64 trials per session. The data of S2 were considered as the Pre-RSS session data. To prevent desensitization of the skin area under assessment due to repeated indentation, short breaks were allowed every 20-30 trials.

Each probe was tested 8 times in pseudo-randomized order, resulting in 64 trials per session. Tips were presented aligned to the longitudinal axis of the finger. Participants were blindfolded and asked to indicate whether they perceived “one” or “two” tips at each trial with the specific instruction of saying “two” only when the tips were clearly distinguishable. They did not receive feedback about their performance and had no time constraint to answer. The 2PDT data were collected through Matlab (MathWorks<sup>®</sup>, version 2015b).

For each participant, the average of the verbal responses (“one” or “two”) was computed and the percentage of “two” responses was plotted as a function of the distance between the probes. The psychometric function was fitted with a binary logistic regression. From these fitted data, the PSE was determined for each session (Pre & Post) and finger (r/ID2, r/ID3).

### *Statistical analysis*

No outliers (data falling outside 3SD around the average per condition) were found in the 2PDT and SSI datasets. After verification of the normality (Shapiro-Wilk test), homoscedasticity (Levene’s test), and sphericity assumptions (Mauchly’s test), repeated-measures ANOVAs (rmANOVAs) were conducted. Both experiments were first analyzed together, with a factor Experiment to account for the difference in the protocol. For the 2PDT thresholds, four-way rmANOVAs with the factors Experiment (Exp1/Exp2), Finger (rD2/ID2/rD3/ID3), Group (Sham/RSS) and Session (Pre/Post) was applied. Because a main effect of Experiment was found, a separate three-way rmANOVA was additionally conducted for each Experiment. For the SSI, four-way rmANOVA with the factors Experiment (Exp1/Exp2), Pair (rD2-rD3/ID2-ID3/rD2-ID2/rD3-ID3), Group (Sham/RSS) and Session (Pre/Post) was used. No main effect or interaction involving the factor Experiment were found. Separate three-way rmANOVAs for the each experiment were also reported for the sake of completeness. For the SSI, additional Pearson’s correlation tests were performed between the Post-Pre changes. When significant main effects or interactions were found, two-tailed t-tests were conducted with alpha levels Bonferroni-corrected for the number of tests performed ( $\alpha_{Bonf}$ ). Effect sizes were computed using Cohen’s d (Cohen, 1988), and based on benchmarks suggested by Cohen, a large effect size was defined as greater than 0.8. Except when specified otherwise, the threshold for statistical significance was set at  $p \leq 0.05$ . Statistical analyses were performed using Jamovi (version 2.2.5).

The 2PDT thresholds obtained in the sessions S1 and S2 (before intervention) were statistically analyzed for stability with a four-way rmANOVA with the factors Experiment (Exp1/Exp2), Finger (rD2/ID2/rD3/ID3), Group (Sham/RSS) and Time (S1/S2). A significant main effect of

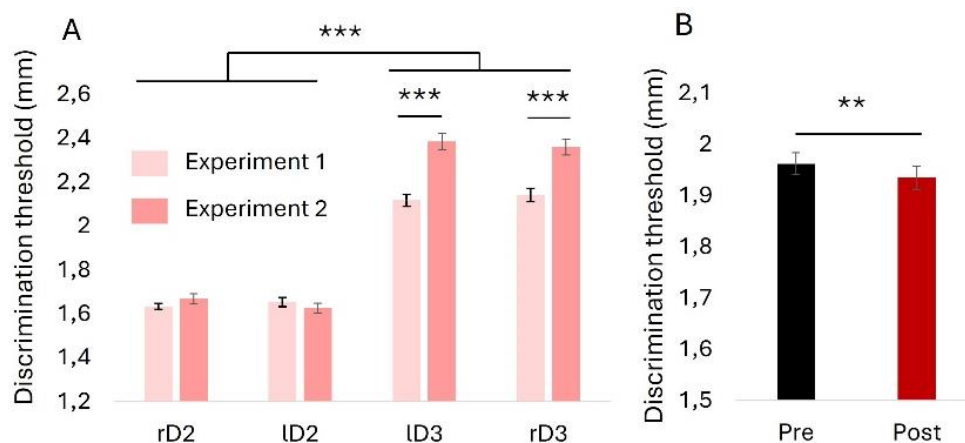
Time ( $F_{(1,78)} = 12.88$ ,  $p < 0.001$ ,  $\eta^2 = 0.002$ ) was found, as well as a significant Time\*Finger interaction ( $F_{(3,234)} = 4.33$ ,  $p = 0.005$ ,  $\eta^2 = 0.001$ ). Post-hoc tests revealed a significant reduction of threshold from S1 to S2 at ID3 ( $t_{(81)} = 3.68$ ,  $p < 0.001$ ,  $\alpha_{\text{Bonf}} = 0.013$ ,  $d = 0.41$ ) and a stable threshold for the three other fingers (all  $t_{(81)} \leq 2.23$ ,  $p \geq 0.029$ ,  $\alpha_{\text{Bonf}} = 0.017$ ,  $d \leq 0.25$ ). Thus, S2 was taken as the baseline performance.

## Results

### *The 2PDT thresholds vary across fingers, sessions and experiments*

The four-way rmANOVA including both experiments revealed a significant main effect of Finger ( $F_{(3,234)} = 377.99$ ,  $p < 0.001$ ,  $\eta^2 = 0.42$ ) arising from higher 2PDT thresholds for D3s than for D2s (all  $t_{(81)} \geq -19.00$ ,  $p < 0.001$ ,  $\alpha_{\text{Bonf}} = 0.008$ ,  $d \leq -2.10$ ; Figure 2A). A significant main effect of Session was also found ( $F_{(1,78)} = 6.77$ ,  $p = 0.011$ ,  $\eta^2 = 0.001$ ) with thresholds being lower after either intervention than before (Figure 2B). Additionally, a main effect of Experiment was revealed ( $F_{(1,78)} = 9.68$ ,  $p = 0.003$ ,  $\eta^2 = 0.08$ ) indicating that the thresholds were lower in the second experiment. The Experiment\*Finger interaction further clarified this effect ( $F_{(3,234)} = 15.54$ ,  $p < 0.001$ ,  $\eta^2 = 0.017$ ) revealing that only the D3s were better in the second experiment (all  $t_{(80)} \leq -3.47$ ,  $p < 0.001$ ,  $\alpha_{\text{Bonf}} = 0.013$ ,  $d \leq -0.77$ ; Figure 2A). Because of this difference across experiments, separate analyses were performed on each experiment.

Similarly to the global analysis, in both experiments, the three-way rmANOVAs revealed a significant main effect of Finger (all  $F_{(3,117)} \geq 19.44$ ,  $p < 0.001$ ,  $\eta^2 \geq 0.57$ ) arising from higher 2PDT thresholds at D3s than at D2s (all  $t_{(40)} \leq -12.48$ ,  $p < 0.001$ ,  $\alpha_{\text{Bonf}} = 0.008$ ,  $d \leq -1.95$ ). Additionally, a significant Finger\*Session interaction ( $F_{(3,117)} = 3.27$ ,  $p = 0.024$ ,  $\eta^2 = 0.003$ ) was found in Experiment 1. However, post-hoc tests revealed no significant difference between sessions within each finger (all  $t_{(40)} \leq 1.95$ ,  $p \geq 0.058$ ,  $\alpha_{\text{Bonf}} = 0.0125$ ,  $d \leq 0.31$ ). In Experiment 2, a main effect of Session was observed ( $F_{(1,39)} = 5.24$ ,  $p = 0.028$ ,  $\eta^2 = 0.002$ ) with lower thresholds after either intervention.

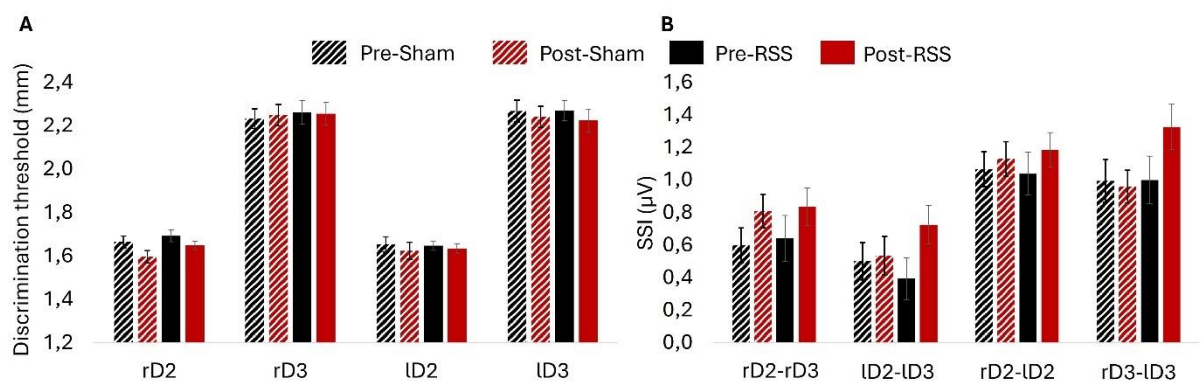


**Figure 2. The 2PDT thresholds vary across fingers, sessions and experiments.** (A) Average ( $\pm$  SEM) 2PDT thresholds on the fingers obtained in Experiment 1 and 2. Data were averaged across groups and sessions (B) Average ( $\pm$  SEM) 2PDT thresholds obtained before (Pre) and after (Post) intervention. Data were averaged across experiments, groups and fingers. \*\*\*  $p < 0.001$  ; \*\*  $p < 0.01$  (paired t-tests for the Finger and Session effect; independent t-tests for the Experiment effect).

*RSS did not affect the 2PDT thresholds and the SSIs*

To further investigate the effect of RSS on the 2PDT thresholds, we explored the above described rmANOVA (Figure 3A). No significant Group\*Session\*Finger ( $F_{(3,234)} = 0.37$ ,  $p = 0.772$ ,  $\eta^2 = 0.00$ ) or Group\*Session ( $F_{(1,78)} = 0.005$ ,  $p = 0.944$ ,  $\eta^2 = 0.00$ ) interactions were found. Similarly, when both studies were analyzed separately, no significant Group\*Session\*Finger (all  $F_{(3,117)} \leq 1.86$ ,  $p \geq 0.146$ ,  $\eta^2 = 0.001$ ) or Group\*Session (all  $F_{(1,39)} \leq 0.21$ ,  $p \leq 0.647$ ,  $\eta^2 = 0.00$ ) interactions were found.

To investigate the effect of RSS on the SSIs, Pre and Post SSIs were compared across pairs of fingers and groups through a four-way rmANOVA including both experiments (Figure 3B). Although not significant, larger SSIs after RSS than after Sham were visible for the ID2-ID3 and rD3-ID3 pairs (Figure 3B). Similarly to the 2PDT results, no significant Group\*Session\*Pair ( $F_{(3,234)} = 0.88$ ,  $p = 0.453$ ,  $\eta^2 = 0.001$ ) or Group\*Session ( $F_{(1,78)} = 1.29$ ,  $p = 0.260$ ,  $\eta^2 = 0.002$ ) interactions were found. Similarly, when both experiments were analyzed separately, no significant Group\*Session\*Pair (all  $F_{(3,117)} \leq 1.46$ ,  $p \leq 0.23$ ,  $\eta^2 \leq 0.007$ ) or Group\*Session (all  $F_{(1,39)} \leq 1.66$ ,  $p \leq 0.21$ ,  $\eta^2 = 0.007$ ) interactions were found.

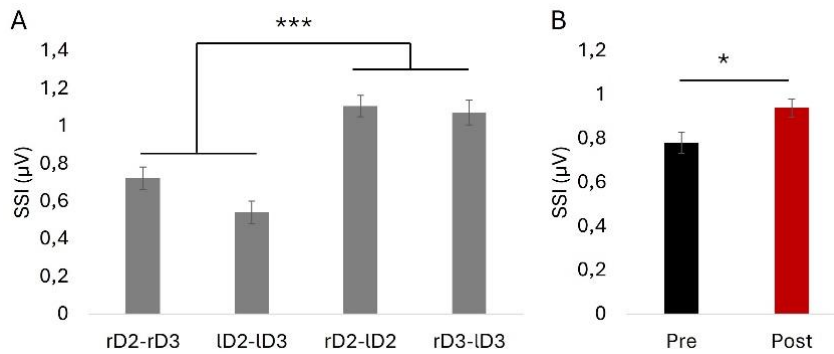


**Figure 3. RSS did not affect the 2PDT thresholds and the SSIs.** (A) Average ( $\pm$  SEM) 2PDT thresholds on the fingers obtained Pre and Post RSS or Sham interventions. (B) Average ( $\pm$  SEM) SSIs obtained in each pair of fingers Pre and Post RSS or Sham interventions.

*The SSI varies across pairs and session*

The four-way rmANOVA including both experiments revealed also a significant main effect of Pair ( $F_{(3,234)} = 31.74$ ,  $p < 0.001$ ,  $\eta^2 = 0.06$ ) arising from higher SSIs between hemispheres (rD2-ID2 and rD3-ID3) than within hemispheres (rD2-rD3 and rD3-ID3); all  $t_{(81)} \leq -5.58$ ,  $p < 0.001$ ,

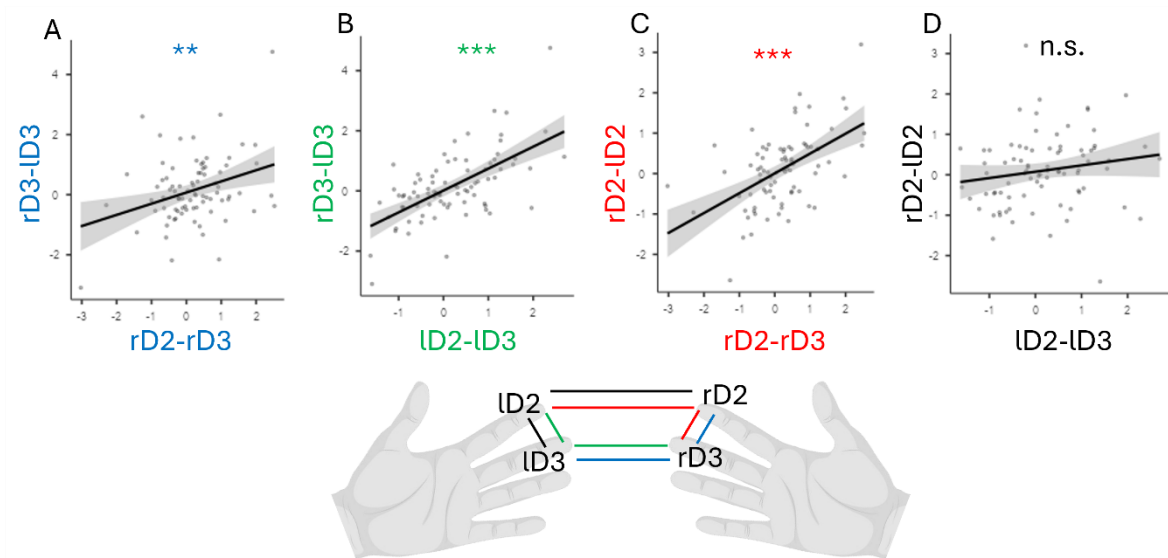
$\alpha_{\text{Bonf}} = 0.008$ ,  $d \geq -0.62$ ; Figure 4A). Besides, a main effect of Session was also observed ( $F_{(3,117)} = 4.04$ ,  $p = 0.048$ ,  $\eta^2 = 0.006$ ), with larger SSIs after either intervention than before (Figure 4B). No main effect or interaction involving the factor Experiment were found (all  $F_{(3,234)} \leq 2.08$ ,  $p \geq 0.104$ ,  $\eta^2 \leq 0.003$ ). Separate analyses on each Experiment revealed similar effects of Pair (both  $F_{(3,117)} \geq 12.74$ ,  $p < 0.001$ ,  $\eta^2 \geq 0.08$ ), while the Session main effect was significant in Experiment 1 ( $F_{(1,39)} = 4.39$ ,  $p = 0.043$ ,  $\eta^2 = 0.02$ ), but not in Experiment 2 ( $F_{(1,39)} = 0.57$ ,  $p = 0.454$ ,  $\eta^2 = 0.003$ ).



**Figure 4. The SSIs vary across fingers pairs and sessions.** (A) Average ( $\pm$  SEM) SSIs within the pairs of fingers. Data were averaged across experiments, groups and sessions (B) Average ( $\pm$  SEM) SSIs obtained before (Pre) and after (Post) intervention. Data were averaged across experiments, groups and pairs of fingers. \*\*\*  $p < 0.001$  ; \*  $p < 0.05$  (paired t-tests).

*SSI Post-Pre changes within pairs involving the rD2 and the ID3 are correlated*

To further explore the seemingly larger SSIs after RSS within the ID2-ID3 and rD3-ID3 pairs, Pearson's correlation tests were conducted between Post-Pre changes in all pairs, with data from both experiments being included. These tests revealed that the SSI Post-Pre change in the ID2-ID3 pair was strongly correlated with the SSI Post-Pre change in the rD3-ID3 pair, both in the Sham ( $r = 0.56$ ,  $p < 0.001$ ,  $\alpha_{\text{Bonf}} = 0.008$ ) and in the RSS ( $r = 0.65$ ,  $p < 0.001$ ,  $\alpha_{\text{Bonf}} = 0.008$ ) groups. Additionally, the SSI change in the rD2-rD3 pair is strongly correlated with the SSI change in the rD2-ID2 pair both in the Sham ( $r = 0.57$ ,  $p < 0.001$ ,  $\alpha_{\text{Bonf}} = 0.008$ ) and RSS ( $r = 0.51$ ,  $p < 0.001$ ,  $\alpha_{\text{Bonf}} = 0.008$ ) groups (Figure 5C). A third correlation, non-significant but trending, was found between the rD2-rD3 and rD3-ID3 pairs ( $r = 0.40$ ,  $p = 0.009$ ,  $\alpha_{\text{Bonf}} = 0.008$ ) in the RSS group and not in the Sham ( $r = 0.24$ ,  $p = 0.138$ ,  $\alpha_{\text{Bonf}} = 0.008$ ). When both groups were included in a same correlation test, this last correlation became significant ( $r = 0.33$ ,  $p = 0.003$ ,  $\alpha_{\text{Bonf}} = 0.008$ ; Figure 5A), along with the first two (all  $r \geq 0.53$ ,  $p < 0.001$ ,  $\alpha_{\text{Bonf}} = 0.008$ ; Figure 5B-C), while the remaining correlations (ID2-ID3 and ID2-rD2; ID2-ID3 and rD2-rD3; rD2-ID2 and rD3-ID3; example in Figure 5D) remained non-significant (all  $r \leq 0.17$ ,  $p \leq 0.127$ ,  $\alpha_{\text{Bonf}} = 0.008$ ).



**Figure 5. The SSI Post-Pre changes within pairs involving the rD2 and ID3 strongly correlate.** Scatterplots of individual SSI changes obtained within the finger pairs, represented two-by-two (from A to D), and regression lines  $\pm$  SD (shaded area). Data are averaged across experiments, groups and sessions. \*\*\*  $p < 0.001$  ; \*\*  $p < 0.01$  (Pearson's correlations,  $\alpha_{\text{Bonf}} = 0.008$ ).

## Discussion

The present study aimed to investigate a candidate physiological mechanism, possibly responsible for the remote tactile improvement observed after RSS (i.e., on left hand fingers), by testing the hypothesis of a modulation of lateral and inter-hemispheric inhibition between the RSS-stimulated finger (right index) and unstimulated ones. After briefly discussing the findings that replicate the known differences in 2PDT thresholds (across fingers and sessions), we will discuss the difference in performance across the experiments. Then, we will turn to discussing the possible reasons for the failure to replicate the well-established local perceptual effect of RSS on this task, highlighting potential methodological issues and advising caution when interpreting these results. On a more solid basis, we will discuss more deeply the RSS-unrelated findings about the SSI, such as the difference in magnitude of intra- and inter-hemispheric inhibition, the increase of inhibition along sessions, as well as the pattern of correlations of inhibition changes between pairs of fingers.

### *The 2PDT thresholds vary across fingers, sessions and individuals*

Showing higher 2PDT thresholds for the middle than for the index fingers, our results replicate previous findings reporting such a difference in tactile acuity between fingers both when measured using the 2PDT (Kalisch et al., 2007) and the grating orientation task (Vega-Bermudez et al., 2001). Besides, our results also showed that the performance on the task

improved in the second session, regardless of the fingers and groups. This is consistent with the known effect of test-retest learning discriminative tasks (e.g., Braun et al., 2000; Dempsey-Jones et al., 2021) and confirms the need for a Sham procedure or a control finger to account for this training effect when investigating the effect of an intervention.

Interestingly, we observed that performance in the second experiment was superior to that in the first. Given that the materials and setup were identical for both experiments, this discrepancy is likely attributable to participants' differences. Indeed, 2PDT performance is known to exhibit interindividual variability, although this variation appears to be less pronounced compared to other tactile acuity tasks (Azaroual-Sentucq et al., unpublished, see Study 2). What is curious however is that this difference in performance was observed only for the middle fingers and not for the index fingers. We speculate this could be due to the higher thresholds leaving more room for inter-individual variability, which we observed in our previous study (i.e., significantly higher variability for ID3 than for D2s; Azaroual-Sentucq et al., unpublished, not mentioned in Study 2).

#### *RSS did not affect tactile acuity or inhibition processes*

Because our experimental design failed to replicate the well-established local improvement in tactile acuity on the stimulated finger (rD2) following RSS, we suggest that either the RSS was ineffective or its effects were hindered or disrupted by the electrocutaneous stimuli used in the EEG sessions. Concerning the first possibility, since the RSS device undergoes regular maintenance and the battery levels are consistently monitored and replaced if necessary before the sessions, it is highly unlikely that the RSS protocol was malfunctioning. A more likely explanation could be that the electrocutaneous stimuli delivered during the EEG interfered with the effects of RSS. Indeed, because they are low frequency ( $\approx 2$  Hz), they can be detrimental to the plasticity and subsequent perceptual effects, even leading to an LTD-like effect (Ragert et al., 2008). Indeed, by applying a 1 Hz twenty-minute stimulation over the index finger, Ragert et al. (2008) even observed an impairment in the 2PDT. A previous study from our group used similarly protracted stimulations coupled with MEG before and after RSS and found smaller than usual -though still significant- RSS-induced improvement in the 2PDT (Muret et al., 2016; this study was used in our sample size calculation). In light of these findings, we hypothesized that the effect of such stimuli could have interfered with two phases: (i) either during the Pre-session of EEG, hindering the induction of RSS-induced plasticity and associated perceptual changes, or (ii) during the Post-session of EEG, possibly cancelling the effect of RSS. To test



each of these hypotheses, one has to either (i) perform EEG recordings at the very end only, after the Post-intervention 2PDT session, or (ii) reverse the order of EEG and 2PDT only in the Post-session. Because the more complete design to test is the second (as it includes Pre- and Post-RSS EEG recordings), we implemented it in our second experiment, but we obtained similar results (lack of perceptual local effect of RSS). The next step is to test the first hypothesis by running a final experiment in which the EEG session will be applied only at the end of the experiment (pre-2PDT, RSS, post-2PDT, EEG) and differences will be analyzed between subjects rather than within subjects.

Overall, because of these potential methodological biases, we believe that the RSS-related results (both on the 2PDT and on the SSI) should be taken with caution and considered preliminary at this stage. The difference between lateral and inter-hemispheric inhibition, the increase of inhibition across sessions, as well as the correlations between SSI changes, which are consistent across experiments, seem quite stable and can thus be considered more confidently.

#### *Inhibition levels vary across type (lateral and inter-hemispheric) and session*

Regardless of session and group, our results revealed a higher level of inhibition (larger SSI) between two fingers on opposite hands than between two fingers within the same hand. To the best of our knowledge, this has not been tested and reported in the literature. Studies using the double stimulation paradigm did not investigate inter-hemispheric inhibition, but essentially assessed inhibition between two fingers of the same hand (Gandevia et al., 1983; Ishibashi et al., 2000) or assessed inhibition between two fingers of both hands but measured the interaction at only one hemisphere (Hoechstetter et al., 2001; Simões et al., 2001). However, since the level of inhibition varies with cortical proximity (Ishibashi et al., 2000), it is likely that the degree of inter-hemispheric inhibition differs significantly from that of lateral inhibition, though it would be expected to be lower. Besides, some studies used the double stimulation paradigm to investigate inter-hemispheric interactions at the behavioral level. Tamè et al. (2011, 2013) observed poorer performance in a tactile detection task (go/no-go task to detect a tactile stimulus delivered to one target finger) when adjacent fingers were stimulated simultaneously, compared to a single stimulation of the target finger or to simultaneous stimulation of homologous fingers. This suggests that inhibitory interaction may have occurred only between adjacent fingers and not between homologous ones.

Our results additionally revealed a higher level of inhibition, both lateral and inter-hemispheric, on the Post-session, regardless of the group. This change of inhibition between the Pre- (performed in the morning) and the Post- (performed in the late afternoon) sessions, may reflect a physiological circadian fluctuation of cortical inhibition. Indeed, the excitatory-inhibitory cortical balance varies along the day (Lang et al., 2011; Chellapa et al., 2016; Bridi et al., 2020).

#### *Inhibition within pairs involving the rD2 and the lD3 are correlated*

We explored the seemingly different SSI post-pre change between pairs through pairs correlations. In both Sham and RSS groups, we observed a strong correlation between pairs involving the right index finger and between those involving the left middle finger. Such correlation was not found to be significant for the other two fingers tested, the pairs involving the lD2 showing no such correlation while the pairs involving the rD3 displayed a trend towards a correlation in the RSS group only. When performing correlation analyses on the whole population (both groups included), the latter correlation between pairs involving the rD3 became significant, but still expressed a lower Pearson's R correlation factor in comparison with the first ones, suggesting a potentially weaker link. The fact that the relationship (here inhibitory) between a finger and its adjacent finger is correlated with its relationship to its homologous finger is not surprising *per se*. Given the preliminary nature of these results, these findings will need to be reevaluated in light of the results from the upcoming experiment.

#### **Overview**

The present study aimed at testing the hypothesis of a modulation of inhibition in SI as the potential neural basis for the transfer of training-independent RSS-induced tactile learning across fingers. No change in inhibition or tactile acuity was found in any finger following RSS application on rD2. Given that this study did not replicate the well-established perceptual effect of RSS on the stimulated finger, possibly due to methodological issues, we recommend interpreting these results as preliminary. An additional experiment is planned to address these concerns and enable a more definitive conclusion regarding the initial hypothesis. Nevertheless, this study showed a RSS-unrelated difference in magnitude between lateral and inter-hemispheric inhibition, an increase of inhibition across sessions, as well as a specific pattern of correlations of inhibition between pairs of fingers. Overall, although further investigation is needed to conclude on the effects of RSS on lateral and inter-hemispheric inhibition, this study brings some insights about the somatosensory inhibitory interactions between fingers of both hands.

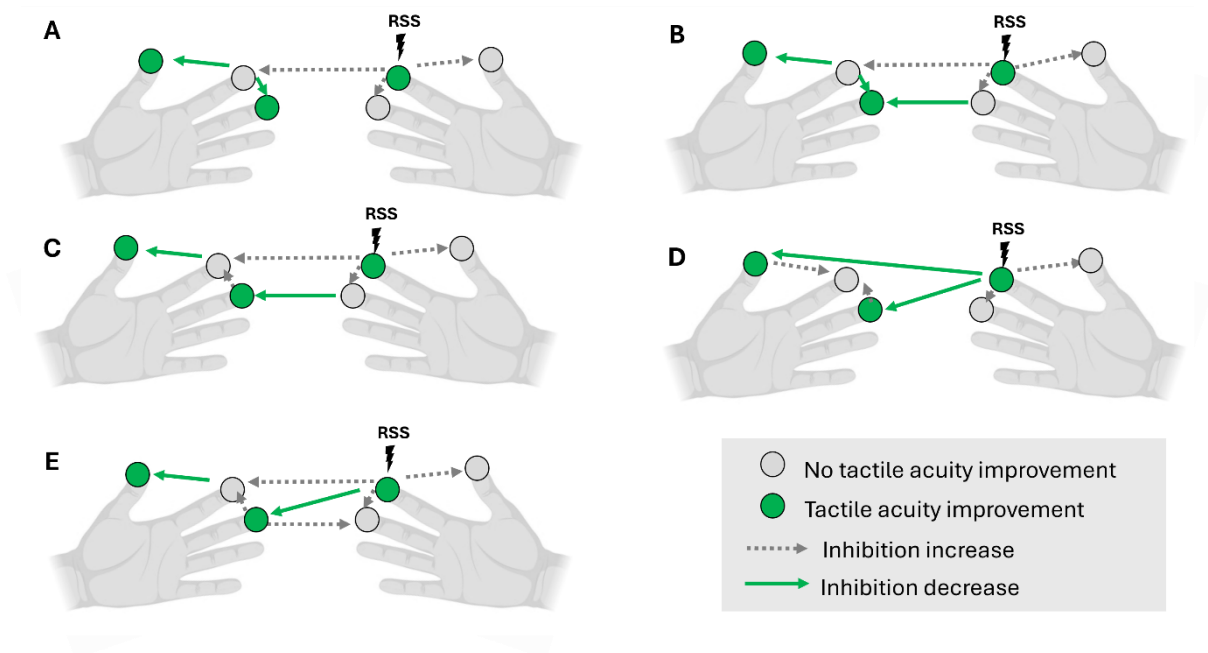
## References

- Beste, C., & Dinse, H. R. (2013). Learning without training. *Current Biology: CB*, 23(11), R489-499. <https://doi.org/10.1016/j.cub.2013.04.044>
- Arslanova, I., Wang, K., Gomi, H. & Haggard, P. (2020): Somatosensory evoked potentials that index lateral inhibition are modulated according to the mode of perceptual processing: comparing or combining multi-digit tactile motion, *Cognitive Neuroscience*. <https://doi.org/10.1080/17588928.2020.1839403>
- Braun, C., Schweizer, R., Elbert, T., Birbaumer, N., & Taub, E. (2000). Differential Activation in Somatosensory Cortex for Different Discrimination Tasks. *The Journal of Neuroscience*, 20(1), 446-450. <https://doi.org/10.1523/JNEUROSCI.20-01-00446.2000>
- Bridi, M. C. D., Zong, F.-J., Min, X., Luo, N., Tran, T., Qiu, J., Severin, D., Zhang, X.-T., Wang, G., Zhu, Z.-J., He, K.-W., & Kirkwood, A. (2020). Daily Oscillation of the Excitation-Inhibition Balance in Visual Cortical Circuits. *Neuron*, 105(4), 621-629.e4. <https://doi.org/10.1016/j.neuron.2019.11.011>
- Cardini, F., Longo, M. R., & Haggard, P. (2011). Vision of the Body Modulates Somatosensory Intracortical Inhibition. *Cerebral Cortex*, 21(9), 2014-2022. <https://doi.org/10.1093/cercor/bhq267>
- Delorme A, Makeig S. 2004. EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *J Neurosci Methods*. 134:9--21
- Dempsey-Jones, H., Stuedte-Schmiedgen, S., Browning, M., Makin, T. R., Woud, M. L., Harmer, C. J., Margraf, J., & Reinecke, A. (2021). Human perceptual learning is delayed by the N-methyl-D-aspartate receptor partial agonist D-cycloserine. *Journal of Psychopharmacology*, 35(3), 253-264. <https://doi.org/10.1177/0269881120986349>
- Dinse, H. R., Ragert, P., Pleger, B., Schwenkreis, P., & Tegenthoff, M. (2003). Pharmacological Modulation of Perceptual Learning and Associated Cortical Reorganization. *Science*, 301(5629), 91-94. <https://doi.org/10.1126/science.1085423>
- Dinse, H. R., & Tegenthoff, M. (2018). Repetitive Sensory Stimulation—A Canonical Approach to Control the Induction of Human Learning at a Behavioral and Neural Level. In *Handbook of Behavioral Neuroscience* (Vol. 28, p. 389-413). Elsevier. <https://doi.org/10.1016/B978-0-12-812028-6.00021-5>
- Gandevia, S. C., Burke, D., & McKeon, B. B. (1983). Convergence in the somatosensory pathway between cutaneous afferents from the index and middle fingers in man. *Experimental Brain Research*, 50-50(2-3). <https://doi.org/10.1007/BF00239208>
- Godde, B., Ehrhardt, J., & Braun, C. (s. d.). *Behavioral significance of input-dependent plasticity of human somatosensory cortex*.
- Harrar, V., Spence, C., & Makin, T. R. (2014). Topographic generalization of tactile perceptual learning. *Journal of Experimental Psychology: Human Perception and Performance*, 40(1), 15-23. <https://doi.org/10.1037/a0033200>
- Harris, J. A., Harris, I. M., & Diamond, M. E. (2001). The Topography of Tactile Learning in Humans. *The Journal of Neuroscience*, 21(3), 1056-1061. <https://doi.org/10.1523/JNEUROSCI.21-03-01056.2001>
- Hoechstetter, K., Rupp, A., Stančák, A., Meinck, H.-M., Stippich, C., Berg, P., & Scherg, M. (2001). Interaction of Tactile Input in the Human Primary and Secondary Somatosensory Cortex—A Magnetoencephalographic Study. *NeuroImage*, 14(3), 759-767. <https://doi.org/10.1006/nimg.2001.0855>
- Ishibashi, H., Tobimatsu, S., Shigeto, H., Morioka, T., Yamamoto, T., & Fukui, M. (2000). Differential interaction of somatosensory inputs in the human primary sensory cortex: A magnetoencephalographic study. *Clinical Neurophysiology*, 111(6), 1095-1102. [https://doi.org/10.1016/S1388-2457\(00\)00266-2](https://doi.org/10.1016/S1388-2457(00)00266-2)
- Kalisch, T., Tegenthoff, M., & Dinse, H. R. (2007). Differential effects of synchronous and asynchronous multifinger coactivation on human tactile performance. *BMC Neuroscience*, 8(1), 58. <https://doi.org/10.1186/1471-2202-8-58>
- Krubitzer, L., Clarey, J. C., Tweedale And, R., & Calford, M. B. (1998). Interhemispheric connections of somatosensory cortex in the flying fox. *The Journal of Comparative Neurology*, 402(4), 538-559. [https://doi.org/10.1002/\(SICI\)1096-9861\(19981228\)402:4<538::AID-CNE7>3.0.CO;2-T](https://doi.org/10.1002/(SICI)1096-9861(19981228)402:4<538::AID-CNE7>3.0.CO;2-T)
- Lang, N., Rothkegel, H., Reiber, H., Hasan, A., Sueske, E., Tergau, F., Ehrenreich, H., Wuttke, W., & Paulus, W. (2011). Circadian Modulation of GABA-Mediated Cortical Inhibition. *Cerebral Cortex*, 21(10), 2299-2306. <https://doi.org/10.1093/cercor/bhr003>

- Lipton, M. L., Liszewski, M. C., O'Connell, M. N., Mills, A., Smiley, J. F., Branch, C. A., Isler, J. R., & Schroeder, C. E. (2010). Interactions within the Hand Representation in Primary Somatosensory Cortex of Primates. *The Journal of Neuroscience*, *30*(47), 15895-15903. <https://doi.org/10.1523/JNEUROSCI.4765-09.2010>
- Muret, D., Daligault, S., Dinse, H. R., Delpuech, C., Mattout, J., Reilly, K. T., & Farnè, A. (2016). Neuromagnetic correlates of adaptive plasticity across the hand-face border in human primary somatosensory cortex. *Journal of Neurophysiology*, *115*(4), 2095-2104. <https://doi.org/10.1152/jn.00628.2015>
- Muret, D., Dinse, H. R., Macchione, S., Urquizar, C., Farnè, A., & Reilly, K. T. (2014). Touch improvement at the hand transfers to the face. *Current Biology*, *24*(16), R736-R737. <https://doi.org/10.1016/j.cub.2014.07.021>
- Muret, D., Macchione, S., Dinse, H. R., Koun, E., Salemme, R., Reilly, K., & Farne, A. (2024). Hand to Hand : A novel pattern of remote tactile improvement following training-independent learning. <https://doi.org/10.31234/osf.io/hbsy>
- Oldfield, R. C. (1971). The assessment and analysis of handedness : The Edinburgh inventory. *Neuropsychologia*, *9*(1), 97-113. [https://doi.org/10.1016/0028-3932\(71\)90067-4](https://doi.org/10.1016/0028-3932(71)90067-4)
- Parianen Lesemann, F. H., Reuter, E.-M., & Godde, B. (2015). Tactile stimulation interventions : Influence of stimulation parameters on sensorimotor behavior and neurophysiological correlates in healthy and clinical samples. *Neuroscience & Biobehavioral Reviews*, *51*, 126-137. <https://doi.org/10.1016/j.neubiorev.2015.01.005>
- Pleger, B., Dinse, H. R., Ragert, P., Schwenkreis, P., Malin, J. P., & Tegenthoff, M. (2001). Shifts in cortical representations predict human discrimination improvement. *Proceedings of the National Academy of Sciences*, *98*(21), 12255-12260. <https://doi.org/10.1073/pnas.191176298>
- Pleger, B., Foerster, A.-F., Ragert, P., Dinse, H. R., Schwenkreis, P., Malin, J.-P., Nicolas, V., & Tegenthoff, M. (2003). Functional Imaging of Perceptual Learning in Human Primary and Secondary Somatosensory Cortex. *Neuron*, *40*(3), 643-653. [https://doi.org/10.1016/S0896-6273\(03\)00677-9](https://doi.org/10.1016/S0896-6273(03)00677-9)
- Pruszynski, J. A., Flanagan, J. R., & Johansson, R. S. (2018). Fast and accurate edge orientation processing during object manipulation. *eLife*, *7*, e31200. <https://doi.org/10.7554/eLife.31200>
- Ragert, P., Kalisch, T., Bliem, B., Franzkowiak, S., & Dinse, H. R. (2008). Differential effects of tactile high- and low-frequency stimulation on tactile discrimination in human subjects. *BMC Neuroscience*, *9*(1), 9. <https://doi.org/10.1186/1471-2202-9-9>
- Recanzone, G. H., Merzenich, M. M., & Jenkins, W. M. (1992). Frequency discrimination training engaging a restricted skin surface results in an emergence of a cutaneous response zone in cortical area 3a. *Journal of Neurophysiology*, *67*(5), 1057-1070. <https://doi.org/10.1152/jn.1992.67.5.1057>
- Severens, M., Farquhar, J., Desain, P., Duysens, J., & Gielen, C. (2010). Transient and steady-state responses to mechanical stimulation of different fingers reveal interactions based on lateral inhibition. *Clinical Neurophysiology*, *121*(12), 2090-2096. <https://doi.org/10.1016/j.clinph.2010.05.016>
- Tremblay, F., Wong, K., Sanderson, R., & Coté, L. (2003). Tactile spatial acuity in elderly persons : Assessment with grating domes and relationship with manual dexterity. *Somatosensory & Motor Research*, *20*(2), 127-132. <https://doi.org/10.1080/0899022031000105154>
- Vega-Bermudez, F., & Johnson, K. O. (2001). Differences in spatial acuity between digits. *Neurology*, *56*(10), 1389-1391. <https://doi.org/10.1212/WNL.56.10.1389>

SUPPLEMENTARY MATERIALS for  
**Exploring the intra and inter-hemispheric inhibitory interactions  
between fingers' representations**

Malika Azaroual-Sentucq, Luke E. Miller, Eric Koun, Romeo Salemme,  
Alessandro Farnè & Dollyane Muret



**Supplementary Figure S1. Hypothetical models of inhibition modulation potentially accounting for the pattern of transfer of RSS-induced tactile learning across fingers.** Models A to E of inhibitory processes modulation may account for the pattern of transfer of learning to fingers of the other hand observed after RSS.

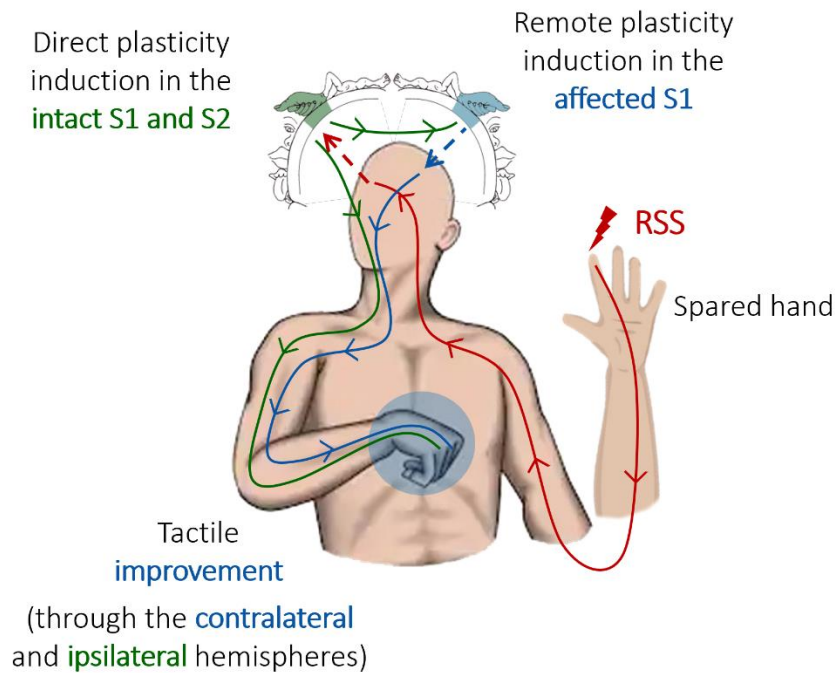
## **STUDY 4: CLINICAL STUDY**

### **Stimulating one hand to improve tactile perception on the other in stroke patients**

While this last study is not directly part of my thesis, I helped developing it and I piloted it during my PhD work, and I just began collecting data on one patient. This section provides a concise overview of the project.

Stroke is a prevalent and drastically life-changing neurological condition leading to severe functional consequences affecting mainly the upper limbs (Kessner et al., 2016). One of the most disabling outcomes of a stroke is the loss of touch and more precisely tactile acuity, where patients struggle to perceive fine tactile stimuli through their fingers. Because tactile acuity is crucial for manual dexterity, these deficits dramatically impact motor performance and hinder motor rehabilitation (Celnik et al., 2007). Currently, there are only a limited number of effective rehabilitation strategies available to address the somatosensory deficits following stroke. One of these strategies involves applying RSS to the affected finger to enhance its tactile acuity by inducing plasticity in the somatosensory cortex (Smith et al., 2009; Kattenstroth et al., 2018).

However, since the hemisphere contralateral to the affected hand is lesioned, rehabilitating this hand through plasticity induction in the damaged hemisphere may prove to be less effective than directly engaging the intact hemisphere. For this reason, a potentially interesting strategy could be to target and induce direct plasticity in the intact hemisphere through RSS application at the intact hand, leveraging the recently discovered remote effect of RSS (Muret et al., 2024). Engaging directly this intact hemisphere offers an additional advantage, as this hemisphere has been shown to play a role in the recovery of tactile function. In fact, the recovery of touch was found to be associated with inter-hemispheric functional connectivity between areas of the somatosensory cortex (Bannister et al., 2015). By applying RSS on the intact hand, we aim to improve tactile perception of the affected hand through both ipsilateral (intact) and contralateral (lesioned) hemispheres (Figure 1). The main hypothesis of this study is that the application of electrocutaneous RSS on the index finger of the spared hand improves tactile perception of fingers on the affected hand (especially the thumb and middle finger).



**Figure 1. Illustration of our strategy of applying RSS on the spared hand to improve tactile perception on the affected hand.**

To test this hypothesis, we are conducting a randomized sham-controlled double-blind study in which tactile acuity, absolute tactile detection, and manual dexterity are assessed on index and middle fingers of both hands before and after the administration of RSS/Sham on the intact index finger of stroke patients. The recruitment of patients is currently ongoing.

## References

- Bannister, L. C., Crewther, S. G., Gavrilescu, M., & Carey, L. M. (2015). Improvement in Touch Sensation after Stroke is Associated with Resting Functional Connectivity Changes. *Frontiers in Neurology*, 6. <https://doi.org/10.3389/fneur.2015.00165>
- Celnik, P., Hummel, F., Harris-Love, M., Wolk, R., & Cohen, L. G. (2007). Somatosensory Stimulation Enhances the Effects of Training Functional Hand Tasks in Patients With Chronic Stroke. *Archives of Physical Medicine and Rehabilitation*, 88(11), 1369-1376. <https://doi.org/10.1016/j.apmr.2007.08.001>
- Kattenstroth, J. C., Kalisch, T., Sczesny-Kaiser, M., Greulich, W., Tegenthoff, M., & Dinse, H. R. (2018). Daily repetitive sensory stimulation of the paretic hand for the treatment of sensorimotor deficits in patients with subacute stroke: RESET, a randomized, sham-controlled trial. *BMC Neurology*, 18(1), 2. <https://doi.org/10.1186/s12883-017-1006-z>
- Kessner, S. S., Bingel, U., & Thomalla, G. (2016). Somatosensory deficits after stroke : A scoping review. *Topics in Stroke Rehabilitation*, 23(2), 136-146. <https://doi.org/10.1080/10749357.2015.1116822>
- Muret, D., Silvia, M., Dinse, H. R., Koun, E., Salemme, R., Reilly, K., & Farne, A. (2024). Hand to Hand : A novel pattern of remote tactile improvement following training-independent learning. *BioRxiv*. <https://doi.org/10.31234/osf.io/hbsya>
- Smith, P. S., Dinse, H. R., Kalisch, T., Johnson, M., & Walker-Batson, D. (2009). Effects of Repetitive Electrical Stimulation to Treat Sensory Loss in Persons Poststroke. *Archives of Physical Medicine and Rehabilitation*, 90(12), 2108-2111. <https://doi.org/10.1016/j.apmr.2009.07.017>

## GENERAL DISCUSSION

In this thesis, I addressed theoretical questions regarding mental body representations (MBRs) and tactile acuity, using RSS to induce somatosensory plasticity. Additionally, I explored the mechanisms underlying the remote effects of RSS through electroencephalography (EEG).

In addition to addressing these main research aims, this work uncovered several noteworthy findings. Study 1 revealed a novel pattern of tactile localization bias on the finger and showed that training-independent tactile learning can extend to higher-level cognitive MBRs. Study 2 confirmed the remote effects of RSS on 2PDT using an electrocutaneous version of RSS. This study additionally reported different patterns of improvement across fingers and tasks, bringing important implications regarding the mechanisms underlying local and remote effects of RSS. These findings will be discussed after the main results in the next sections.

### **I- How do somatosensory inputs feed MBRs?**

While somatosensory processes are known to contribute to the building and maintenance of MBRs, whether different MBRs are equally - or differentially - influenced by tactile inputs through SI remains unknown. In my first study, we addressed this question by testing the following hypothesis: if MBRs are equally fed by somatosensory inputs despite their respective differential roles, then altering this input would similarly affect them. Alternatively, we should observe a non-uniform impact across different MBRs. To this aim, we investigated the impact of RSS applied to the right index finger on the body image, body model, and superficial schema associated with this finger. The results indicated that RSS had a specific effect on the body image, as evidenced by a decrease in the perceived size of the finger, but did not alter the body model and the superficial schema.

The selective impact on the body image, as opposed to the body model and superficial schema, aligns with studies on patients who exhibit a selective disruption in the body image without any change to their body model (Augière et al., 2024) or superficial schema (Mergen et al., 2018). In a population of patients suffering from fibromyalgia, the body image -as assessed through drawings of the whole body- was observed to be altered, while the body model -as assessed through tactile distance judgement- was found to be preserved, compared to healthy controls (Augière et al., 2024). Similarly, patients suffering from anorexia nervosa, which are known to have body image disturbance (e.g., Keizer et al., 2012; Risso et al., 2020; but not tested in Mergen et al.'s study) displayed preserved superficial schema -as assessed through tactile



localization- compared to healthy controls (Mergen et al., 2018). Although this does not indicate that the alteration of body image stems from an alteration of low-level somatosensory processes, this indicates that the body image can be selectively affected by a condition.

In our study, showing that RSS selectively altered the body image, the findings suggest that this MBR would have a different functional connection to SI, as compared to the other two MBRs. In light of this finding, we propose an updated model that revises the initial conception of the SI-MBR relationship, transforming it from a single common link into one that includes at least two distinct links: one specific to the body image and another that may equally connect the body model and superficial schema. The way SI exerts its modulatory effects differently on MBRs may depend on three possible scenarios.

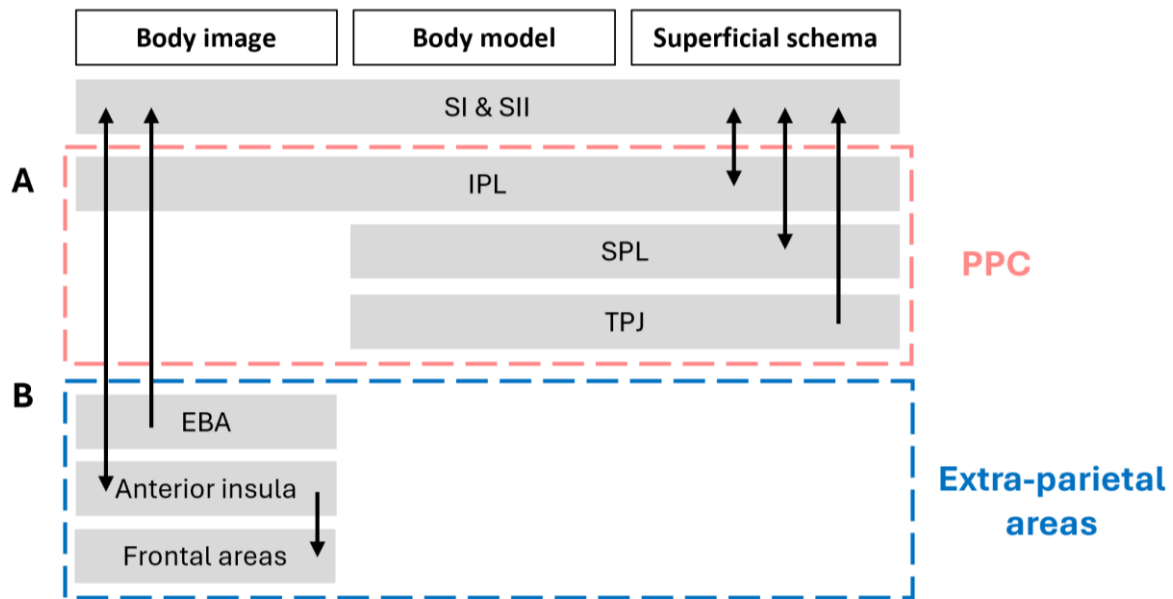
A first possibility is that the body image may be more vulnerable to tactile manipulations than the other two MBRs. This may reflect either (i) the relative “immunity” of the other two MBRs to changes in tactile inputs; or (ii) their higher susceptibility to sensory correction (i.e. the altered tactile information could be compensated for by the intact proprioceptive and visual information). Regarding the susceptibility of the body model and superficial schema to changes in tactile inputs, to the best of our knowledge, only two studies investigated the effect of a disruption of SI on tactile localization (superficial schema), but no study investigated its effect on the body model. After TMS application over SI, Seyal et al. (1997) reported an impaired localization performance in a task requiring to identify the finger receiving an electric shock among two fingers. In contrast, a more recent study using the same task showed reduced but still above-chance level tactile localization performances following TMS application over SI (Ro & Koenig, 2021). While the tasks used in these two studies may involve the superficial schema, their comparability to our tactile localization task requiring to localize touch within a finger is limited. As for the possibility of a higher susceptibility to sensory correction, it is known that these MBRs are multisensory, built and maintained from tactile, proprioceptive, visual and auditory information (Bremner et al., 2012; Azañón et al., 2016). Additionally, a change in visual (Taylor-Clarke et al., 2004), proprioceptive (De Vignemont et al., 2005) or auditory (Tajadura-Jimenez et al., 2012) inputs has been shown to alter the body model, further emphasizing its reliance on these modalities (see Chapter II. Section II.3. for details about these studies). However, the relative influence of inputs from these modalities in shaping and maintaining these two MBRs is still unclear and deserves further investigation.

Another possibility is that RSS affects differently the distinct subregions of the PPC which potentially support the body image and the other MBRs. Indeed, while there is no definitive

consensus about the specific subregions of the PPC housing these MBRs, there is some evidence supporting that the SPL and TPJ (Van Boven et al., 2005; Spitoni et al., 2010) would house specifically spatial body representations (from the model of De Haan & Dijkerman, 2020) corresponding to the body model and superficial schema in the nomenclature adopted in this thesis, while the IPL would contribute to all three MBRs (De Haan & Dijkerman, 2020; see Chapter II, section II.2., Figure 10). In this view, RSS may have affected only the IPL, but not the SPL and TPJ, and we speculate that the intact information from both these unaffected areas could have “corrected” the potential effect of input change in the IPL on the body model and superficial schema (Figure 18A).

A third possibility is that the effects of RSS may spread to extra-parietal cortical areas that are exclusively involved in the body image. While no evidence of an involvement of extra-parietal areas were reported for the body model and the superficial schema, the body image may indeed rely on cortical areas beyond the PPC, such as the extrastriate body area in the occipital lobe (Moayedi et al., 2021; Hamamoto et al., 2023), the anterior insula (Hamamoto et al., 2023) and other areas in the frontal lobe (Mohr et al., 2010, 2011). As for the extent of the effects of RSS, the enlargement of RFs and cortical representations were predominantly reported in SI and SII as they were investigated specifically in these areas (e.g., Pleger et al., 2001, 2003; Hodzic et al., 2004; Muret et al., 2016). However, studies reported that RSS reduced inherent functional connectivity in the left insular cortex (Heba et al., 2017) and that the amount of RSS-induced tactile improvement (2PDT) was potentially correlated (trend) with a decrease in the gray matter volume in the insular cortex (Schmidt-Wilcke et al., 2018). Taken together, this suggests that RSS-induced plasticity in SI may have influenced the body image potentially through changes in the insular cortex (Figure 18B).

Future research will be needed to explore these possibilities in detail using both behavioral and neuroimaging approaches.



**Figure 18. Cortical areas thought to be involved in the body image, body model and superficial schema.** Besides relying on the primary (SI) and secondary (SII) somatosensory cortices, the three MBRs rely on the posterior parietal cortex (PPC; A) specifically on the inferior parietal lobule (IPL). Moreover the body model and superficial schema further rely on the superior parietal lobule (SPL) and the temporoparietal junction (TPJ), while only the body image seem to rely on extra-parietal areas such as the extrastriate body area (EBA), the anterior insula, and frontal areas (B). The arrows represent anatomical connections between areas (taken from De Haan & Dijkerman, 2020).

## II- Training-independent tactile learning spreads to high-level cognitive MBRs

Since the development of RSS, its perceptual effects were mainly investigated at the perceptual level, through tactile spatial and temporal discrimination tasks (e.g., Godde et al., 2000; Reuter et al., 2014), as well as tactile absolute detection tasks (e.g., Kalisch et al., 2007; Kowalewski et al., 2012), but until recently not at the cognitive level. Indeed, the most recent study using RSS investigated its effects on the body image (Mora et al., 2024). The authors showed that 20 minutes of mechanical high-frequency RSS (> 10 Hz) applied synchronously at twelve locations on the hand induced a reduction in the perceived size of the hand, suggesting an alteration of the body image. In contrast to their study, we applied three hours of RSS at a lower frequency (average 1 Hz over the three hours, up to 10 Hz), only at the right index fingertip. Our template matching task also differed from theirs in the experimental setup, order of presentation of distorted pictures, and threshold computation. Despite these methodological differences, we found similar effects of reduced perceived size of the stimulated body part, indicating that the effect of RSS on body image may be robust and strictly dependent on the stimulated body part. It implies a strong selectivity/independence in the way the different body

parts are represented in the body image. This may pave the way for more targeted rehabilitation of body image disturbances, allowing focused stimulation where needed.

This is the first result, along with ours (manuscript under revision), to reveal that a passive training-independent tactile stimulation induces changes in MBRs. This holds therapeutic potential, as it may help addressing body image disturbances, particularly in individuals who overestimate the size of their body (e.g., anorexia nervosa or bulimia). Investigating the effects of RSS on these clinical populations could serve as a proof of concept leading to the development of passive protocols for treating body image distortions.

Furthermore, given that the low-level perceptual effects of RSS are known to extend to unstimulated body parts (such as the other hand and face; Muret et al., 2014, 2016, 2024), and given the present finding that RSS also influences the body image, a compelling direction for future research would be to explore whether body image plasticity similarly transfers to the other hand and face. Indeed, while no definitive evidence of such transfer of training-independent MBR plasticity has been described, some cases of transfer of tool use-dependent MBR plasticity were reported. Trained baseball players repeatedly using a baseball glove were found to exhibit a shrunk body model at both the trained and the untrained hand, suggesting a transfer of MBR plasticity (Coelho et al., 2019). Similarly, a transfer of tool-use induced change in body schema to untrained body part has been observed after repeatedly using a cane (Sun & Tang, 2019). In contrast, no such transfer of body model change was found after a repeated use of a hand-shaped tool from the hand to the cheek (Miller et al., 2017). This suggests that plastic changes in some but not all MBRs may transfer to some but not all body parts.

In this direction, Mora et al. (2024) investigated such a possibility and found no transfer of changes in size perception to either the face or the other hand after RSS on the hand. However, the RSS protocol used in their study was applied to the whole hand while so far, the transfer of training-independent learning was found to follow a specific topographic pattern. Indeed, stimulating the whole hand through RSS did not lead to a transfer of tactile learning to the other hand (e.g., Kattenstroth et al., 2018), while stimulating only one finger led to such a transfer to specific fingers of the other hand (Muret et al., 2024). This may be explained by the fact that applying RSS to a limited skin area likely engages different mechanisms than applying it to multiple regions (i.e., temporal pairing). While the former alters local tactile processing through Hebbian-like plasticity, the latter alters tactile synergy and the likelihood of coactivation between the stimulated skin regions. Evidence supporting the distinct mechanisms of RSS and temporal pairing comes from the differential perceptual effects of synchronous versus

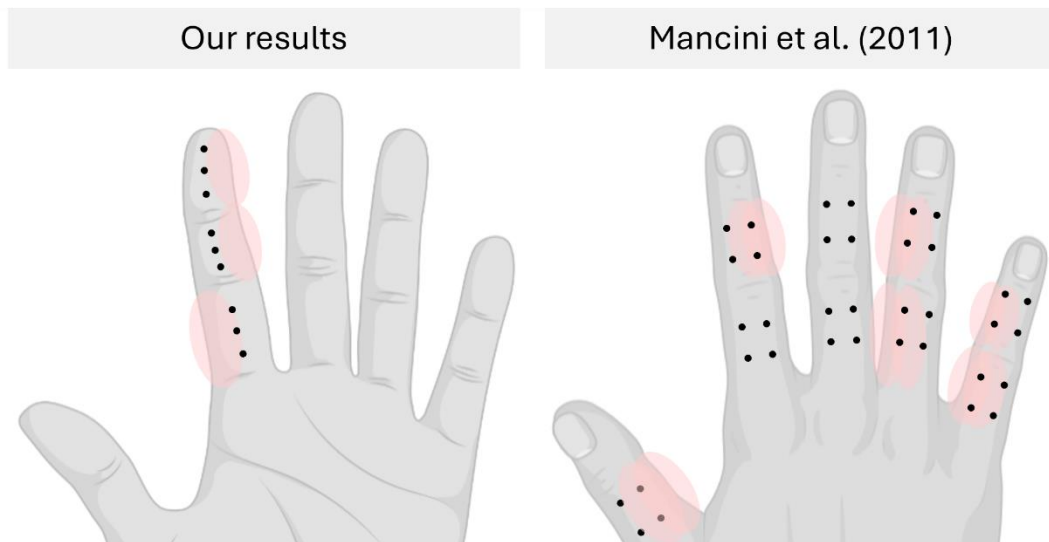
asynchronous RSS application across fingers (Kalisch et al., 2007; see Chapter IV, section II.2. for details). Therefore, in Mora et al. (2024)'s study, both RSS and pairing mechanisms might have interacted with one another. Consequently, it is plausible that stimulating one finger may result in a transfer of changes in size perception (body image) at fingers of the other hand or at the face, despite the absence of such effects following stimulation of the entire hand. This question deserves further investigation.

### **III- A novel pattern of tactile localization bias at the finger**

The superficial schema of the hand has been repeatedly shown to be distorted, as revealed through tactile localization tasks (Mancini et al., 2011; Margolis & Longo, 2015; Medina & Duckett, 2017; Kang & Longo, 2023). While many reports in the literature investigated tactile localization at the whole hand, either at the back of the hand (Margolis & Longo, 2015; Kang & Longo, 2023) or at the dorsal surface of fingers with two points to localize per finger (Dupin et al., 2022), very few studies investigated tactile localization at the scale of one finger with several points to localize (Mancini et al., 2011; Miller et al., 2022). At the scale of the hand, localization biases towards the tips (distal bias) and thumb (radial bias) were reported on the hand dorsum (Mancini et al., 2011). It is however unknown if similar distortions would be found on the hand palmar surface of fingers.

Indeed, it is possible that palmar and dorsal surfaces do not exhibit the same distortions, as it is the case for the body model, assessed through landmark localization tasks, showing a reduced perceived length of fingers when assessed on the dorsal, but not the palmar surface (Longo & Haggard, 2012). In the same study, the authors noted that the perceived width of the hand was increased on both the dorsal and palmar surfaces, although the effect was less pronounced on the palmar side (Longo & Haggard, 2012). In our study, when using a tactile localization task on the palmar surface of the index finger at all three phalanges, we found a proximal bias on the distal and middle phalanges but no proximo-distal bias on the proximal phalanx. As for the radio-ulnar direction of bias, we found an ulnar bias on the distal and middle phalanges, but a radial bias on the thumb. These findings might originate from a bias towards adjacent fingers, where informative tactile (co)stimulation is more likely to occur in everyday activities due to postural and finger movement synergies. In a typical hands shape and posture, the proximal phalanx of the index finger may indeed be more likely to make contact with both the middle finger and the thumb, while the other two phalanges may preferentially contact the middle finger. Therefore, this newly reported mislocalization pattern raises new questions about how tactile “synergies” may contribute to the distortions observed in the superficial schema.

We know from monkey studies that fusing the skin of two adjacent fingers through surgery induces an extension of some RFs across the limit between the two fingers because of the induced synchronous co-stimulation patterns between these fingers (Clark et al., 1988; Allard et al., 1991). Comparable observations were reported in humans with webbed fingers who displayed non-somatotopic hand cortical representations (Mogilner et al., 1993). Weeks after surgical separation of their fingers, their finger representations underwent reorganization correlating with the new functional status of their separated digits (Mogilner et al., 1993). Similar reorganization of finger cortical representations was also reported after temporarily webbing fingers by using gloves (Stavrinou et al., 2007). Besides these specific cases, studies in healthy population reported the presence of shared RFs across adjacent fingers (Iwamura, 2000; Trczinski et al., 2023) and more frequent localization errors towards adjacent fingers than towards non-adjacent fingers (Schweizer et al., 2000). Completing these findings, our results on the index finger tend to indicate that differential localization bias patterns can be seen within a finger, with the proximal phalanx displaying a radial bias while the other two phalanges displayed an ulnar bias. To test the hypothesis of an effect of tactile co-stimulation on tactile localization bias, one could investigate the tactile localization pattern on the palmar surface of all fingers. If this hypothesis is confirmed, the middle finger should exhibit no mislocalization bias along the ulnar-radial (radio-ulnar) axis, whereas the thumb and little finger should display a radial bias and an ulnar bias respectively. One study investigated tactile localization biases on the dorsal surface of proximal and middle phalanges of all fingers and found that both phalanges of little and ring fingers exhibited radial bias while the thumb and the middle phalanx of the index finger exhibited an ulnar bias (Mancini et al., 2011; Figure 19). Though these results obtained on the dorsal hairy surface of the fingers may not be completely comparable to the palmar glabrous surface, they can be seen as supporting our hypothesis (Figure 19).



**Figure 19. Schematic representation of our localization bias pattern on the palmar surface across phalanges of the index finger (left) and of mislocalization pattern on the dorsal surface of fingers (right).** We observed a radial bias on the proximal phalanx and an ulnar bias on the other two phalanges. Using a similar tactile localization task on the dorsal surface, Mancini et al. (2011) reported a radial bias on the thumb and middle phalanx of the index finger and an ulnar bias on the ring and little finger (tactile localization on distal phalanges was not investigated). Black dots represent the applied stimuli, and light pink ovals represent the directions towards which touch was mislocalized.

#### **IV- Do 2PDT, 2POT and GOT similarly measure tactile acuity?**

Although tactile acuity tasks are commonly used, there is limited understanding of the specific features that contribute to this acuity and the relationships between these tasks. In my second study, we assessed similarities and differences between the two-point discrimination (2PDT), the two-point orientation (2POT) and the grating orientation (GOT) tasks in order to establish whether they capture similar aspects of tactile acuity and whether they are similarly sensitive measures.

Comparing the performance in these three tasks and investigating their relation to anatomical measures at the fingertips, we found that the most similar tasks are the GOT and 2POT as their thresholds correlated, displayed the same interindividual variability, and depended on the fingertip area. In this respect, they are likely to measure similar, possibly the same, aspects of tactile acuity, which is most likely linked to their shared orientation aspect (Figure 20). Regarding the fingertip area, the lack of correlation with the 2PDT suggests that this task may be less reliant on mechanoreceptor density compared to the other two tasks. This could be possible since tactile acuity is determined not only by mechanoreceptor density, but also by the complex shape of RFs (Pruszynski et al., 2018) and spike timing coding (Foffani et al., 2008), as discussed in the introductory Chapter II (section I.3.). Alternatively, another potential

explanation for the differences in correlations between tasks could be the differences in the skin areas being stimulated during each task. Indeed, the task that most strongly correlated to fingertip area was the GOT, which is the task in which the largest skin surface is stimulated, while the 2POT, stimulating a smaller area, was less strongly and less consistently (across fingers) correlated to the fingertip area. In the 2PDT, the stimulated area is even smaller, as it is restricted to a single axis, which may require even greater statistical power to identify such a correlation. To test for this, a possibility would be to apply the 2PDT at different positions on the fingertip to cover a larger surface and equate the stimulated area in the other tasks.

Comparing the modulation of these tasks by RSS, we observed that all three tasks were modulated, suggesting that they all grasp some relevant information from SI. However, they displayed different patterns of changes across fingers. On the stimulated finger, both the GOT and 2PDT displayed a significant threshold reduction, suggesting that they are similarly sensitive to tactile acuity improvement (Figure 20). Since the established mechanisms driving RSS-induced changes in tactile acuity involve an increase in the size of RFs and cortical representation (e.g., Godde et al., 1996; Pleger et al., 2001), the improvement in performance for both tasks at the stimulated finger suggests that these two tasks may be sensitive to alterations in the size of RF and cortical representation, unlike the 2POT. Since the 2POT did not exhibit local improvement following RSS, it may be less sensitive to detecting changes in tactile acuity related to alterations in the size of RFs.

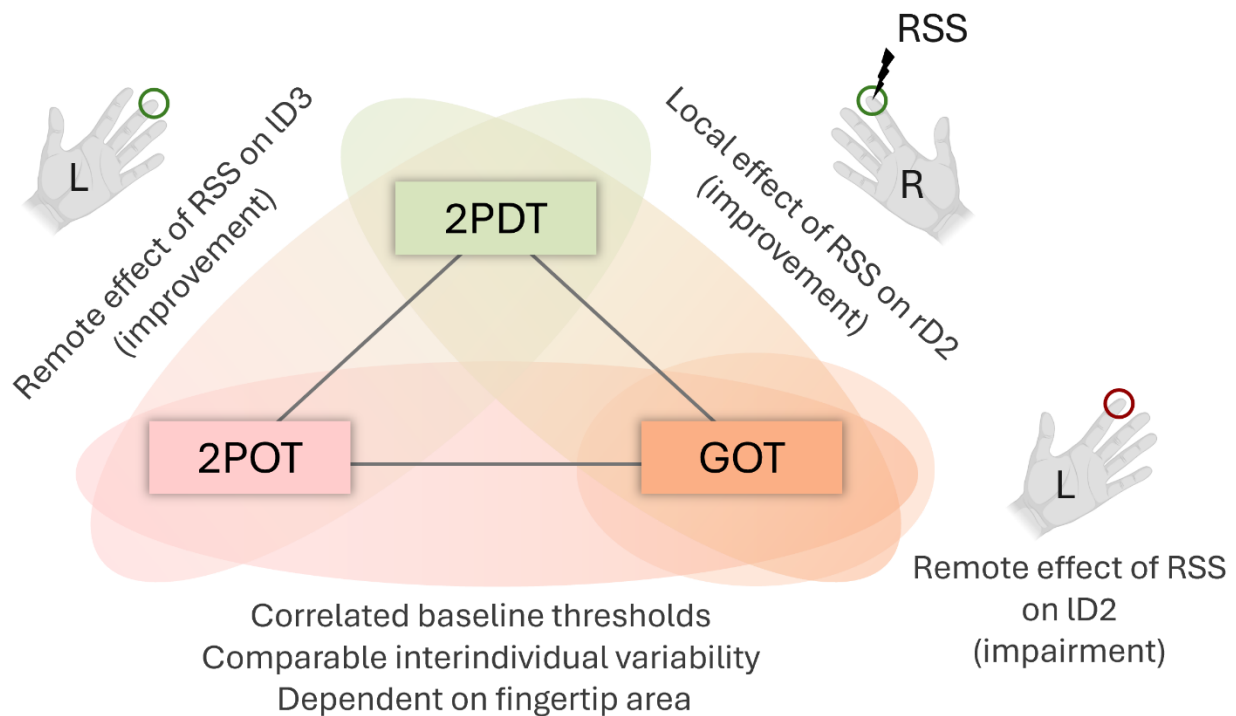
As discussed in the introductory Chapter II, while the increase in RF size can be seen as paradoxical in regards to the improvement of tactile acuity, recent evidence weakens the long held assumption that the smallest RFs support the highest tactile spatial acuity. In an electrophysiological study on rats, Foffani et al. (2008) showed that although large RFs reduce the spatial selectivity of individual neurons, they offer a compensatory advantage through a more complex temporal coding mechanism. This sophisticated temporal code leverages latency differences across large neuronal populations, allowing the retention of essential information about stimulus location without necessarily sacrificing it. They additionally found that the spike timing populational code is particularly informative when RFs are large, or when discriminating between close locations, allowing for a high tactile acuity even with large RFs (Foffani et al., 2008). Additional recent evidence showed that training-dependent tactile improvement in a texture discrimination task in monkeys was supported by both an increase and a decrease in the size of SI RFs depending on the active or passive modes of touch used during the training (Cybulska-Klosowicz et al., 2020). Indeed, while the monkeys trained on the task using passive



touch (surfaces displaced under the immobile fingertips) displayed the smallest RFs, the ones trained using active touch (fingertips scanned over the surfaces) exhibited the largest RFs, potentially due to the higher cortical firing rates induced by active touch (Cybulska-Klosowicz et al., 2020). Together, these findings indicate that an increase in the size of RFs can indeed support tactile acuity improvement.

As for the remote effect of RSS on these tasks, RSS improved the performance in 2PDT and 2POT, but not GOT on the unstimulated left middle finger, while it impaired the performance in GOT on the unstimulated left index finger (Figure 20). Since the 2PDT and 2POT seem to capture similar changes in tactile acuity for the unstimulated fingers, we suggest that they may assess a similar aspect of tactile acuity modulated by RSS (though the underlying physiological mechanisms are unknown yet) that GOT may not capture. Since both tasks share the two-point stimuli, the change they are both sensitive to may relate to the nature of the stimuli. In contrast, the fact that RSS impaired GOT performance suggests that this task may be more sensitive in detecting impaired tactile acuity on unstimulated fingers, either on the other hand specifically, or on the neighboring finger of the stimulated one as well, where 2PDT thresholds typically remain stable (Godde et al., 2000; Muret et al., 2024). Indeed, while we did not assess acuity on the adjacent right middle finger, it is possible that the GOT performance would also be impaired on this finger. To the best of our knowledge, the effect of RSS on GOT has never been investigated on the adjacent finger. Investigating the effect of RSS on GOT performance across all four fingers (both index and middle fingers) would provide a more thorough understanding of the pattern of changes and help determine whether this task is more sensitive to tactile acuity impairment than the other two tasks.

In summary, while the 2POT and GOT may capture an aspect of tactile acuity linked to the density of mechanoreceptors (correlation with fingertip area), the 2PDT and GOT would capture an aspect of tactile acuity linked to the size of RFs (improved by RSS at the stimulated finger). The last aspect captured by the 2PDT and 2POT (improved by RSS at an unstimulated finger) would rely on mechanisms that are unknown yet but seem distinct from RFs and mechanoreceptor density. Given the observed similarities and differences between the tasks, we conclude that they measure at least partially overlapping rather than entirely distinct aspects of tactile acuity. This emphasizes the complexity of tactile acuity and highlights the importance of using multiple, methodologically consistent tasks to comprehensively capture its various aspects.



**Figure 20.** Our results showed that aspects measured by each task are not entirely separate but rather partially overlapping. The GOT and 2POT thresholds were correlated, exhibited comparable interindividual variability and depended on fingertip area, the GOT and 2PDT demonstrating similar sensitivity to RSS at the stimulated finger (right index finger; rD2), and the 2PDT and 2POT showing similar sensitivity to RSS at the unstimulated fingers (improvement at the left middle finger; rD3). The GOT was additionally found to be more sensitive in detecting impaired performance at the left index finger (ID2) than the two other tasks. Green circle: tactile acuity improvement; Red circle: tactile acuity impairment.

#### V- Does the 2PDT measure tactile acuity? Our contribution to the discussion

Additionally to the main aim of the study, on a more methodological perspective, our study brings some elements to the long-held controversy about biases in the 2PDT questioning its reliability as a tactile acuity task (Tawney, 1895; Johnson & Phillips, 1981; Craig & Johnson, 2000; Tong et al., 2013).

One of the main criticisms raised against the 2PDT is that since the single and double stimuli differ in perceived intensity (one pin is felt more intense than two pins), this could provide a non-spatial cue to solve the task. This may lead some participants to answer “two” even when there is no distance between the two points (Tawney, 1895; Johnson & Phillips, 1981; Craig & Johnson, 2000) bringing to the paradoxical results of observing some thresholds at zero values. In contrast to this criticism, we did not observe a “zero” threshold in the current study, nor in previous studies conducted by our team (Muret et al., 2014, 2016, 2024; Muret & Dinse, 2018) nor others that used the same device, instructions, and procedures (Godde et al., 2000; Pleger et al., 2003; Bruns et al., 2014). The instruction to say “two” only when the tips are clearly

distinguishable, may have limited the issue related to intensity cues, since the sensations other than “clear two tips” (i.e. the circle, line or dumbbell elicited by two close tips; Boring, 1942; Craig & Johnson, 2000) were asked to be considered as “one”. Since the 2PDT thresholds obtained in this manner showed similar patterns across fingers to those of the 2POT, which is considered more reliable due to the absence of intensity cues (while using similar stimuli), this further supports the 2PDT as a reliable measure of tactile acuity. Additionally, the fact that these 2PDT thresholds at the stimulated finger are affected by RSS similarly to the GOT, which is also considered more reliable for the same reason, further reinforces the validity of 2PDT as a reliable measure of tactile acuity.

The second main criticism relates to the influence of the individual criteria, as the participants have to split their sensation continuum into “one” vs. “two” categories, which is thought to increase the variability among participants (Tawney, 1895; Johnson & Phillips, 1981; Craig & Johnson, 2000). This criticism, however, only applied to subjective methods, which we did not use. Nevertheless, in our study, we did not observe such a high interindividual variability, and instead we even found the variability to be lower than in the other two tasks. Likewise, in Bruns et al. (2014)’s study, which is the only one to compare the GOT and 2PDT using the same methodology as ours, the 2PDT showed lower interindividual variability compared to the GOT (see Discussion of Study 2). This suggests that the instruction given may mitigate the “criterion issue”. Nonetheless, it is possible that reducing the variability too much may have inadvertently reduced also relevant tactile acuity-related information, such as the interindividual variability related to mechanoreceptor density. This might be a potential explanation for the absence of correlation between the 2PDT thresholds and the fingertip area, although the smaller surface area involved in the task seems a more likely explanation, since the correlation weakened as the engaged surface area decreased (see section IV). Though this is only speculative, this deserves further investigation.

Our results therefore emphasize the importance of standardizing the 2PDT methodology and of using conservative instructions to limit the influence of the intensity cues and criterion biases to get reliable results.

## **VI- Different patterns at stimulated and unstimulated fingers: different mechanisms?**

Following RSS on the right index finger, we reported different patterns of improvements across tasks and fingers. Besides showing that these tasks may measure overlapping rather than entirely distinct aspects of tactile acuity (which was discussed in section IV), this result also reveals that the local and remote perceptual effects of RSS may rely on different mechanisms. Indeed, altering differently the performance in the three tasks at the stimulated and unstimulated fingers through RSS suggests that the mechanisms at play are likely not the same (or partly different).

While the local effect of RSS is believed to depend on an increase in the size of RFs and cortical representation of the stimulated finger (e.g., Godde et al., 1996; Pleger et al., 2001, 2003), the absence of an effect on the homologous left index finger has been associated with a lack of change in the size of its cortical representation (e.g., Pleger et al., 2001, 2003). Nonetheless, in light of these findings and our observation of impaired GOT performance for the left index finger, it appears that this change in performance may not result from changes in the size of its RFs and cortical representation, but may instead depend on other mechanisms. Furthermore, our finding that RSS worsened tactile acuity as measured by GOT strengthens our hypothesis regarding the modulation of inhibition (Study 3, ongoing). Specifically, an increased inhibition towards the left index finger could explain the observed decline in performance for that finger.

## **VII- Replication of RSS-induced remote effects in its electrocutaneous version**

While tactile acuity improvements (remote effects) were observed following RSS applied in its mechanical version, it was not known whether the same effects could be observed following electrocutaneous RSS. When comparing the effects of both versions of RSS, it is evident that they result in similar local improvements of tactile acuity on the stimulated finger, which are thought to be supported by an enlargement of the stimulated RFs and cortical representations (e.g., Godde et al., 1996; Pleger et al., 2003). However, in the case of the remote effects, because the underlying mechanisms are not known, the possibility that the electrocutaneous version could have resulted in different effects could not be ignored. Moreover, a recent study showed that electrical and mechanical stimulations induced opposite changes in corticospinal excitability, with the mechanical one increasing it while the electrocutaneous one decreasing it (Kojima et al., 2021). Given these considerations, it remained to be determined whether remote effects would be observed following electrical RSS. Through our Study 2, we did observe an improvement on the 2PDT and 2POT performance following electrical RSS. We also

additionally observed for the first time that tactile acuity at the homologous finger was impaired as measured through the GOT, which contrasts with previous works that repeatedly reported stable tactile acuity at the homologous finger both using 2PDT (e.g., Godde et al., 2000; Muret et al., 2024) and GOT (Hodzic et al., 2004; Ross et al., 2022). It is still unclear whether this impairment stems from the electrocutaneous version of RSS, is specifically detected through GOT, or is a result of both (could be detected only through GOT after electrocutaneous RSS). Since both studies finding stable GOT thresholds after RSS used its mechanical version, we hypothesize that the impairment in tactile acuity may be specifically induced by the electrocutaneous version of RSS and specifically detected through GOT. A comparative study investigating the effects of both versions of RSS across all three tasks would help clarify this issue.

Besides strengthening the quite recent results of mechanical RSS-induced improvement on the unstimulated left middle finger (Muret et al., 2024), this replication with electrical RSS holds therapeutic potential as the electrocutaneous version is shorter and thus more adapted to clinical populations (Smith et al., 2009; Kattenstroth et al., 2018). This replication enabled us to implement the electrocutaneous version of RSS in our recently started clinical study (Study 4).

### **VIII- Inducing plasticity through RSS: methodological considerations**

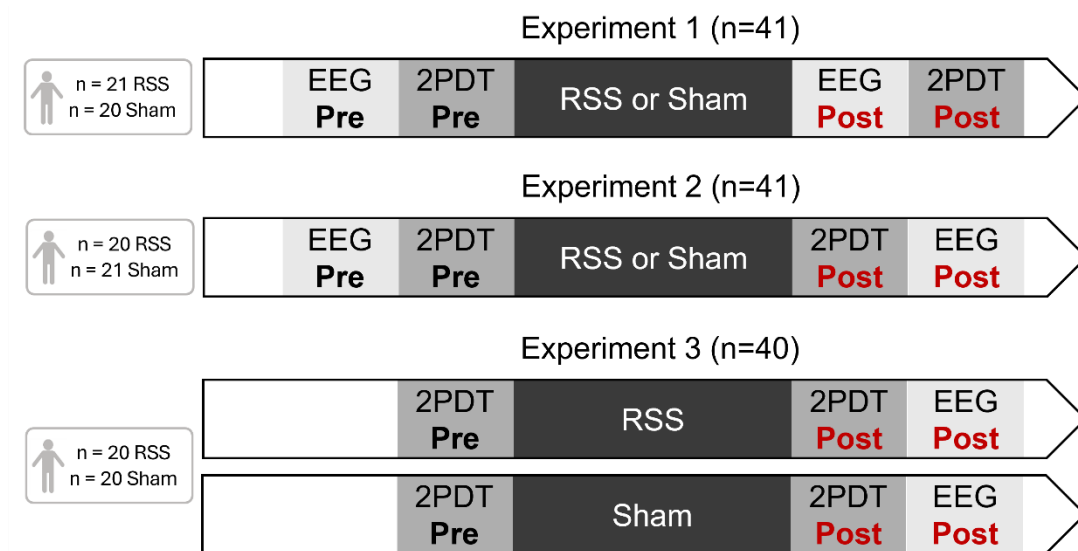
Since RSS was used as a tool to induce plasticity in the somatosensory system for both studies, it is crucial to understand its mechanisms of action. While the local effects of RSS have been shown to rely on Hebbian-like cortical changes in SI and SII representations of the stimulated finger (Godde et al., 1996; Pleger et al., 2003), the physiological mechanisms behind its remote effects on the unstimulated hand remain unexplored. Given the specific pattern of improvement transfer between fingers of both hands and the close relationship between Hebbian and homeostatic plasticity, we hypothesized that this transfer might be facilitated by homeostatic modulations of lateral (within fingers of the same hand) and inter-hemispheric (between fingers of opposite hands) inhibition. My third study aimed at testing this hypothesis, but it did not show any effect of RSS on the tactile acuity (2PDT) of the tested fingers and on the inhibition between these fingers. Given that the well-established perceptual effect of RSS on the stimulated finger was not replicated, potentially due to methodological issues, these results should be considered preliminary. We plan another experiment to solve the issue and conclude on the question. In this final section, I discuss potential methodological issues that may have hindered the RSS-induced tactile learning on the stimulated finger, possibly by preventing the induction of somatosensory plasticity.

In the experimental design of study 2, RSS was applied in between two sessions of EEG recordings and two sessions of 2PDT testing (Figure 21). During the EEG sessions, tactile electrocutaneous stimuli were applied to elicit somatosensory potentials, which were used to calculate a somatosensory suppression index which served to quantify the strength of inhibitory processes. Each finger tested, including the one stimulated by RSS, received low-frequency tactile stimuli at around 2 Hz for a total duration of approximately 40 minutes (corresponding to the duration of the EEG recording during single and paired electrocutaneous stimulations). As we know from the literature (Ragert et al., 2008), a low frequency stimulation may hinder the induction of plasticity and subsequent perceptual effects as it tends to promote the induction of LTD rather than LTP, which can lead to impaired tactile perception. Ragert et al. (2008) reported that applying a 1 Hz, 20-minute stimulation to the index finger impaired 2PDT performance. In our experiments, however, 2PDT performance was not significantly worsened, suggesting that while the low-frequency stimulation may have been sufficient to prevent LTP, it may not have been low or efficient enough to induce LTD. This reflects a delicate balance, ranging from effective LTD to effective LTP, with intermediate levels of weak LTD and LTP (see introductory Chapter III, section IV, Figure 14B). It is possible that the EEG stimulation prior to RSS heightened the level of excitation in SI, which may have limited the induction of somatosensory plasticity by RSS. Indeed, a history of enhanced postsynaptic activity can raise the threshold for LTP induction, thereby increasing the chances of triggering LTD instead (Ragert et al., 2009).

A previous study from our group used mechanical stimuli (coupled with MEG) with similar temporal pattern before and after RSS and found lower -though still significant- RSS-induced improvement in the 2PDT (Muret et al., 2016). Another example in the literature observed a reduced effect of RSS on 2PDT thresholds when RSS was applied following electrocutaneous stimulations. Indeed, Gatica Tossi et al. (2013) applied 2 Hz stimuli for a few minutes before and after RSS and reported a reduction of 2PDT thresholds lower than usually found (but still significant). In another group of their experiment, they increased cortical excitability through rTMS before applying RSS and found no effect of RSS on the 2PDT (Gatica Tossi et al., 2013).

Altogether, these findings support our hypothesis that the tactile stimulation may have interfered with RSS in two potential ways: (i) during the EEG pre-session, potentially hindering the subsequent induction of plasticity by RSS and its associated perceptual changes, or (ii) during the EEG post-session, possibly cancelling the cortical and perceptual effects of RSS. To investigate these possibilities, we had to either (i) perform EEG recordings at the very end only,

after the Post-intervention 2PDT session (Figure 21; Experiment 3), or (ii) reverse the order of EEG and 2PDT only in the Post-session (Figure 21; Experiment 2). Since the second design, incorporating both Pre- and Post-RSS EEG recordings, was the most comprehensive for testing, we implemented it in our second experiment of study 2. However, we still observed similar results, showing no perceptual local effect of RSS. The next step is thus to investigate the first hypothesis in a final experiment, where EEG recordings will be performed only at the end of the experiment, in which case we will analyze differences between subjects rather than within the same subjects (Figure 21). Additionally, by contrasting the results of the three experiments, we will be able to isolate the effects of RSS on cortical inhibition and hopefully bring a more conclusive answer to our question of whether RSS acts remotely by modulating lateral and inter-hemispheric inhibition between fingers of both hands.



**Figure 21. Experimental timeline of our EEG experiments.** Participants underwent the EEG and the 2-point discrimination task (2PDT) before (Pre) and after (Post) receiving either RSS or Sham intervention on their right index finger (rD2). After the intervention, they either underwent the EEG and the 2PDT in the same order as in the Pre session (Experiment 1), or the converse (Experiment 2). In the Experiment 3, the EEG will be conducted only after the RSS or Sham and both pre- and post-2PDT sessions to avoid the potential detrimental effects of the electrocutaneous stimulations on the induction of somatosensory plasticity.

## CONCLUSION & PERSPECTIVES

To conclude, we found that modulating tactile information through RSS affected selectively the body image and left the body model and superficial schema unchanged, indicating that MBRs are not equally fed by tactile inputs through SI. On this basis, we proposed an updated model that revises the initial conception of the SI-MBR relationship, transforming it from a single common link to one that includes at least two distinct relationships: one specific to the body image and another that may equally connect the body model and superficial schema. The way SI acts differently on these MBRs may be explained by multiple scenarios. A first possibility is that the body image may be linked to SI in a different way than the other two MBRs, making it more sensitive to alterations in tactile inputs. Another possibility is that RSS affects differently the different subregions of the posterior parietal cortex potentially supporting the body image and the other two MBRs. Alternatively, the effects of RSS may spread to other extra-parietal cortical areas that are exclusively involved in the body image. Further investigations using both behavioral and neuroimaging approaches should help disentangle these alternatives. In addition, we reported a novel mislocalization pattern, with a bias towards the middle finger in distal phalanges that reversed towards the thumb in the proximal phalanx, enriching the known distortions of the superficial schema. This may reflect an effect of the tactile co-stimulation of the index finger's proximal phalanx with the thumb's distal phalanx, and raises new questions about how tactile "synergies" may contribute to the distortions observed in the superficial schema. This needs to be further investigated through assessing tactile localization performance across all fingers. From a clinical perspective, the finding that passive, training-independent tactile learning influences body image offers promising potential for treating body image disorders, specifically in cases of overestimated size of one's own body (e.g., in patients suffering from anorexia nervosa or bulimia). The effect of RSS on such clinical populations should be investigated and could bring a first step towards developing a passive protocol helping to treat body image alterations. Besides, an interesting direction for future research could be to investigate the potential transfer of body image plasticity from the stimulated finger to the unstimulated fingers and face.

At a lower level, we reported that different tactile acuity tasks capture similar aspects of tactile acuity in pairs, with (i) the GOT and 2POT thresholds being correlated, exhibiting comparable interindividual variability and associations with fingertip area, (ii) the GOT and 2PDT demonstrating similar sensitivity to RSS's local effect at the stimulated finger, and (iii) the



2PDT and 2POT showing similar sensitivity to RSS's remote effects at the unstimulated fingers. The GOT was additionally found to be more sensitive in detecting impaired performance than the two other tasks. Considering these similarities and differences between the tasks, we concluded that the aspects measured by each task are not entirely separate but rather partially overlapping. Based on our findings, we point to the necessity of using multiple tasks to assess tactile acuity and fully capture its complexity, and we stress the need for using the same methodologies across tasks. Additionally, answering some criticisms made towards the 2PDT, we suggest that this task provides relevant and informative measures of acuity when using a standardized methodology to limit the biases attributed to this task.

While we were not able to conclude on whether the remote effects of RSS on tactile acuity occur via the modulation of lateral and inter-hemispheric inhibition, potentially due to methodological issues, the last experiment will hopefully bring a more conclusive answer to this question.

Finally, since RSS is a non-invasive, passive intervention with significant potential for tactile rehabilitation, and since remote effects could provide additional benefits, we are currently conducting a clinical study to investigate these remote effects in stroke patients with somatosensory deficits. This study has recently started and aims at providing a proof of concept for a remote application of RSS on the intact hand to enhance tactile perception on the affected hand.

## REFERENCES

- Abraira, V. E., & Ginty, D. D. (2013). The Sensory Neurons of Touch. *Neuron*, 79(4), 618-639. <https://doi.org/10.1016/j.neuron.2013.07.051>
- Adhikari, B. M., Sathian, K., Epstein, C. M., Lamichhane, B., & Dhamala, M. (2014). Oscillatory activity in neocortical networks during tactile discrimination near the limit of spatial acuity. *NeuroImage*, 91, 300-310. <https://doi.org/10.1016/j.neuroimage.2014.01.007>
- Akatsuka, K., Noguchi, Y., Harada, T., Sadato, N., & Kakigi, R. (2008). Neural codes for somatosensory two-point discrimination in inferior parietal lobule: An fMRI study. *NeuroImage*, 40(2), 852-858. <https://doi.org/10.1016/j.neuroimage.2007.12.013>
- Akatsuka, K., Wasaka, T., Nakata, H., Kida, T., Hoshiyama, M., Tamura, Y., & Kakigi, R. (2007). Objective examination for two-point stimulation using a somatosensory oddball paradigm: An MEG study. *Clinical Neurophysiology*, 118(2), 403-411. <https://doi.org/10.1016/j.clinph.2006.09.030>
- Akshay Baweja. (2020). *Haptic Glove Display: Enabling Sensory Substitution*. 673427 Bytes. <https://doi.org/10.6084/M9.FIGSHARE.13303445.V3>
- Alitto, H. J., & Usrey, W. M. (2003). Corticothalamic feedback and sensory processing. *Current Opinion in Neurobiology*, 13(4), 440-445. [https://doi.org/10.1016/S0959-4388\(03\)00096-5](https://doi.org/10.1016/S0959-4388(03)00096-5)
- Allard, T., Clark, S. A., Jenkins, W. M., & Merzenich, M. M. (1991). Reorganization of somatosensory area 3b representations in adult owl monkeys after digital syndactyly. *Journal of Neurophysiology*, 66(3), 1048-1058. <https://doi.org/10.1152/jn.1991.66.3.1048>
- Ambron, E., Schettino, L. F., Coyle, M., Jax, S., & Coslett, H. B. (2017). When perception trips action! The increase in the perceived size of both hand and target matters in reaching and grasping movements. *Acta Psychologica*, 180, 160-168. <https://doi.org/10.1016/j.actpsy.2017.09.011>
- Ambron, E., White, N., Faseyitan, O., Kessler, S. K., Medina, J., & Coslett, H. B. (2018). Magnifying the View of the Hand Changes Its Cortical Representation. A Transcranial Magnetic Stimulation Study. *Journal of Cognitive Neuroscience*, 30(8), 1098-1107. [https://doi.org/10.1162/jocn\\_a\\_01266](https://doi.org/10.1162/jocn_a_01266)
- Amoruso, E., Terhune, D. B., Kromm, M., Kirker, S., Muret, D., & Makin, T. R. (2023). Reassessing referral of touch following peripheral deafferentation: The role of contextual bias. *Cortex*, 167, 167-177. <https://doi.org/10.1016/j.cortex.2023.04.019>
- Anani, A., Körner, L. (1979). Discrimination of phantom hand sensations elicited by afferent electrical nerve stimulation in below-elbow amputees. *Medical Progress through Technology*, 6(3), 131-135.
- Andersen, P., Eccles, J. C., & Sears, T. A. (1964). The ventro-basal complex of the thalamus: Types of cells, their responses and their functional organization. *The Journal of Physiology*, 174(3), 370-399. <https://doi.org/10.1113/jphysiol.1964.sp007493>
- Anema, H. A., Van Zandvoort, M. J. E., De Haan, E. H. F., Kappelle, L. J., De Kort, Paul. L. M., Jansen, B. P. W., & Dijkerman, H. C. (2009). A double dissociation between somatosensory processing for perception and action. *Neuropsychologia*, 47(6), 1615-1620. <https://doi.org/10.1016/j.neuropsychologia.2008.11.001>
- Arkachar, P., & Wagh, M. D. (2007). Criticality of lateral inhibition for edge enhancement in neural systems. *Neurocomputing*, 70(4-6), 991-999. <https://doi.org/10.1016/j.neucom.2006.03.017>
- Arnold, G., & Auvray, M. (2014). Perceptual Learning: Tactile Letter Recognition Transfers Across Body Surfaces. *Multisensory Research*, 27(1), 71-90. <https://doi.org/10.1163/22134808-00002443>
- Arslanova, I., Takamuku, S., Gomi, H., & Haggard, P. (2022). Multidigit tactile perception I: Motion integration benefits for tactile trajectories presented bimanually. *Journal of Neurophysiology*, 128(2), 418-433. <https://doi.org/10.1152/jn.00022.2022>
- Arslanova, I., Wang, K., Gomi, H., & Haggard, P. (2020). Somatosensory evoked potentials that index lateral inhibition are modulated according to the mode of perceptual processing: Comparing or combining multi-digit tactile motion. *Cognitive Neuroscience*, 13(1), 47-59. <https://doi.org/10.1080/17588928.2020.1839403>
- Augière, T., Metral, M., Simoneau, M., & Mercier, C. (2024). Preserved tactile distance estimation despite body representation distortions in individuals with fibromyalgia. *Frontiers in Pain Research*, 5, 1414927. <https://doi.org/10.3389/fpain.2024.1414927>
- Avanzini, P., Abdollahi, R. O., Sartori, I., Caruana, F., Pelliccia, V., Casaceli, G., Mai, R., Lo Russo, G., Rizzolatti, G., & Orban, G. A. (2016). Four-dimensional maps of the human somatosensory system. *Proceedings of the National Academy of Sciences*, 113(13). <https://doi.org/10.1073/pnas.1601889113>
- Azañón, E., Longo, M. R., Soto-Faraco, S., & Haggard, P. (2010). The Posterior Parietal Cortex Remaps Touch into External Space. *Current Biology*, 20(14), 1304-1309. <https://doi.org/10.1016/j.cub.2010.05.063>
- Azañón, E., Tamè, L., Maravita, A., Linkenauger, S. A., Ferrè, E. R., Tajadura-Jiménez, A., & Longo, M. R. (2016). Multimodal Contributions to Body Representation. *Multisensory Research*, 29(6-7), 635-661. <https://doi.org/10.1163/22134808-00002531>

- Badde, S., & Heed, T. (2016). Towards explaining spatial touch perception : Weighted integration of multiple location codes. *Cognitive Neuropsychology*, 33(1-2), 26-47. <https://doi.org/10.1080/02643294.2016.1168791>
- Badde, S., & Heed, T. (2023). The hands' default location guides tactile spatial selectivity. *Proceedings of the National Academy of Sciences*, 120(15), e2209680120. <https://doi.org/10.1073/pnas.2209680120>
- Bahia, C. P., Vianna-Barbosa, R. J., Tovar-Moll, F., & Lent, R. (2019). Terminal Arbors of Callosal Axons Undergo Plastic Changes in Early-Amputated Rats. *Cerebral Cortex*, 29(4), 1460-1472. <https://doi.org/10.1093/cercor/bhy043>
- Bassolino, M., & Becchio, C. (2023). The 'hand paradox' : Distorted representations guide optimal actions. *Trends in Cognitive Sciences*, 27(1), 7-8. <https://doi.org/10.1016/j.tics.2022.09.010>
- Beauchamp, M. S., LaConte, S., & Yasar, N. (2009). Distributed representation of single touches in somatosensory and visual cortex. *Human Brain Mapping*, 30(10), 3163-3171. <https://doi.org/10.1002/hbm.20735>
- Beck, J., & Schwartz, T. (1979). Vernier acuity with dot test objects. *Vision Research*, 19(3), 313-319. [https://doi.org/10.1016/0042-6989\(79\)90176-7](https://doi.org/10.1016/0042-6989(79)90176-7)
- Békésy, G. V. (1960). Neural Inhibitory Units of the Eye and Skin Quantitative Description of Contrast Phenomena\*. *Journal of the Optical Society of America*, 50(11), 1060. <https://doi.org/10.1364/JOSA.50.001060>
- Bensmaia, S. J., Craig, J. C., Yoshioka, T., & Johnson, K. O. (2006). SA1 and RA Afferent Responses to Static and Vibrating Gratings. *Journal of Neurophysiology*, 95(3), 1771-1782. <https://doi.org/10.1152/jn.00877.2005>
- Bensmaia, S. J., Hsiao, S. S., Denchev, P. V., Killebrew, J. H., & Craig, J. C. (2008). The tactile perception of stimulus orientation. *Somatosensory & Motor Research*, 25(1), 49-59. <https://doi.org/10.1080/08990220701830662>
- Berlucchi, G., & Aglioti, S. (1997). The body in the brain : Neural bases of corporeal awareness. *Trends in Neurosciences*, 20(12), 560-564. [https://doi.org/10.1016/S0166-2236\(97\)01136-3](https://doi.org/10.1016/S0166-2236(97)01136-3)
- Beste, C., & Dinse, H. R. (2013). Learning without training. *Current Biology: CB*, 23(11), R489-499. <https://doi.org/10.1016/j.cub.2013.04.044>
- Biermann, K., Schmitz, F., Witte, O. W., Konczak, J., Freund, H.-J., & Schnitzler, A. (1998). Interaction of finger representation in the human first somatosensory cortex : A neuromagnetic study. *Neuroscience Letters*, 251(1), 13-16. [https://doi.org/10.1016/S0304-3940\(98\)00480-7](https://doi.org/10.1016/S0304-3940(98)00480-7)
- Birznieks, I., Logina, I., & Wasner, G. (2012). Somatotopic mismatch following stroke : A pathophysiological condition escaping detection. *BMJ Case Reports*, bcr2012006304. <https://doi.org/10.1136/bcr-2012-006304>
- Björkman, A., Rosén, B., ven Westen, D., Larsson, E-M., Lundborg, G. (2004). Acute improvement of contralateral hand function after deafferentation. *Clinical Neuroscience and Neuropathology*, 15(12).
- Björkman, A., Weibull, A., Rosén, B., Svensson, J., & Lundborg, G. (2009). Rapid cortical reorganisation and improved sensitivity of the hand following cutaneous anaesthesia of the forearm. *European Journal of Neuroscience*, 29(4), 837-844. <https://doi.org/10.1111/j.1460-9568.2009.06629.x>
- Blake, D. T., Strata, F., Kempter, R., & Merzenich, M. M. (2005). Experience-Dependent Plasticity in S1 Caused by Noncoincident Inputs. *Journal of Neurophysiology*, 94(3), 2239-2250. <https://doi.org/10.1152/jn.00172.2005>
- Blankenburg, F. (2003). Evidence for a Rostral-to-Caudal Somatotopic Organization in Human Primary Somatosensory Cortex with Mirror-reversal in Areas 3b and 1. *Cerebral Cortex*, 13(9), 987-993. <https://doi.org/10.1093/cercor/13.9.987>
- Bliem, B., Müller-Dahlhaus, J. F. M., Dinse, H. R., & Ziemann, U. (2008). Homeostatic Metaplasticity in the Human Somatosensory Cortex. *Journal of Cognitive Neuroscience*, 20(8), 1517-1528. <https://doi.org/10.1162/jocn.2008.20106>
- Bliss T V, Collingridge GL (1993) A synaptic model of memory: long-term potentiation in the hippocampus. *Nature* 361:31–39.
- Bolton, C.F., Winkelmann, R. K., and Dyck, P.J. (1966). A quantitative study of Meissner's corpuscles in man. *Neurology*, 16(1). <https://doi.org/10.1212/WNL.16.1.1>
- Boring, E.G. (1942). *Sensation and perception in the history of experimental psychology*. New York: Appleton-Century-Crofts
- Botvinick, M., & Cohen, J. (1998). Rubber hands 'feel' touch that eyes see. *Nature*, 391(6669), 756-756. <https://doi.org/10.1038/35784>
- Bramati, I. E., Rodrigues, E. C., Simões, E. L., Melo, B., Höfle, S., Moll, J., Lent, R., & Tovar-Moll, F. (2019). Lower limb amputees undergo long-distance plasticity in sensorimotor functional connectivity. *Scientific Reports*, 9(1), 2518. <https://doi.org/10.1038/s41598-019-39696-z>
- Bratch, A., Chen, Y., Engel, S. A., & Kersten, D. J. (2021). Visual adaptation selective for individual limbs reveals hierarchical human body representation. *Journal of Vision*, 21(5), 18. <https://doi.org/10.1167/jov.21.5.18>

- Braun, C., Schweizer, R., Elbert, T., Birbaumer, N., & Taub, E. (2000). Differential Activation in Somatosensory Cortex for Different Discrimination Tasks. *The Journal of Neuroscience*, 20(1), 446-450. <https://doi.org/10.1523/JNEUROSCI.20-01-00446.2000>
- Bremner, A. J. (2016). Developing body representations in early life : Combining somatosensation and vision to perceive the interface between the body and the world. *Developmental Medicine & Child Neurology*, 58(S4), 12-16. <https://doi.org/10.1111/dmcn.13041>
- Bremner, A. J., Holmes, N. P., & Spence, C. (2012). The development of multisensory representations of the body and of the space around the body. In A. J. Bremner, D. J. Lewkowicz, & C. Spence (Éds.), *Multisensory Development* (p. 113-136). Oxford University Press. <https://doi.org/10.1093/acprof:oso/9780199586059.003.0005>
- Brickwedde, M., Krüger, M. C., & Dinse, H. R. (2019). Somatosensory alpha oscillations gate perceptual learning efficiency. *Nature Communications*, 10(1), 263. <https://doi.org/10.1038/s41467-018-08012-0>
- Brodman, K. (1909). Vergleichende Lokalisationslehre der Grosshirnrinde in ihren Prinzipien dargestellt auf Grund des Zellenbaues. Johann Ambrosius Barth Verlag, Leipzig.
- Brooks, V.B., Rudomin, P., Slayman, C.L. (1961). Peripheral receptive fields of neurons in the cat's cerebral cortex. *J. Neurophysiol.* 24, 302-325
- Bruns, P., Camargo, C. J., Campanella, H., Esteve, J., Dinse, H. R., & Röder, B. (2014). Tactile Acuity Charts : A Reliable Measure of Spatial Acuity. *PLoS ONE*, 9(2), e87384. <https://doi.org/10.1371/journal.pone.0087384>
- Buxbaum, L. J., & Branch Coslett, H. (2001). Specialised structural descriptions for human body parts : Evidence from autotopagnosia. *Cognitive Neuropsychology*, 18(4), 289-306. <https://doi.org/10.1080/02643290126172>
- Byrne, J. A., & Calford, M. B. (1991). Short-term expansion of receptive fields in rat primary somatosensory cortex after hindpaw digit denervation. *Brain Research*, 565(2), 218-224. [https://doi.org/10.1016/0006-8993\(91\)91652-H](https://doi.org/10.1016/0006-8993(91)91652-H)
- Caggiano, P., & Cocchini, G. (2020). The functional body : Does body representation reflect functional properties? *Experimental Brain Research*, 238(1), 153-169. <https://doi.org/10.1007/s00221-019-05705-w>
- Calford, M. B., & Tweedale, R. (1990). Interhemispheric Transfer of Plasticity in the Cerebral Cortex. *Science*, 249(4970), 805-807. <https://doi.org/10.1126/science.2389146>
- Calford, M. B., & Tweedale, R. (1991). Acute changes in cutaneous receptive fields in primary somatosensory cortex after digit denervation in adult flying fox. *Journal of Neurophysiology*, 65(2), 178-187. <https://doi.org/10.1152/jn.1991.65.2.178>
- Calford, M.B., Tweedale, R. (1988) Immediate and chronic changes in responses of somatosensory cortex in adult flying-fox after digit amputation. *Nature*, 332.
- Callier, T., Suresh, A. K., & Bensmaia, S. J. (2019). Neural Coding of Contact Events in Somatosensory Cortex. *Cerebral Cortex*, 29(11), 4613-4627. <https://doi.org/10.1093/cercor/bhy337>
- Canzoneri, E., Marzolla, M., Amoresano, A., Verni, G., & Serino, A. (2013a). Amputation and prosthesis implantation shape body and peripersonal space representations. *Scientific Reports*, 3(1), 2844. <https://doi.org/10.1038/srep02844>
- Canzoneri, E., Ubaldi, S., Rastelli, V., Finisguerra, A., Bassolino, M., & Serino, A. (2013b). Tool-use reshapes the boundaries of body and peripersonal space representations. *Experimental Brain Research*, 228(1), 25-42. <https://doi.org/10.1007/s00221-013-3532-2>
- Capaday, C., Richardson, M. P., Rothwell, J. C., & Brooks, D. J. (2000). Long-term changes of GABAergic function in the sensorimotor cortex of amputees. *Experimental Brain Research*, 133(4), 552-556. <https://doi.org/10.1007/s002210000477>
- Cardinali, L., Brozzoli, C., Luauté, J., Roy, A. C., & Farnè, A. (2016). Proprioception Is Necessary for Body Schema Plasticity : Evidence from a Deafferented Patient. *Frontiers in Human Neuroscience*, 10. <https://doi.org/10.3389/fnhum.2016.00272>
- Cardinali, L., Brozzoli, C., Urquizar, C., Salemme, R., Roy, A. C., & Farnè, A. (2011). When action is not enough : Tool-use reveals tactile-dependent access to Body Schema. *Neuropsychologia*, 49(13), 3750-3757. <https://doi.org/10.1016/j.neuropsychologia.2011.09.033>
- Cardinali, L., Frassinetti, F., Brozzoli, C., Urquizar, C., Roy, A. C., & Farnè, A. (2009). Tool-use induces morphological updating of the body schema. *Current Biology*, 19(13), 1157. <https://doi.org/10.1016/j.cub.2009.06.048>
- Cash, T. F., & Deagle, E. A. (1997). The nature and extent of body-image disturbances in anorexia nervosa and bulimia nervosa : A meta-analysis. *International Journal of Eating Disorders*, 22(2), 107-126. [https://doi.org/10.1002/\(SICI\)1098-108X\(199709\)22:2<107::AID-EAT1>3.0.CO;2-J](https://doi.org/10.1002/(SICI)1098-108X(199709)22:2<107::AID-EAT1>3.0.CO;2-J)
- Cataldo, A., Frier, W., & Haggard, P. (2023). Quantifying spatial acuity of frequency resolved midair ultrasound vibrotactile stimuli. *Scientific Reports*, 13(1), 21149. <https://doi.org/10.1038/s41598-023-48037-0>

- Catani, M. (2017). A little man of some importance. *Brain*, *140*(11), 3055-3061. <https://doi.org/10.1093/brain/awx270>
- Catley, M. J., O'Connell, N. E., Berryman, C., Ayhan, F. F., & Moseley, G. L. (2014). Is Tactile Acuity Altered in People With Chronic Pain? A Systematic Review and Meta-analysis. *The Journal of Pain*, *15*(10), 985-1000. <https://doi.org/10.1016/j.jpain.2014.06.009>
- Cauna, N. & Mannan, G. (1958). The structure of human digital Pacinian corpuscles and its functional significance. *J. Anat.* *92*, 1-20
- Celnik, P., Hummel, F., Harris-Love, M., Wolk, R., & Cohen, L. G. (2007). Somatosensory Stimulation Enhances the Effects of Training Functional Hand Tasks in Patients With Chronic Stroke. *Archives of Physical Medicine and Rehabilitation*, *88*(11), 1369-1376. <https://doi.org/10.1016/j.apmr.2007.08.001>
- Chand, P., & Jain, N. (2015). Intracortical and Thalamocortical Connections of the Hand and Face Representations in Somatosensory Area 3b of Macaque Monkeys and Effects of Chronic Spinal Cord Injuries. *The Journal of Neuroscience*, *35*(39), 13475-13486. <https://doi.org/10.1523/JNEUROSCI.2069-15.2015>
- Chang, K-C., Longo, M.R. (2022). Similar tactile distance anisotropy across segments of the arm. *Perception*, *51*(5), 300-312. [10.1177/03010066221088164](https://doi.org/10.1177/03010066221088164).
- Chatterjee, K., Stockley, R. C., Lane, S., Watkins, C., Cottrell, K., Ankers, B., Davies, S., Morris, M. F., Fallon, N., & Nurmikko, T. (2019). PULSE-I - Is repetitive Upper Limb Sensory stimulation early after stroke feasible and acceptable? A stratified single-blinded randomised controlled feasibility study. *Trials*, *20*(1), 388. <https://doi.org/10.1186/s13063-019-3428-y>
- Ching-Liang Hsieh, Fumio Shima, Shozo Tobimatsu, Shu-Jian Sun, & Motohiro Kato. (1995). The interaction of the somatosensory evoked potentials to simultaneous finger stimuli in the human central nervous system. A study using direct recordings. *Electroencephalography and Clinical Neurophysiology/ Evoked Potentials Section*, *96*(2), 135-142. [https://doi.org/10.1016/0168-5597\(94\)00251-9](https://doi.org/10.1016/0168-5597(94)00251-9)
- Chirila, A. M., Rankin, G., Tseng, S.-Y., Emanuel, A. J., Chavez-Martinez, C. L., Zhang, D., Harvey, C. D., & Ginty, D. D. (2022). Mechanoreceptor signal convergence and transformation in the dorsal horn flexibly shape a diversity of outputs to the brain. *Cell*, *185*(24), 4541-4559.e23. <https://doi.org/10.1016/j.cell.2022.10.012>
- Cholewiak, R. W., & Collins, A. A. (2003). Vibrotactile localization on the arm : Effects of place, space, and age. *Perception & Psychophysics*, *65*(7), 1058-1077. <https://doi.org/10.3758/BF03194834>
- Cholewiak, R. W., Brill, J. C., & Schwab, A. (2004). Vibrotactile localization on the abdomen : Effects of place and space. *Perception & Psychophysics*, *66*(6), 970-987. <https://doi.org/10.3758/BF03194989>
- Chung YG, Han SW, Kim H-S, Chung S-C, Park J-Y, Wallraven C, Kim S-P (2014) Intra- and interhemispheric effective connectivity in the human somatosensory cortex during pressure stimulation. *BMC Neurosci* *15*:43
- Clark, S. A., Allard, T., Jenkins, W. M., and Merzenich, M. M. (1988). Receptive fields in the bodysurface map in adult cortex defined by temporally correlated inputs. *Nature* *332*, 444-5.
- Clarke, J. M., & Zaidel, E. (1994). Anatomical-behavioral relationships : Corpus callosum morphometry and hemispheric specialization. *Behavioural Brain Research*, *64*(1-2), 185-202. [https://doi.org/10.1016/0166-4328\(94\)90131-7](https://doi.org/10.1016/0166-4328(94)90131-7)
- Coelho, L. A., & Gonzalez, C. L. R. (2024). Perception, action, and the body model. *Neuropsychologia*, *196*, 108853. <https://doi.org/10.1016/j.neuropsychologia.2024.108853>
- Coelho, L. A., Schacher, J. P., Scammel, C., Doan, J. B., & Gonzalez, C. L. R. (2019). Long- but not short-term tool-use changes hand representation. *Experimental Brain Research*, *237*(1), 137-146. <https://doi.org/10.1007/s00221-018-5408-y>
- Conti, F., Fabri, M., & Manzoni, T. (1986). Bilateral Receptive Fields and Callosal Connectivity of the Body Midline Representation in the First Somatosensory Area of Primates. *Somatosensory Research*, *3*(4), 273-289. <https://doi.org/10.3109/07367228609144588>
- Corniani, G., & Saal, H. P. (2020). Tactile innervation densities across the whole body. *Journal of Neurophysiology*, *124*(4), 1229-1240. <https://doi.org/10.1152/jn.00313.2020>
- Corradi-Dell'Acqua, C., Hesse, M. D., Rumiati, R. I., & Fink, G. R. (2008). Where is a Nose with Respect to a Foot? The Left Posterior Parietal Cortex Processes Spatial Relationships among Body Parts. *Cerebral Cortex*, *18*(12), 2879-2890. <https://doi.org/10.1093/cercor/bhn046>
- Corradi-Dell'Acqua, C., Tomasino, B., & Fink, G. R. (2009). What Is the Position of an Arm Relative to the Body? Neural Correlates of Body Schema and Body Structural Description. *The Journal of Neuroscience*, *29*(13), 4162-4171. <https://doi.org/10.1523/JNEUROSCI.4861-08.2009>
- Craig, J. C. (1985). Attending to two fingers : Two hands are better than one. *Perception & Psychophysics*, *38*(6), 496-511. <https://doi.org/10.3758/BF03207059>
- Craig, J. C. (1993). Anomalous sensations following prolonged tactile stimulation. *Neuropsychologia*, *31*(3), 277-291. [https://doi.org/10.1016/0028-3932\(93\)90092-E](https://doi.org/10.1016/0028-3932(93)90092-E)

- Craig, J. C. (1999). Grating orientation as a measure of tactile spatial acuity. *Somatosensory & Motor Research*, 16(3), 197-206. <https://doi.org/10.1080/08990229970456>
- Craig, J. C., & Lyle, K. B. (2001). A comparison of tactile spatial sensitivity on the palm and fingerpad. *Perception & Psychophysics*, 63(2), 337-347. <https://doi.org/10.3758/BF03194474>
- Craig, J. C., & Lyle, K. B. (2002). A correction and a comment on Craig and Lyle (2001). *Perception & Psychophysics*, 64(3), 504-506. <https://doi.org/10.3758/BF03194721>
- Critchley, M. (1953). The parietal lobes. London: Edward Arnold & Co
- Cunningham, D. A., Machado, A., Yue, G. H., Carey, J. R., & Plow, E. B. (2013). Functional somatotopy revealed across multiple cortical regions using a model of complex motor task. *Brain Research*, 1531, 25-36. <https://doi.org/10.1016/j.brainres.2013.07.050>
- Cybulska-Klosowicz, A., Tremblay, F., Jiang, W., Bourgeon, S., Meftah, E.-M., & Chapman, C. E. (2020). Differential effects of the mode of touch, active and passive, on experience-driven plasticity in the S1 cutaneous digit representation of adult macaque monkeys. *Journal of Neurophysiology*, 123(3), 1072-1089. <https://doi.org/10.1152/jn.00014.2019>
- Darian-Smith, C. (2004). Primary afferent terminal sprouting after a cervical dorsal rootlet section in the macaque monkey. *Journal of Comparative Neurology*, 470(2), 134-150. <https://doi.org/10.1002/cne.11030>
- De Haan, E. H. F., & Dijkerman, H. C. (2020). Somatosensation in the Brain : A Theoretical Re-evaluation and a New Model. *Trends in Cognitive Sciences*, 24(7), 529-541. <https://doi.org/10.1016/j.tics.2020.04.003>
- De Klerk, C. C. J. M., Filippetti, M. L., & Rigato, S. (2021). The development of body representations : An associative learning account. *Proceedings of the Royal Society B: Biological Sciences*, 288(1949), rspb.2021.0070, 20210070. <https://doi.org/10.1098/rspb.2021.0070>
- De Vignemont, F. (2010). Body schema and body image—Pros and cons. *Neuropsychologia*, 48(3), 669-680. <https://doi.org/10.1016/j.neuropsychologia.2009.09.022>
- De Vignemont, F., & Farne, A. (2010). Widening the body to rubber hands and tools : What's the difference?: *Revue de Neuropsychologie, Volume 2*(3), 203-211. <https://doi.org/10.1684/nrp.2010.0087>
- De Vignemont, F., Ehrsson, H. H., & Haggard, P. (2005). Bodily Illusions Modulate Tactile Perception. *Current Biology*, 15(14), 1286-1290. <https://doi.org/10.1016/j.cub.2005.06.067>
- DeCosta-Fortune, T. M., Ramshur, J. T., Li, C. X., De Jongh Curry, A., Pellicer-Morata, V., Wang, L., & Waters, R. S. (2020). Repetitive microstimulation in rat primary somatosensory cortex (SI) strengthens the connection between homotopic sites in the opposite SI and leads to expression of previously ineffective input from the ipsilateral forelimb. *Brain Research*, 1732, 146694. <https://doi.org/10.1016/j.brainres.2020.146694>
- Deflorio, D., Di Luca, M., & Wing, A. M. (2022). Skin and Mechanoreceptor Contribution to Tactile Input for Perception : A Review of Simulation Models. *Frontiers in Human Neuroscience*, 16, 862344. <https://doi.org/10.3389/fnhum.2022.862344>
- Deflorio, D., Di Luca, M., & Wing, A. M. (2023). Skin properties and afferent density in the deterioration of tactile spatial acuity with age. *The Journal of Physiology*, 601(3), 517-533. <https://doi.org/10.1113/JP283174>
- Del Gratta C, Penna S Della, Tartaro A, Ferretti A, Torquati K, Bonomo L, Romani GL, Rossini PM (2000) Topographic organization of the human primary and secondary somatosensory areas. *Neuroreport* 11:2035–2043.
- Delhaye, B. P., Long, K. H., & Bensmaia, S. J. (2018). Neural Basis of Touch and Proprioception in Primate Cortex. In Y. S. Prakash (Éd.), *Comprehensive Physiology* (1re éd., p. 1575-1602). Wiley. <https://doi.org/10.1002/cphy.c170033>
- Delhaye, B. P., Xia, X., & Bensmaia, S. J. (2019). Rapid geometric feature signaling in the simulated spiking activity of a complete population of tactile nerve fibers. *Journal of Neurophysiology*, 121(6), 2071-2082. <https://doi.org/10.1152/jn.00002.2019>
- Dempsey-Jones, H., Stuedte-Schmiedgen, S., Browning, M., Makin, T. R., Woud, M. L., Harmer, C. J., Margraf, J., & Reinecke, A. (2021). Human perceptual learning is delayed by the N-methyl-D-aspartate receptor partial agonist D-cycloserine. *Journal of Psychopharmacology*, 35(3), 253-264. <https://doi.org/10.1177/0269881120986349>
- Dempsey-Jones, H., Themistocleous, A. C., Carone, D., Ng, T. W. C., Harrar, V., & Makin, T. R. (2019). Blocking tactile input to one finger using anaesthetic enhances touch perception and learning in other fingers. *Journal of Experimental Psychology: General*, 148(4), 713-727. <https://doi.org/10.1037/xge0000514>
- Dennis, M. (1976). Dissociated naming and locating of body parts after left anterior temporal lobe resection : An experimental case study. *Brain and Language*, 3(2), 147-163. [https://doi.org/10.1016/0093-934X\(76\)90013-4](https://doi.org/10.1016/0093-934X(76)90013-4)
- Dettmers, C., Adler, T., Rzanny, R., Van Schayck, R., Gaser, C., Weiss, T., Miltner, W. H., Brückner, L., & Weiller, C. (2001). Increased excitability in the primary motor cortex and supplementary motor area in patients with phantom limb pain after upper limb amputation. *Neuroscience Letters*, 307(2), 109-112. [https://doi.org/10.1016/S0304-3940\(01\)01953-X](https://doi.org/10.1016/S0304-3940(01)01953-X)

- Dhillon, G. S., Lawrence, S. M., Hutchinson, D. T., & Horch, K. W. (2004). Residual function in peripheral nerve stumps of amputees : Implications for neural control of artificial limbs. *The Journal of Hand Surgery*, 29(4), 605-615. <https://doi.org/10.1016/j.jhbs.2004.02.006>
- Di Vita, A., Boccia, M., Palermo, L., & Guariglia, C. (2016). To move or not to move, that is the question! Body schema and non-action oriented body representations : An fMRI meta-analytic study. *Neuroscience & Biobehavioral Reviews*, 68, 37-46. <https://doi.org/10.1016/j.neubiorev.2016.05.005>
- Dijkerman, H. C., & De Haan, E. H. F. (2007). Somatosensory processes subserving perception and action. *Behavioral and Brain Sciences*, 30(2), 189-201. <https://doi.org/10.1017/S0140525X07001392>
- Dillon, Y. K., Haynes, J., & Henneberg, M. (2001). The relationship of the number of Meissner's corpuscles to dermatoglyphic characters and finger size. *Journal of Anatomy*, 199(5), 577-584. <https://doi.org/10.1046/j.1469-7580.2001.19950577.x>
- Dimwamwa, E. D., Pala, A., Chundru, V., Wright, N. C., & Stanley, G. B. (2024). Dynamic corticothalamic modulation of the somatosensory thalamocortical circuit during wakefulness. *Nature Communications*, 15(1), 3529. <https://doi.org/10.1038/s41467-024-47863-8>
- Dinse, H. R., Kleibel, N., Kalisch, T., Ragert, P., Wilimzig, C., & Tegenthoff, M. (2006). Tactile coactivation resets age-related decline of human tactile discrimination. *Annals of Neurology*, 60(1), 88-94. <https://doi.org/10.1002/ana.20862>
- Dinse, H. R., Kraß, D., Maachaoui, R., Van Der Berg, I., and Ragert, P. (2005). Tactile 2-point discrimination and localization are differentially affected by synchronous and asynchronous coactivation. In Proceedings of the 6th Meeting of the German Neuroscience Society/30th Göttingen Neurobiology Conference 2005, H. Zimmermann and K. Krieglstein, Eds. *Neuroforum Suppl 1*, 62A
- Dinse, H. R., Ragert, P., Pleger, B., Schwenkreis, P., & Tegenthoff, M. (2003). Pharmacological Modulation of Perceptual Learning and Associated Cortical Reorganization. *Science*, 301(5629), 91-94. <https://doi.org/10.1126/science.1085423>
- Dinse, H.R., Tegenthoff, M. (2019). Repetitive Sensory Stimulation A Canonical Approach to Control the Induction of Human Learning at a Behavioral and Neural Level. In: Handbook of In Vivo Neural Plasticity Techniques. Elsevier B.V.
- Disbrow E a, Hinkley LBN, Roberts TPL (2003) Ipsilateral representation of oral structures in human anterior parietal somatosensory cortex and integration of inputs across the midline. *J Comp Neurol* 467:487–495.
- Doehler, J., Northall, A., Liu, P., Fracasso, A., Chrysidou, A., Speck, O., Lohmann, G., Wolbers, T., & Kuehn, E. (2023). The 3D Structural Architecture of the Human Hand Area Is Nontopographic. *The Journal of Neuroscience*, 43(19), 3456-3476. <https://doi.org/10.1523/JNEUROSCI.1692-22.2023>
- Duncan, R. O., & Boynton, G. M. (2007). Tactile Hyperacuity Thresholds Correlate with Finger Maps in Primary Somatosensory Cortex (S1). *Cerebral Cortex*, 17(12), 2878-2891. <https://doi.org/10.1093/cercor/bhm015>
- Dupin, L., Cuenca, M., Baron, J.-C., Maier, M. A., & Lindberg, P. G. (2022). Shrinking of spatial hand representation but not of objects across the lifespan. *Cortex*, 146, 173-185. <https://doi.org/10.1016/j.cortex.2021.10.009>
- Ehrsson, H. H., Kito, T., Sadato, N., Passingham, R. E., & Naito, E. (2005). Neural Substrate of Body Size : Illusory Feeling of Shrinking of the Waist. *PLoS Biology*, 3(12), e412. <https://doi.org/10.1371/journal.pbio.0030412>
- Eickhoff, S.B., Heim, S., Zilles, K., Amunts, K. (2006) Testing anatomically specified hypotheses in functional imaging using cytoarchitectonic maps. *Neuroimage*, 32, 570–582.
- Elbert, T., Pantev, C., Wienbruch, C., Rockstroh, B., & Taub, E. (1995). Increased Cortical Representation of the Fingers of the Left Hand in String Players. *Science*, 270(5234), 305-307. <https://doi.org/10.1126/science.270.5234.305>
- Elbert, T., Sterr, A., Flor, H., Rockstroh, B., Knecht, S., Pantev, C., Wienbruch, C., & Taub, E. (1997). Input-increase and input-decrease types of cortical reorganization after upper extremity amputation in humans. *Experimental Brain Research*, 117(1), 161-164. <https://doi.org/10.1007/s002210050210>
- Emanuel, A. J., Lehnert, B. P., Panzeri, S., Harvey, C. D., & Ginty, D. D. (2021). Cortical responses to touch reflect subcortical integration of LTMR signals. *Nature*, 600(7890), 680-685. <https://doi.org/10.1038/s41586-021-04094-x>
- Enander, J. M. D., & Jörntell, H. (2019). Somatosensory Cortical Neurons Decode Tactile Input Patterns and Location from Both Dominant and Non-dominant Digits. *Cell Reports*, 26(13), 3551-3560.e4. <https://doi.org/10.1016/j.celrep.2019.02.099>
- Engel, M. M., Gadsby, S., Corcoran, A. W., Keizer, A., Dijkerman, H. C., & Hohwy, J. (2022). Waiting longer, feeling fatter : Effects of response delay on tactile distance estimation and confidence in females with anorexia nervosa. *Brain and Behavior*, 12(3), e2422. <https://doi.org/10.1002/brb3.2422>
- Erro, R., Rocchi, L., Antelmi, E., Palladino, R., Tinazzi, M., Rothwell, J., & Bhatia, K. P. (2016). High frequency repetitive sensory stimulation improves temporal discrimination in healthy subjects. *Clinical Neurophysiology*, 127(1), 817-820. <https://doi.org/10.1016/j.clinph.2015.06.023>

- Esposito, R., Cieri, F., Di Giannantonio, M., & Tartaro, A. (2018). The role of body image and self-perception in anorexia nervosa: The neuroimaging perspective. *Journal of Neuropsychology*, *12*(1), 41-52. <https://doi.org/10.1111/jnp.12106>
- Faggin, B. M., Nguyen, K. T., & Nicolelis, M. A. L. (1997). Immediate and simultaneous sensory reorganization at cortical and subcortical levels of the somatosensory system. *Proceedings of the National Academy of Sciences*, *94*(17), 9428-9433. <https://doi.org/10.1073/pnas.94.17.9428>
- Fasold, O., Heinau, J., Trenner, M. U., Villringer, A., & Wenzel, R. (2008). Proprioceptive head posture-related processing in human polysensory cortical areas. *NeuroImage*, *40*(3), 1232-1242. <https://doi.org/10.1016/j.neuroimage.2007.12.060>
- Feldman, D. E. (2012). The Spike-Timing Dependence of Plasticity. *Neuron*, *75*(4), 556-571. <https://doi.org/10.1016/j.neuron.2012.08.001>
- Felician, O., Romaguère, P., Anton, J., Nazarian, B., Roth, M., Poncet, M., & Roll, J. (2004). The role of human left superior parietal lobule in body part localization. *Annals of Neurology*, *55*(5), 749-751. <https://doi.org/10.1002/ana.20109>
- Fitzgerald, P. J., Lane, J. W., Thakur, P. H., & Hsiao, S. S. (2004). Receptive Field Properties of the Macaque Second Somatosensory Cortex: Evidence for Multiple Functional Representations. *The Journal of Neuroscience*, *24*(49), 11193-11204. <https://doi.org/10.1523/JNEUROSCI.3481-04.2004>
- Fitzgerald, P. J., Lane, J. W., Thakur, P. H., & Hsiao, S. S. (2006). Receptive Field (RF) Properties of the Macaque Second Somatosensory Cortex: RF Size, Shape, and Somatotopic Organization. *Journal of Neuroscience*, *26*(24), 6485-6495. <https://doi.org/10.1523/JNEUROSCI.5061-05.2006>
- Fletcher, S. N., Collinger, J. L., Foldes, S. T., Weiss, J. M., Downey, J. E., Tyler-Kabara, E. C., Bensmaia, S. J., Schwartz, A. B., Boninger, M. L., & Gaunt, R. A. (2016). Intracortical microstimulation of human somatosensory cortex. *Science Translational Medicine*, *8*(361). <https://doi.org/10.1126/scitranslmed.aaf8083>
- Flor, H., Elbert, T., Knecht, S., Wienbruch, C., Pantev, C., Birbaumers, N., Larbig, W., & Taub, E. (1995). Phantom-limb pain as a perceptual correlate of cortical reorganization following arm amputation. *Nature*, *375*(6531), 482-484. <https://doi.org/10.1038/375482a0>
- Flor, H., Nikolajsen, L., & Staehelin Jensen, T. (2006). Phantom limb pain: A case of maladaptive CNS plasticity? *Nature Reviews Neuroscience*, *7*(11), 873-881. <https://doi.org/10.1038/nrn1991>
- Florence, S. L., Hackett, T. A., & Strata, F. (2000). Thalamic and Cortical Contributions to Neural Plasticity After Limb Amputation. *Journal of Neurophysiology*, *83*(5), 3154-3159. <https://doi.org/10.1152/jn.2000.83.5.3154>
- Florence, S. L., Taub, H. B., & Kaas, J. H. (1998). Large-Scale Sprouting of Cortical Connections After Peripheral Injury in Adult Macaque Monkeys. *Science*, *282*(5391), 1117-1121. <https://doi.org/10.1126/science.282.5391.1117>
- Florence, S. L., Wall, J. T., & Kaas, J. H. (1989). Somatotopic organization of inputs from the hand to the spinal gray and cuneate nucleus of monkeys with observations on the cuneate nucleus of humans. *Journal of Comparative Neurology*, *286*(1), 48-70. <https://doi.org/10.1002/cne.902860104>
- Florence, S. L., Wall, J. T., & Kaas, J. H. (1991). Central projections from the skin of the hand in squirrel monkeys. *Journal of Comparative Neurology*, *311*(4), 563-578. <https://doi.org/10.1002/cne.903110410>
- Florence, S.L., Kaas, J.H. (1995). Large-Scale Reorganization at Multiple Levels of the Somatosensory Pathway Follows Therapeutic Amputation of the Hand in Monkeys. *The Journal of Neuroscience*, *15*(12), 8083-8095
- Foffani, G., Chapin, J. K., & Moxon, K. A. (2008). Computational Role of Large Receptive Fields in the Primary Somatosensory Cortex. *Journal of Neurophysiology*, *100*(1), 268-280. <https://doi.org/10.1152/jn.01015.2007>
- Foffani, G., Morales-Botello, M. L., & Aguilar, J. (2009). Spike Timing, Spike Count, and Temporal Information for the Discrimination of Tactile Stimuli in the Rat Ventrobasal Complex. *The Journal of Neuroscience*, *29*(18), 5964-5973. <https://doi.org/10.1523/JNEUROSCI.4416-08.2009>
- Forss, N., Jousmäki, V., & Hari, R. (1995). Interaction between afferent input from fingers in human somatosensory cortex. *Brain Research*, *685*(1-2), 68-76. [https://doi.org/10.1016/0006-8993\(95\)00424-O](https://doi.org/10.1016/0006-8993(95)00424-O)
- Frank, S. M. (2024). Transfer of Tactile Learning to Untrained Body Parts: Emerging Cortical Mechanisms. *The Neuroscientist*, *10738584241256277*. <https://doi.org/10.1177/10738584241256277>
- Frank, S. M., Otto, A., Volberg, G., Tse, P. U., Watanabe, T., & Greenlee, M. W. (2022). Transfer of Tactile Learning from Trained to Untrained Body Parts Supported by Cortical Coactivation in Primary Somatosensory Cortex. *The Journal of Neuroscience*, *42*(31), 6131-6144. <https://doi.org/10.1523/JNEUROSCI.0301-22.2022>
- Freeman, A. W., & Johnson, K. O. (1982). A model accounting for effects of vibratory amplitude on responses of cutaneous mechanoreceptors in macaque monkey. *The Journal of Physiology*, *323*(1), 43-64. <https://doi.org/10.1113/jphysiol.1982.sp014060>



- Friedman, D. P., & Murray, E. A. (1986). Thalamic connectivity of the second somatosensory area and neighboring somatosensory fields of the lateral sulcus of the macaque. *Journal of Comparative Neurology*, 252(3), 348-373. <https://doi.org/10.1002/cne.902520305>
- Friedman, R. M., Chen, L. M., & Roe, A. W. (2008). Responses of Areas 3b and 1 in Anesthetized Squirrel Monkeys to Single- and Dual-Site Stimulation of the Digits. *Journal of Neurophysiology*, 100(6), 3185-3196. <https://doi.org/10.1152/jn.90278.2008>
- Fukuda, S., Tsujinaka, R., Oda, H., Hamada, N., Matsuoka, M., & Hiraoka, K. (2023). Suppression of perceptual sensitivity to digital nerve stimulation induced by afferent volley from digital nerve of contralateral homologous finger. *NeuroReport*, 34(8), 436-440. <https://doi.org/10.1097/WNR.0000000000001909>
- Gadsby, S. (2017). Distorted body representations in anorexia nervosa. *Consciousness and Cognition*, 51, 17-33. <https://doi.org/10.1016/j.concog.2017.02.015>
- Gadsby, S. (2019). Body representations and cognitive ontology : Drawing the boundaries of the body image. *Consciousness and Cognition*, 74, 102772. <https://doi.org/10.1016/j.concog.2019.102772>
- Gallagher, S. How the Body Shapes the Mind; Oxford University Press: Oxford, UK, 2005; Volume 284, ISBN 0199271941.
- Gallagher, S., Cole, J., (1995). Body schema and body image in a deafferented subject. *Journal of Mind & Behavior*, 16, 369-390.
- Gandevia, S. C., Burke, D., & McKeon, B. B. (1983). Convergence in the somatosensory pathway between cutaneous afferents from the index and middle fingers in man. *Experimental Brain Research*, 50-50(2-3). <https://doi.org/10.1007/BF00239208>
- Gandevia, S. C., Phegan C. M. L. (1999). Perceptual distortions of the human body image produced by local anaesthesia, pain and cutaneous stimulation. *The Journal of Physiology*, 514(Pt 2), 609-616.
- García-Piqueras, J., García-Mesa, Y., Cárcaba, L., Feito, J., Torres-Parejo, I., Martín-Biedma, B., Cobo, J., García-Suárez, O., & Vega, J. A. (2019). Ageing of the somatosensory system at the periphery : Age-related changes in cutaneous mechanoreceptors. *Journal of Anatomy*, 234(6), 839-852. <https://doi.org/10.1111/joa.12983>
- Gardner, E. P., & Palmer, C. I. (1989). Simulation of motion on the skin. I. Receptive fields and temporal frequency coding by cutaneous mechanoreceptors of OPTACON pulses delivered to the hand. *Journal of Neurophysiology*, 62(6), 1410-1436. <https://doi.org/10.1152/jn.1989.62.6.1410>
- Gatica Tossi, M. A., Stude, P., Schwenkreis, P., Tegenthoff, M., & Dinse, H. R. (2013). Behavioural and neurophysiological markers reveal differential sensitivity to homeostatic interactions between centrally and peripherally applied passive stimulation. *European Journal of Neuroscience*, 38(6), 2893-2901. <https://doi.org/10.1111/ejn.12293>
- Gaudio, S., & Quattrocchi, C. C. (2012). Neural basis of a multidimensional model of body image distortion in anorexia nervosa. *Neuroscience & Biobehavioral Reviews*, 36(8), 1839-1847. <https://doi.org/10.1016/j.neubiorev.2012.05.003>
- Geyer S, Schleicher A, Zilles K (1999) Areas 3a, 3b, and 1 of human primary somatosensory cortex. Microstructural organization and interindividual variability. *Neuroimage* 10:63–83.
- Gharbawie, O. A., Stepniewska, I., Qi, H., & Kaas, J. H. (2011). Multiple Parietal–Frontal Pathways Mediate Grasping in Macaque Monkeys. *The Journal of Neuroscience*, 31(32), 11660-11677. <https://doi.org/10.1523/JNEUROSCI.1777-11.2011>
- Ghazanfar, A., Krupa, D., & Nicolelis, M. (2001). Role of cortical feedback in the receptive field structure and nonlinear response properties of somatosensory thalamic neurons. *Experimental Brain Research*, 141(1), 88-100. <https://doi.org/10.1007/s002210100849>
- Gibson, G. O., Makinson, C. D., & Sathian, K. (2009). Tactile co-activation improves detection of afferent spatial modulation. *Experimental Brain Research*, 194(3), 409-417. <https://doi.org/10.1007/s00221-009-1717-5>
- Giurgola, S., Pisoni, A., Maravita, A., Vallar, G., & Bolognini, N. (2019). Somatosensory cortical representation of the body size. *Human Brain Mapping*, 40(12), 3534-3547. <https://doi.org/10.1002/hbm.24614>
- Glasser, M. F., Coalson, T. S., Robinson, E. C., Hacker, C. D., Harwell, J., Yacoub, E., Ugurbil, K., Andersson, J., Beckmann, C. F., Jenkinson, M., Smith, S. M., & Van Essen, D. C. (2016). A multi-modal parcellation of human cerebral cortex. *Nature*, 536(7615), 171-178. <https://doi.org/10.1038/nature18933>
- Godde, B., Ehrhardt, J., Braun, C. (2003). Behavioral significance of input-dependent plasticity of human somatosensory cortex. *NeuroReport*, 14(4). 10.1097/01.wnr.0000060833.03650.f7.
- Godde, B., Spengler, F., Dinse, H. R. (1996). Associative pairing of tactile stimulation induces somatosensory cortical reorganization in rats and humans. *NeuroReport*, 8(1), 281-285.
- Godde, B., Stauffenberg, B., Spengler, F., & Dinse, H. R. (2000). Tactile Coactivation-Induced Changes in Spatial Discrimination Performance. *The Journal of Neuroscience*, 20(4), 1597-1604. <https://doi.org/10.1523/JNEUROSCI.20-04-01597.2000>
- Goodwin, A. W., & Wheat, H. E. (1999). Effects of Nonuniform Fiber Sensitivity, Innervation Geometry, and Noise on Information Relayed by a Population of Slowly Adapting Type I Primary Afferents from the

- Fingerpad. *The Journal of Neuroscience*, 19(18), 8057-8070. <https://doi.org/10.1523/JNEUROSCI.19-18-08057.1999>
- Goodwin, A. W., & Wheat, H. E. (2004). Sensory signals in neural populations underlying tactile perception and manipulation. *Annual Review of Neuroscience*, 27(1), 53-77. <https://doi.org/10.1146/annurev.neuro.26.041002.131032>
- Haag, L. M., Heba, S., Lenz, M., Glaubitz, B., Höffken, O., Kalisch, T., Puts, N. A., Edden, R. A. E., Tegenthoff, M., Dinse, H., & Schmidt-Wilcke, T. (2015). Resting BOLD fluctuations in the primary somatosensory cortex correlate with tactile acuity. *Cortex*, 64, 20-28. <https://doi.org/10.1016/j.cortex.2014.09.018>
- Handler, A., & Ginty, D. D. (2021). The mechanosensory neurons of touch and their mechanisms of activation. *Nature Reviews Neuroscience*, 22(9), 521-537. <https://doi.org/10.1038/s41583-021-00489-x>
- Hari, R., Karhu, J., Hämäläinen, M., Knuutila, J., Salonen, O., Sams, M., & Vilkmann, V. (1993). Functional Organization of the Human First and Second Somatosensory Cortices: A Neuromagnetic Study. *European Journal of Neuroscience*, 5(6), 724-734. <https://doi.org/10.1111/j.1460-9568.1993.tb00536.x>
- Harrar, V., Spence, C., & Makin, T. R. (2014). Topographic generalization of tactile perceptual learning. *Journal of Experimental Psychology: Human Perception and Performance*, 40(1), 15-23. <https://doi.org/10.1037/a0033200>
- Harris, J. A., Harris, I. M., & Diamond, M. E. (2001). The Topography of Tactile Learning in Humans. *The Journal of Neuroscience*, 21(3), 1056-1061. <https://doi.org/10.1523/JNEUROSCI.21-03-01056.2001>
- Härtner, J., Strauss, S., Pfannmöller, J., & Lotze, M. (2021). Tactile acuity of fingertips and hand representation size in human Area 3b and Area 1 of the primary somatosensory cortex. *NeuroImage*, 232, 117912. <https://doi.org/10.1016/j.neuroimage.2021.117912>
- Hayward, V., Terekhov, A. V., Wong, S.-C., Geborek, P., Bengtsson, F., & Jörntell, H. (2014). Spatio-temporal skin strain distributions evoke low variability spike responses in cuneate neurons. *Journal of The Royal Society Interface*, 11(93), 20131015. <https://doi.org/10.1098/rsif.2013.1015>
- Head, H., & Holmes, G. (1911). Sensory disturbances from cerebral lesions. *Brain*, 34, 102-254. doi:10.1093/brain/34.2-3.102.
- Health M, Murray EA, Mishkin M (1984) Relative contributions of SII and area 5 to tactile discrimination in monkeys. *Behav Brain Res* 11:67-83.
- Heba, S., Lenz, M., Kalisch, T., Höffken, O., Schweizer, L. M., Glaubitz, B., Puts, N. A. J., Tegenthoff, M., Dinse, H. R., & Schmidt-Wilcke, T. (2017). Regionally Specific Regulation of Sensorimotor Network Connectivity Following Tactile Improvement. *Neural Plasticity*, 2017, 1-11. <https://doi.org/10.1155/2017/5270532>
- Hebb, D. O. (1949). *The organization of behavior; a neuropsychological theory*. Wiley and Sons, New York.
- Heed, T., & Röder, B. (2012). *Chapter 28 The Body in a Multisensory World*.
- Henderson, J., Mari, T., Hewitt, D., Newton-Fenner, A., Giesbrecht, T., Marshall, A., Stancak, A., & Fallon, N. (2023). The neural correlates of texture perception: A systematic review and activation likelihood estimation meta-analysis of functional magnetic resonance imaging studies. *Brain and Behavior*, 13(11), e3264. <https://doi.org/10.1002/brb3.3264>
- Henley, C. (2021). *Foundations of Neuroscience*. Michigan State University Libraries. ISBN: 978-1-62610-109-8
- Hicks, T. P., & Dykes, R. W. (1983). Receptive field size for certain neurons in primary somatosensory cortex is determined by GABA-mediated intracortical inhibition. *Brain Research*, 274(1), 160-164. [https://doi.org/10.1016/0006-8993\(83\)90533-4](https://doi.org/10.1016/0006-8993(83)90533-4)
- Hirai, D., Nakamura, K. C., Shibata, K., Tanaka, T., Hioki, H., Kaneko, T., & Furuta, T. (2018). Shaping somatosensory responses in awake rats: Cortical modulation of thalamic neurons. *Brain Structure and Function*, 223(2), 851-872. <https://doi.org/10.1007/s00429-017-1522-z>
- Hlushchuk, Y., & Hari, R. (2006). Transient Suppression of Ipsilateral Primary Somatosensory Cortex during Tactile Finger Stimulation. *The Journal of Neuroscience*, 26(21), 5819-5824. <https://doi.org/10.1523/JNEUROSCI.5536-05.2006>
- Hodzic, A., Veit, R., Karim, A. A., Erb, M., & Godde, B. (2004). Improvement and Decline in Tactile Discrimination Behavior after Cortical Plasticity Induced by Passive Tactile Coactivation. *The Journal of Neuroscience*, 24(2), 442-446. <https://doi.org/10.1523/JNEUROSCI.3731-03.2004>
- Hoechstetter, K., Rupp, A., Stančák, A., Meinck, H.-M., Stippich, C., Berg, P., & Scherg, M. (2001). Interaction of Tactile Input in the Human Primary and Secondary Somatosensory Cortex—A Magnetoencephalographic Study. *NeuroImage*, 14(3), 759-767. <https://doi.org/10.1006/nimg.2001.0855>
- Höffken, O., Veit, M., Knossalla, F., Lissek, S., Bliem, B., Ragert, P., Dinse, H. R., & Tegenthoff, M. (2007). Sustained increase of somatosensory cortex excitability by tactile coactivation studied by paired median nerve stimulation in humans correlates with perceptual gain. *The Journal of Physiology*, 584(2), 463-471. <https://doi.org/10.1113/jphysiol.2007.140079>

- Holmes, N. P., & Tamè, L. (2023). Detection, Discrimination & Localization : The Psychophysics of Touch. In N. P. Holmes (Ed.), *Somatosensory Research Methods* (Vol. 196, p. 3-33). Springer US. [https://doi.org/10.1007/978-1-0716-3068-6\\_1](https://doi.org/10.1007/978-1-0716-3068-6_1)
- Holmes, N. P., Snijders, H. J., & Spence, C. (2006). Reaching with alien limbs : Visual exposure to prosthetic hands in a mirror biases proprioception without accompanying illusions of ownership. *Perception & Psychophysics*, *68*(4), 685-701. <https://doi.org/10.3758/BF03208768>
- Hong, J. H., Kwon, H. G., & Jang, S. H. (2011). Probabilistic Somatotopy of the Spinothalamic Pathway at the Ventroposterolateral Nucleus of the Thalamus in the Human Brain. *American Journal of Neuroradiology*, *32*(7), 1358-1362. <https://doi.org/10.3174/ajnr.A2497>
- Hordacre, B., Bradnam, L. V., Barr, C., Patriitti, B. L., & Crotty, M. (2015). Intracortical inhibition is modulated by phase of prosthetic rehabilitation in transtibial amputees. *Frontiers in Human Neuroscience*, *09*. <https://doi.org/10.3389/fnhum.2015.00276>
- Hsiao, S. S., Lane, J., & Fitzgerald, P. (2002). Representation of orientation in the somatosensory system. *Behavioural Brain Research*, *135*(1-2), 93-103. [https://doi.org/10.1016/S0166-4328\(02\)00160-2](https://doi.org/10.1016/S0166-4328(02)00160-2)
- Huber, L., Finn, E. S., Handwerker, D. A., Bönstrup, M., Glen, D. R., Kashyap, S., Ivanov, D., Petridou, N., Marrett, S., Goense, J., Poser, B. A., & Bandettini, P. A. (2020). Sub-millimeter fMRI reveals multiple topographical digit representations that form action maps in human motor cortex. *NeuroImage*, *208*, 116463. <https://doi.org/10.1016/j.neuroimage.2019.116463>
- Hyvärinen, J., & Poranen, A. (1978). Receptive field integration and submodality convergence in the hand area of the post-central gyrus of the alert monkey. *The Journal of Physiology*, *283*(1), 539-556. <https://doi.org/10.1113/jphysiol.1978.sp012518>
- Ionta, S., Villiger, M., Jutzeler, C. R., Freund, P., Curt, A., & Gassert, R. (2016). Spinal cord injury affects the interplay between visual and sensorimotor representations of the body. *Scientific Reports*, *6*(1), 20144. <https://doi.org/10.1038/srep20144>
- Iwamura Y (1998) Hierarchical somatosensory processing. *Curr Opin Neurobiol* 8:522–528.
- Iwamura Y, Taoka M, Iriki A (2001) Bilateral activity and callosal connections in the somatosensory cortex. *Neuroscience*. 7:419–429.
- Iwamura, Y. (2000). *Bilateral receptive field neurons and callosal connections in the somatosensory cortex*.
- Jain, N., Florence, S. L., & Kaas, J. H. (1998). Reorganization of Somatosensory Cortex After Nerve and Spinal Cord Injury. *Physiology*, *13*(3), 143-149. <https://doi.org/10.1152/physiologyonline.1998.13.3.143>
- Jain, N., Florence, S. L., Qi, H.-X., & Kaas, J. H. (2000). Growth of new brainstem connections in adult monkeys with massive sensory loss. *Proceedings of the National Academy of Sciences*, *97*(10), 5546-5550. <https://doi.org/10.1073/pnas.090572597>
- Jain, N., Qi, H.-X., Collins, C. E., & Kaas, J. H. (2008). Large-Scale Reorganization in the Somatosensory Cortex and Thalamus after Sensory Loss in Macaque Monkeys. *The Journal of Neuroscience*, *28*(43), 11042-11060. <https://doi.org/10.1523/JNEUROSCI.2334-08.2008>
- Janig, W., Spencer, W. A., & Younkin, S. G. (1979). Spatial and temporal features of afferent inhibition of thalamocortical relay cells. *Journal of Neurophysiology*, *42*(5), 1450-1460. <https://doi.org/10.1152/jn.1979.42.5.1450>
- Jarocka, E., Pruszyński, J. A., & Johansson, R. S. (2021). Human Touch Receptors Are Sensitive to Spatial Details on the Scale of Single Fingerprint Ridges. *The Journal of Neuroscience*, *41*(16), 3622-3634. <https://doi.org/10.1523/JNEUROSCI.1716-20.2021>
- Jenkins, W. M., Merzenich, M. M., Ochs, M. T., Allard, T., & Guic-Robles, E. (1990). Functional reorganization of primary somatosensory cortex in adult owl monkeys after behaviorally controlled tactile stimulation. *Journal of Neurophysiology*, *63*(1), 82-104. <https://doi.org/10.1152/jn.1990.63.1.82>
- Jiang, W., Tremblay, F., & Chapman, C. E. (1997). Neuronal Encoding of Texture Changes in the Primary and the Secondary Somatosensory Cortical Areas of Monkeys During Passive Texture Discrimination. *Journal of Neurophysiology*, *77*(3), 1656-1662. <https://doi.org/10.1152/jn.1997.77.3.1656>
- Johansson, R. S., & Vallbo, A. B. (1979). Tactile sensibility in the human hand : Relative and absolute densities of four types of mechanoreceptive units in glabrous skin. *The Journal of Physiology*, *286*(1), 283-300. <https://doi.org/10.1113/jphysiol.1979.sp012619>
- Johansson, R. S., & Vallbo, Å. B. (1983). Tactile sensory coding in the glabrous skin of the human hand. *Trends in Neurosciences*, *6*, 27-32. [https://doi.org/10.1016/0166-2236\(83\)90011-5](https://doi.org/10.1016/0166-2236(83)90011-5)
- Johnson, J. I., Welker, W. I., & Pubols, B. H. (1968). Somatotopic organization of raccoon dorsal column nuclei. *Journal of Comparative Neurology*, *132*(1), 1-43. <https://doi.org/10.1002/cne.901320102>
- Johnson, K. (2001). The roles and functions of cutaneous mechanoreceptors. *Current Opinion in Neurobiology*, *11*(4), 455-461. [https://doi.org/10.1016/S0959-4388\(00\)00234-8](https://doi.org/10.1016/S0959-4388(00)00234-8)
- Johnson, K. O., & Phillips, J. R. (1981). Tactile spatial resolution. I. Two-point discrimination, gap detection, grating resolution, and letter recognition. *Journal of Neurophysiology*, *46*(6), 1177-1192. <https://doi.org/10.1152/jn.1981.46.6.1177>

- Johnson, K.O., Van Boven, R.W., & Hsiao, S.S. (1994). The perception of two points is not the spatial resolution threshold. In J. Boivie, P. Hansson, & U. Lindblom (Eds.), *Touch, temperature, and pain in health and disease: Mechanisms and assessments* (pp. 389–404). Seattle, WA: IASP Press
- Jones, E. G. (1993). GABAergic Neurons and Their Role in Cortical Plasticity in Primates. *Cerebral Cortex*, *3*(5), 361-372. <https://doi.org/10.1093/cercor/3.5.361-a>
- Jones, E. G., Manger, P. R., & Woods, T. M. (1997). Maintenance of a somatotopic cortical map in the face of diminishing thalamocortical inputs. *Proceedings of the National Academy of Sciences*, *94*(20), 11003-11007. <https://doi.org/10.1073/pnas.94.20.11003>
- Jörntell, H., Bengtsson, F., Geborek, P., Spanne, A., Terekhov, A. V., & Hayward, V. (2014). Segregation of Tactile Input Features in Neurons of the Cuneate Nucleus. *Neuron*, *83*(6), 1444-1452. <https://doi.org/10.1016/j.neuron.2014.07.038>
- Jung, S.-C., & Shin, H.-C. (2002). Suppression of temporary deafferentation-induced plasticity in the primary somatosensory cortex of rats by GABA antagonist. *Neuroscience Letters*, *334*(2), 87-90. [https://doi.org/10.1016/S0304-3940\(02\)01108-4](https://doi.org/10.1016/S0304-3940(02)01108-4)
- Kakigi, R., & Jones, S. J. (1985). Effects on median nerve SEPs of tactile stimulation applied to adjacent and remote areas of the body surface. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section*, *62*(4), 252-265. [https://doi.org/10.1016/0168-5597\(85\)90003-6](https://doi.org/10.1016/0168-5597(85)90003-6)
- Kalisch, T., Tegenthoff, M., & Dinse, H. R. (2007). Differential effects of synchronous and asynchronous multifinger coactivation on human tactile performance. *BMC Neuroscience*, *8*(1), 58. <https://doi.org/10.1186/1471-2202-8-58>
- Kambi, N., Halder, P., Rajan, R., Arora, V., Chand, P., Arora, M., & Jain, N. (2014). Large-scale reorganization of the somatosensory cortex following spinal cord injuries is due to brainstem plasticity. *Nature Communications*, *5*(1), 3602. <https://doi.org/10.1038/ncomms4602>
- Kammers, M. P. M., Kootker, J. A., Hogendoorn, H., & Dijkerman, H. C. (2010). How many motoric body representations can we grasp? *Experimental Brain Research*, *202*(1), 203-212. <https://doi.org/10.1007/s00221-009-2124-7>
- Kammers, M. P. M., Longo, M. R., Tsakiris, M., Dijkerman, H. C., & Haggard, P. (2009). Specificity and Coherence of Body Representations. *Perception*, *38*(12), 1804-1820. <https://doi.org/10.1068/p6389>
- Kang, W., & Longo, M. R. (2023). Tactile localization on stretched skin. *Journal of Experimental Psychology: Human Perception and Performance*, *49*(8), 1175-1179. <https://doi.org/10.1037/xhp0001142>
- Karl, A., Birbaumer, N., Lutzenberger, W., Cohen, L. G., & Flor, H. (2001). Reorganization of Motor and Somatosensory Cortex in Upper Extremity Amputees with Phantom Limb Pain. *The Journal of Neuroscience*, *21*(10), 3609-3618. <https://doi.org/10.1523/JNEUROSCI.21-10-03609.2001>
- Kattenstroth, J. C., Kalisch, T., Sczesny-Kaiser, M., Greulich, W., Tegenthoff, M., & Dinse, H. R. (2018). Daily repetitive sensory stimulation of the paretic hand for the treatment of sensorimotor deficits in patients with subacute stroke: RESET, a randomized, sham-controlled trial. *BMC Neurology*, *18*(1), 2. <https://doi.org/10.1186/s12883-017-1006-z>
- Katz, D. B., Simon, S. A., Moody, A., & Nicoletis, M. A. L. (1999). Simultaneous Reorganization in Thalamocortical Ensembles Evolves Over Several Hours After Perioral Capsaicin Injections. *Journal of Neurophysiology*, *82*(2), 963-977. <https://doi.org/10.1152/jn.1999.82.2.963>
- Keizer, A., Smeets, M. A. M., Dijkerman, H. C., Van Elburg, A., & Postma, A. (2012). Aberrant somatosensory perception in Anorexia Nervosa. *Psychiatry Research*, *200*(2-3), 530-537. <https://doi.org/10.1016/j.psychres.2012.05.001>
- Kemmerer, D., & Tranel, D. (2008). Searching for the elusive neural substrates of body part terms: A neuropsychological study. *Cognitive Neuropsychology*, *25*(4), 601-629. <https://doi.org/10.1080/02643290802247052>
- Khoshnejad, M., Piché, M., Saleh, S., Duncan, G., & Rainville, P. (2014). Serial processing in primary and secondary somatosensory cortex : A DCM analysis of human fMRI data in response to innocuous and noxious electrical stimulation. *Neuroscience Letters*, *577*, 83-88. <https://doi.org/10.1016/j.neulet.2014.06.013>
- Kikkert, S., Kolasinski, J., Jbadi, S., Tracey, I., Beckmann, C. F., Johansen-Berg, H., & Makin, T. R. (2016). Revealing the neural fingerprints of a missing hand. *eLife*, *5*, e15292. <https://doi.org/10.7554/eLife.15292>
- Kikkert, S., Pfyffer, D., Verling, M., Freund, P., & Wenderoth, N. (2021). Finger somatotopy is preserved after tetraplegia but deteriorates over time. *eLife*, *10*, e67713. <https://doi.org/10.7554/eLife.67713>
- Killackey, H. P., Gould, H. J., Cusick, C. G., Pons, T. P., & Kaas, J. H. (1983). The relation of corpus callosum connections to architectonic fields and body surface maps in sensorimotor cortex of new and old world monkeys. *Journal of Comparative Neurology*, *219*(4), 384-419. <https://doi.org/10.1002/cne.902190403>
- Kilteni, K., & Ehrsson, H. H. (2020). Functional Connectivity between the Cerebellum and Somatosensory Areas Implements the Attenuation of Self-Generated Touch. *The Journal of Neuroscience*, *40*(4), 894-906. <https://doi.org/10.1523/JNEUROSCI.1732-19.2019>

- Kilteni, K., Maselli, A., Kording, K. P., & Slater, M. (2015). Over my fake body : Body ownership illusions for studying the multisensory basis of own-body perception. *Frontiers in Human Neuroscience*, 9. <https://doi.org/10.3389/fnhum.2015.00141>
- Kim, Y. R., Kim, C.-E., Yoon, H., Kim, S. K., & Kim, S. J. (2020). Multiplexed Processing of Vibrotactile Information in the Mouse Primary Somatosensory Cortex. *Experimental Neurobiology*, 29(6), 425-432. <https://doi.org/10.5607/en20041>
- Klaver, M., & Dijkerman, H. C. (2016). Bodily Experience in Schizophrenia : Factors Underlying a Disturbed Sense of Body Ownership. *Frontiers in Human Neuroscience*, 10. <https://doi.org/10.3389/fnhum.2016.00305>
- Klingner, C. M., Brodoehl, S., Huonker, R., & Witte, O. W. (2016). The Processing of Somatosensory Information Shifts from an Early Parallel into a Serial Processing Mode : A Combined fMRI/MEG Study. *Frontiers in Systems Neuroscience*, 10. <https://doi.org/10.3389/fnsys.2016.00103>
- Klingner, C. M., Huonker, R., Flemming, S., Hasler, C., Brodoehl, S., Preul, C., Burmeister, H., Kastrup, A., & Witte, O. W. (2011). Functional deactivations : Multiple ipsilateral brain areas engaged in the processing of somatosensory information. *Human Brain Mapping*, 32(1), 127-140. <https://doi.org/10.1002/hbm.21006>
- Knecht, S., Henningsen, H., Elbert, T., Flor, H., Hohling, C., Pantev, C., & Taub, E. (1996). Reorganizational and perceptual changes after amputation. *Brain*, 119(4), 1213-1219. <https://doi.org/10.1093/brain/119.4.1213>
- Kolasinski, J., Makin, T. R., Logan, J. P., Jbabdi, S., Clare, S., Stagg, C. J., & Johansen-Berg, H. (2016). Perceptually relevant remapping of human somatotopy in 24 hours. *eLife*, 5, e17280. <https://doi.org/10.7554/eLife.17280>
- Kowalewski, R., Kattenstroth, J.-C., Kalisch, T., & Dinse, H. R. (2012). Improved Acuity and Dexterity but Unchanged Touch and Pain Thresholds following Repetitive Sensory Stimulation of the Fingers. *Neural Plasticity*, 2012, 1-10. <https://doi.org/10.1155/2012/974504>
- Krubitzer, L., & Kaas, J. (1990). The organization and connections of somatosensory cortex in marmosets. *The Journal of Neuroscience*, 10(3), 952-974. <https://doi.org/10.1523/JNEUROSCI.10-03-00952.1990>
- Krupa, D. J., Ghazanfar, A. A., & Nicolelis, M. A. L. (1999). Immediate thalamic sensory plasticity depends on corticothalamic feedback. *Proceedings of the National Academy of Sciences*, 96(14), 8200-8205. <https://doi.org/10.1073/pnas.96.14.8200>
- Kuehn, E. D., Meltzer, S., Abaira, V. E., Ho, C.-Y., & Ginty, D. D. (2019). Tiling and somatotopic alignment of mammalian low-threshold mechanoreceptors. *Proceedings of the National Academy of Sciences*, 116(19), 9168-9177. <https://doi.org/10.1073/pnas.1901378116>
- Kuehn, E., Dinse, J., Jakobsen, E., Long, X., Schäfer, A., Bazin, P.-L., Villringer, A., Sereno, M. I., & Margulies, D. S. (2017). Body Topography Parcellates Human Sensory and Motor Cortex. *Cerebral Cortex*, 27(7), 3790-3805. <https://doi.org/10.1093/cercor/bhx026>
- Kuo, H.-C., Gordon, A. M., Henrionnet, A., Hautfenne, S., Friel, K. M., & Bleyenheuft, Y. (2016). The effects of intensive bimanual training with and without tactile training on tactile function in children with unilateral spastic cerebral palsy : A pilot study. *Research in Developmental Disabilities*, 49-50, 129-139. <https://doi.org/10.1016/j.ridd.2015.11.024>
- Kwak, H., Koh, W., Kim, S., Song, K., Shin, J.-I., Lee, J. M., Lee, E. H., Bae, J. Y., Ha, G. E., Oh, J.-E., Park, Y. M., Kim, S., Feng, J., Lee, S. E., Choi, J. W., Kim, K. H., Kim, Y. S., Woo, J., Lee, D., ... Cheong, E. (2020). Astrocytes Control Sensory Acuity via Tonic Inhibition in the Thalamus. *Neuron*, 108(4), 691-706.e10. <https://doi.org/10.1016/j.neuron.2020.08.013>
- Lackner, J. R. (1988). Some proprioceptive influences on the perceptual representation of body shape and orientation. *Brain*, 111(2), 281-297. <https://doi.org/10.1093/brain/111.2.281>
- Laiacona, M., Allamano, N., Lorenzi, L., & Capitani, E. (2006). A Case of Impaired Naming and Knowledge of Body Parts. Are Limbs a Separate Sub-category? *Neurocase*, 12(5), 307-316. <https://doi.org/10.1080/13554790601125940>
- LaMotte, R. H., & Whitehouse, J. (1986). Tactile detection of a dot on a smooth surface : Peripheral neural events. *Journal of Neurophysiology*, 56(4), 1109-1128. <https://doi.org/10.1152/jn.1986.56.4.1109>
- Lenz, M., Tegenthoff, M., Kohlhaas, K., Stude, P., Höffken, O., Gatica Tossi, M. A., Kalisch, T., & Dinse, H. R. (2012). Increased Excitability of Somatosensory Cortex in Aged Humans is Associated with Impaired Tactile Acuity. *The Journal of Neuroscience*, 32(5), 1811-1816. <https://doi.org/10.1523/JNEUROSCI.2722-11.2012>
- Levy, L. M., Ziemann, U., Chen, R., & Cohen, L. G. (2002). Rapid modulation of GABA in sensorimotor cortex induced by acute deafferentation. *Annals of Neurology*, 52(6), 755-761. <https://doi.org/10.1002/ana.10372>

- Li, C.X., Waters, R.S. (1996). In vivo intracellular recording and labeling of neurons in the forepaw barrel subfield (FBS) of rat somatosensory cortex: possible physiological and morphological substrates for reorganization. *NeuroReport*, 7, 2261-2272.
- Liang, M., Mouraux, A., & Iannetti, G. D. (2011). Parallel Processing of Nociceptive and Non-nociceptive Somatosensory Information in the Human Primary and Secondary Somatosensory Cortices : Evidence from Dynamic Causal Modeling of Functional Magnetic Resonance Imaging Data. *Journal of Neuroscience*, 31(24), 8976-8985. <https://doi.org/10.1523/JNEUROSCI.6207-10.2011>
- Liao, C., Reed, J. L., Kaas, J. H., & Qi, H. (2016). Intracortical connections are altered after long-standing deprivation of dorsal column inputs in the hand region of area 3b in squirrel monkeys. *Journal of Comparative Neurology*, 524(7), 1494-1526. <https://doi.org/10.1002/cne.23921>
- Linkenauger, S. A., Wong, H. Y., Geuss, M., Stefanucci, J. K., McCulloch, K. C., Bühlhoff, H. H., Mohler, B. J., & Proffitt, D. R. (2015). The perceptual homunculus : The perception of the relative proportions of the human body. *Journal of Experimental Psychology: General*, 144(1), 103-113. <https://doi.org/10.1037/xge0000028>
- Lipton, M. L., Fu, K.-M. G., Branch, C. A., & Schroeder, C. E. (2006). Ipsilateral Hand Input to Area 3b Revealed by Converging Hemodynamic and Electrophysiological Analyses in Macaque Monkeys. *The Journal of Neuroscience*, 26(1), 180-185. <https://doi.org/10.1523/JNEUROSCI.1073-05.2006>
- Lipton, M. L., Liszewski, M. C., O'Connell, M. N., Mills, A., Smiley, J. F., Branch, C. A., Isler, J. R., & Schroeder, C. E. (2010). Interactions within the Hand Representation in Primary Somatosensory Cortex of Primates. *The Journal of Neuroscience*, 30(47), 15895-15903. <https://doi.org/10.1523/JNEUROSCI.4765-09.2010>
- Liu, L. C., Gaetz, W. C., Bosnyak, D. J., & Roberts, L. E. (2000). Evidence for fusion and segregation induced by 21 Hz multiple-digit stimulation in humans: *NeuroReport*, 11(10), 2313-2318. <https://doi.org/10.1097/00001756-200007140-00049>
- Liu, Y., Ma, J., Li, H., Shi, W., Xiao, Z., Yang, Q., Zhao, Q., Wang, F., Tao, X., & Bai, Y. (2023). Which sites better represent the sensory function of hands in convalescent stroke patients? A study based on electrophysiological examination. *Frontiers in Neuroscience*, 16, 1065629. <https://doi.org/10.3389/fnins.2022.1065629>
- Longo, M. R. (2020). Tactile distance anisotropy on the palm : A meta-analysis. *Attention, Perception, & Psychophysics*, 82(4), 2137-2146. <https://doi.org/10.3758/s13414-019-01951-w>
- Longo, M. R. (2022). Distortion of mental body representations. *Trends in Cognitive Sciences*, 26(3), 241-254. <https://doi.org/10.1016/j.tics.2021.11.005>
- Longo, M. R. (2023). Motor adaptation and distorted body representations. *Trends in Cognitive Sciences*, 27(1), 9. <https://doi.org/10.1016/j.tics.2022.10.006>
- Longo, M. R., & Haggard, P. (2010). An implicit body representation underlying human position sense. *Proceedings of the National Academy of Sciences*, 107(26), 11727-11732. <https://doi.org/10.1073/pnas.1003483107>
- Longo, M. R., & Haggard, P. (2011). Weber's illusion and body shape : Anisotropy of tactile size perception on the hand. *Journal of Experimental Psychology: Human Perception and Performance*, 37(3), 720-726. <https://doi.org/10.1037/a0021921>
- Longo, M. R., & Haggard, P. (2012a). A 2.5-D representation of the human hand. *Journal of Experimental Psychology: Human Perception and Performance*, 38(1), 9-13. <https://doi.org/10.1037/a0025428>
- Longo, M. R., & Haggard, P. (2012b). Implicit body representations and the conscious body image. *Acta Psychologica*, 141(2), 164-168. <https://doi.org/10.1016/j.actpsy.2012.07.015>
- Longo, M. R., & Holmes, M. (2020). Distorted perceptual face maps. *Acta Psychologica*, 208, 103128. <https://doi.org/10.1016/j.actpsy.2020.103128>
- Longo, M. R., & Morcom, R. (2016). No Correlation between Distorted Body Representations Underlying Tactile Distance Perception and Position Sense. *Frontiers in Human Neuroscience*, 10. <https://doi.org/10.3389/fnhum.2016.00593>
- Longo, M. R., Lulciuc, A., & Sotakova, L. (2019). No evidence of tactile distance anisotropy on the belly. *Royal Society Open Science*, 6(3), 180866. <https://doi.org/10.1098/rsos.180866>
- Longo, M. R., Mancini, F., & Haggard, P. (2015). Implicit body representations and tactile spatial remapping. *Acta Psychologica*, 160, 77-87. <https://doi.org/10.1016/j.actpsy.2015.07.002>
- Loomis, J. (1979). An Investigation of Tactile Hyperacuity. *Sensory processes*, 3, 289-302.
- Loomis, J. M., & Collins, C. C. (1978). Sensitivity to shifts of a point stimulus : An instance of tactile hyperacuity. *Perception & Psychophysics*, 24(6), 487-492. <https://doi.org/10.3758/BF03198771>
- Lotze, M. (2001). Phantom movements and pain An fMRI study in upper limb amputees. *Brain*, 124(11), 2268-2277. <https://doi.org/10.1093/brain/124.11.2268>
- Lundborg, G., & Rosén, B. (2004). The Two-Point Discrimination Test – Time For a Re-Appraisal? *Journal of Hand Surgery*, 29(5), 418-422. <https://doi.org/10.1016/J.JHSB.2004.02.008>

- Mainka, T., Ganos, C., Longo, M.R. (2023). Skin stretch modulates tactile distance perception without central correction mechanisms. *Journal of Experimental Psychology*, 49(2), 226-235.
- Makin, T. R., & Bensmaia, S. J. (2017). Stability of Sensory Topographies in Adult Cortex. *Trends in Cognitive Sciences*, 21(3), 195-204. <https://doi.org/10.1016/j.tics.2017.01.002>
- Makin, T. R., & Flor, H. (2020). Brain (re)organisation following amputation : Implications for phantom limb pain. *NeuroImage*, 218, 116943. <https://doi.org/10.1016/j.neuroimage.2020.116943>
- Makin, T. R., Cramer, A. O., Scholz, J., Hahamy, A., Henderson Slater, D., Tracey, I., & Johansen-Berg, H. (2013). Deprivation-related and use-dependent plasticity go hand in hand. *eLife*, 2, e01273. <https://doi.org/10.7554/eLife.01273>
- Makin, T. R., Scholz, J., Henderson Slater, D., Johansen-Berg, H., & Tracey, I. (2015). Reassessing cortical reorganization in the primary sensorimotor cortex following arm amputation. *Brain*, 138(8), 2140-2146. <https://doi.org/10.1093/brain/awv161>
- Mancini, F., Longo, M. R., Iannetti, G. D., & Haggard, P. (2011). A supramodal representation of the body surface. *Neuropsychologia*, 49(5), 1194-1201. <https://doi.org/10.1016/j.neuropsychologia.2010.12.040>
- Manser-Smith, K., Tamè, L., Longo, M.R. (2021). Tactile distance anisotropy on the feet. *Attention, Perception and Psychophysics*, 83(8), 3227-3239. [10.3758/s13414-021-02339-5](https://doi.org/10.3758/s13414-021-02339-5).
- Margolis, A. N., & Longo, M. R. (2015). Visual detail about the body modulates tactile localisation biases. *Experimental Brain Research*, 233(2), 351-358. <https://doi.org/10.1007/s00221-014-4118-3>
- Marino, B. F. M., Stucchi, N., Nava, E., Haggard, P., & Maravita, A. (2010). Distorting the visual size of the hand affects hand pre-shaping during grasping. *Experimental Brain Research*, 202(2), 499-505. <https://doi.org/10.1007/s00221-009-2143-4>
- Markram, H., Lübke, J., Frotscher, M., & Sakmann, B. (1997). Regulation of Synaptic Efficacy by Coincidence of Postsynaptic APs and EPSPs. *Science*, 275(5297), 213-215. <https://doi.org/10.1126/science.275.5297.213>
- Martel, M., Cardinali, L., Roy, A. C., & Farnè, A. (2016). Tool-use : An open window into body representation and its plasticity. *Cognitive Neuropsychology*, 33(1-2), 82-101. <https://doi.org/10.1080/02643294.2016.1167678>
- Martinetti, L. E., Autio, D. M., & Crandall, S. R. (2024). Motor Control of Distinct Layer 6 Corticothalamic Feedback Circuits. *Eneuro*, 11(7), ENEURO.0255-24.2024. <https://doi.org/10.1523/ENEURO.0255-24.2024>
- Mazer, J., Gallant, J.L. (2000). Object recognition: Seeing us seeing shapes. *Current biology*, 10:R668-R670.
- Medina, J., & Coslett, H. B. (2010). From maps to form to space : Touch and the body schema. *Neuropsychologia*, 48(3), 645-654. <https://doi.org/10.1016/j.neuropsychologia.2009.08.017>
- Medina, J., & Duckett, C. (2017). Domain-general biases in spatial localization : Evidence against a distorted body model hypothesis. *Journal of Experimental Psychology: Human Perception and Performance*, 43(7), 1430-1443. <https://doi.org/10.1037/xhp0000397>
- Medina, S., Tamè, L., & Longo, M. R. (2018). Tactile localization biases are modulated by gaze direction. *Experimental Brain Research*, 236(1), 31-42. <https://doi.org/10.1007/s00221-017-5105-2>
- Mehling, K., Becker, J., Chen, J., Scriba, S., Kindl, G., Jakubietz, R., Sommer, C., Hartmannsberger, B., & Rittner, H. L. (2024). Bilateral deficiency of Meissner corpuscles and papillary microvessels in patients with acute complex regional pain syndrome. *Pain*, 165(7), 1613-1624. <https://doi.org/10.1097/j.pain.0000000000003168>
- Melzer, I. (2004). Postural stability in the elderly : A comparison between fallers and non-fallers. *Age and Ageing*, 33(6), 602-607. <https://doi.org/10.1093/ageing/afh218>
- Mergen, J., Keizer, A., Koelkebeck, K., Van Den Heuvel, M. R. C., & Wagner, H. (2018). Women with Anorexia Nervosa do not show altered tactile localization compared to healthy controls. *Psychiatry Research*, 267, 446-454. <https://doi.org/10.1016/j.psychres.2018.06.007>
- Merzenich, M. M., Kaas, J. H., Sur, M., & Lin, C. (1978). Double representation of the body surface within cytoarchitectonic area 3b and 1 in "SI" in the owl monkey ( *aotus trivirgatus* ). *Journal of Comparative Neurology*, 181(1), 41-73. <https://doi.org/10.1002/cne.901810104>
- Merzenich, M. M., Kaas, J. H., Wall, J. T., Sur, M., Nelson, R. J., & Felleman, D. J. (1983). Progression of change following median nerve section in the cortical representation of the hand in areas 3b and 1 in adult owl and squirrel monkeys. *Neuroscience*, 10(3), 639-665. [https://doi.org/10.1016/0306-4522\(83\)90208-7](https://doi.org/10.1016/0306-4522(83)90208-7)
- Merzenich, M. M., Nelson, R. J., Stryker, M. P., Cynader, M. S., Schoppmann, A., & Zook, J. M. (1984). Somatosensory cortical map changes following digit amputation in adult monkeys. *Journal of Comparative Neurology*, 224(4), 591-605. <https://doi.org/10.1002/cne.902240408>
- Miller, L. E., Cawley-Bennett, A., Longo, M. R., & Saygin, A. P. (2017). The recalibration of tactile perception during tool use is body-part specific. *Experimental Brain Research*, 235(10), 2917-2926. <https://doi.org/10.1007/s00221-017-5028-y>

- Miller, L. E., Fabio, C., Azaroual, M., Muret, D., Van Beers, R. J., Farnè, A., & Medendorp, W. P. (2022). A neural surveyor to map touch on the body. *Proceedings of the National Academy of Sciences*, *119*(1), e2102233118. <https://doi.org/10.1073/pnas.2102233118>
- Miller, L. E., Longo, M. R., & Saygin, A. (2015). Vision during tool use is both necessary and sufficient for recalibration of tactile perception of body size. *Journal of Vision*, *15*(12), 362. doi:10.1167/15.12.362
- Miller, L. E., Longo, M. R., & Saygin, A. P. (2014). Tool morphology constrains the effects of tool use on body representations. *Journal of Experimental Psychology: Human Perception and Performance*, *40*(6), 2143-2153. <https://doi.org/10.1037/a0037777>
- Mima, T., Nagamine, T., Nakamura, K., & Shibasaki, H. (1998). Attention Modulates Both Primary and Second Somatosensory Cortical Activities in Humans: A Magnetoencephalographic Study. *Journal of Neurophysiology*, *80*(4), 2215-2221. <https://doi.org/10.1152/jn.1998.80.4.2215>
- Moayed, M., Noroozbahari, N., Hadjis, G., Themelis, K., Salomons, T. V., Newport, R., & S. Lewis, J. (2021). The structural and functional connectivity neural underpinnings of body image. *Human Brain Mapping*, *42*(11), 3608-3619. <https://doi.org/10.1002/hbm.25457>
- Mogilner, A., Grossman, J. A., Ribary, U., Joliot, M., Volkman, J., Rapaport, D., Beasley, R. W., & Llinás, R. R. (1993). Somatosensory cortical plasticity in adult humans revealed by magnetoencephalography. *Proceedings of the National Academy of Sciences*, *90*(8), 3593-3597. <https://doi.org/10.1073/pnas.90.8.3593>
- Mohr, H. M., Röder, C., Zimmermann, J., Hummel, D., Negele, A., & Grubhorn, R. (2011). Body image distortions in bulimia nervosa: Investigating body size overestimation and body size satisfaction by fMRI. *NeuroImage*, *56*(3), 1822-1831. <https://doi.org/10.1016/j.neuroimage.2011.02.069>
- Mohr, H. M., Zimmermann, J., Röder, C., Lenz, C., Overbeck, G., & Grubhorn, R. (2010). Separating two components of body image in anorexia nervosa using fMRI. *Psychological Medicine*, *40*(9), 1519-1529. <https://doi.org/10.1017/S0033291709991826>
- Molander, C., Grant, G. (1986). Laminar distribution and somatotopic organization of primary afferent fibers from hindlimb nerves in the dorsal horn. A study by transganglionic transport of horseradish peroxidase in the rat. *Neuroscience*, *19*(1), 297-312.
- Mölbert, S. C., Klein, L., Thaler, A., Mohler, B. J., Brozzo, C., Martus, P., Karnath, H.-O., Zipfel, S., & Giel, K. E. (2017). Depictive and metric body size estimation in anorexia nervosa and bulimia nervosa: A systematic review and meta-analysis. *Clinical Psychology Review*, *57*, 21-31. <https://doi.org/10.1016/j.cpr.2017.08.005>
- Mora, L., Committeri, G., L'Abbate, T., & Cocchini, G. (2024). Unlocking the potential of 'passive' modulation: How sensory stimulation shapes hand and face size. *Journal of Neuropsychology*, jnp.12379. <https://doi.org/10.1111/jnp.12379>
- Mountcastle V.B., Darian-Smith I. (1968). Neural mechanisms in somesthesia, in: V.B. Mountcastle (Ed.), *Medical Physiology*, 12th edition, vol. 2, Mosby, St. Louis, pp. 1372-1423.
- Muniak, M. A., Ray, S., Hsiao, S. S., Dammann, J. F., & Bensmaia, S. J. (2007). The Neural Coding of Stimulus Intensity: Linking the Population Response of Mechanoreceptive Afferents with Psychophysical Behavior. *The Journal of Neuroscience*, *27*(43), 11687-11699. <https://doi.org/10.1523/JNEUROSCI.1486-07.2007>
- Murata, A., Gallese, V., Luppino, G., Kaseda, M., & Sakata, H. (2000). Selectivity for the Shape, Size, and Orientation of Objects for Grasping in Neurons of Monkey Parietal Area AIP. *Journal of Neurophysiology*, *83*(5), 2580-2601. <https://doi.org/10.1152/jn.2000.83.5.2580>
- Muret, D., & Dinse, H. R. (2018). Tactile learning transfer from the hand to the face but not to the forearm implies a special hand-face relationship. *Scientific Reports*, *8*(1), 11752. <https://doi.org/10.1038/s41598-018-30183-5>
- Muret, D., Daligault, S., Dinse, H. R., Delpuech, C., Mattout, J., Reilly, K. T., & Farnè, A. (2016). Neuromagnetic correlates of adaptive plasticity across the hand-face border in human primary somatosensory cortex. *Journal of Neurophysiology*, *115*(4), 2095-2104. <https://doi.org/10.1152/jn.00628.2015>
- Muret, D., Dinse, H. R., Macchione, S., Urquizar, C., Farnè, A., & Reilly, K. T. (2014). Touch improvement at the hand transfers to the face. *Current Biology*, *24*(16), R736-R737. <https://doi.org/10.1016/j.cub.2014.07.021>
- Muret, D., Macchione, S., Dinse, H. R., Koun, E., Salemme, R., Reilly, K., & Farne, A. (2024). Hand to Hand: A novel pattern of remote tactile improvement following training-independent learning. <https://doi.org/10.31234/osf.io/hbsy>
- Muret, D., Root, V., Kieliba, P., Clode, D., & Makin, T. R. (2022). Beyond body maps: Information content of specific body parts is distributed across the somatosensory homunculus. *Cell Reports*, *38*(11).
- Nakamura A, Yamada T, Goto A, Kato T, Ito K, Abe Y, Kachi T, Kakigi R (1998) Somatosensory homunculus as drawn by MEG. *Neuroimage* *7*:377-386.



- Nava, E., & Tajadura-Jiménez, A. (2020). Auditory-induced body distortions in children and adults. *Scientific Reports*, *10*(1), 3024. <https://doi.org/10.1038/s41598-020-59979-0>
- Navarro-Guerrero, N., Toprak, S., Josifovski, J., & Jamone, L. (2023). Visuo-haptic object perception for robots : An overview. *Autonomous Robots*, *47*(4), 377-403. <https://doi.org/10.1007/s10514-023-10091-y>
- Neubarth, N. L., Emanuel, A. J., Liu, Y., Springel, M. W., Handler, A., Zhang, Q., Lehnert, B. P., Guo, C., Orefice, L. L., Abdelaziz, A., DeLisle, M. M., Iskols, M., Rhyins, J., Kim, S. J., Cattel, S. J., Regehr, W., Harvey, C. D., Drugowitsch, J., & Ginty, D. D. (2020). Meissner corpuscles and their spatially intermingled afferents underlie gentle touch perception. *Science*, *368*(6497), eabb2751. <https://doi.org/10.1126/science.abb2751>
- Nico, D. (2004). Left and right hand recognition in upper limb amputees. *Brain*, *127*(1), 120-132. <https://doi.org/10.1093/brain/awh006>
- Nicolelis, M. A. L., & Fanselow, E. E. (2002). Dynamic shifting in thalamocortical processing during different behavioural states. *Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences*, *357*(1428), 1753-1758. <https://doi.org/10.1098/rstb.2002.1175>
- Nicula, A., & Longo, M. R. (2021). Perception of Tactile Distance on the Back. *Perception*, *50*(8), 677-689. <https://doi.org/10.1177/03010066211025384>
- Norata, D., Musumeci, G., Todisco, A., Cruciani, A., Motolese, F., Capone, F., Lattanzi, S., Ranieri, F., Di Lazzaro, V., & Pilato, F. (2024). Bilateral median nerve stimulation and High-Frequency Oscillations unveil interhemispheric inhibition of primary sensory cortex. *Clinical Neurophysiology*, *165*, 154-165. <https://doi.org/10.1016/j.clinph.2024.06.011>
- Nyberg, G., & Blomqvist, A. (1985). The somatotopic organization of forelimb cutaneous nerves in the brachial dorsal horn: An anatomical study in the cat. *Journal of Comparative Neurology*, *242*(1), 28-39. <https://doi.org/10.1002/cne.902420103>
- O'Sullivan, B. T., Roland, P. E., & Kawashima, R. (1994). A PET Study of Somatosensory Discrimination in Man. Microgeometry Versus Macrogeometry. *European Journal of Neuroscience*, *6*(1), 137-148. <https://doi.org/10.1111/j.1460-9568.1994.tb00255.x>
- Onishi, H., Nagasaka, K., Yokota, H., Kojima, S., Ohno, K., Sakurai, N., Kodama, N., Sato, D., & Otsuru, N. (2023). Association between somatosensory sensitivity and regional gray matter volume in healthy young volunteers: A voxel-based morphometry study. *Cerebral Cortex*, *33*(5), 2001-2010. <https://doi.org/10.1093/cercor/bhac188>
- Padberg, J., Cerkevich, C., Engle, J., Rajan, A. T., Recanzone, G., Kaas, J., & Krubitzer, L. (2009). Thalamocortical Connections of Parietal Somatosensory Cortical Fields in Macaque Monkeys are Highly Divergent and Convergent. *Cerebral Cortex*, *19*(9), 2038-2064. <https://doi.org/10.1093/cercor/bhn229>
- Paillard, J. (1997) Divided Body Schema and Body Image in Deafferented Patients. In: Brain and Movement: Int. Symp. Motor Control. St.-Petersburg - Moscow (Abstract). In: V.S. Gurfinkel & Yu. S. Levik (Eds). Institute for Information and Transmission problems RAS Moscow.
- Paillard, J. (1999). Body schema and body image—A double dissociation in deafferented patients. *Motor Control Today and Tomorrow*.
- Paillard, J., Michel, F., Stelmach, G. (1983) Localisation without content: a tactile analogue of "blind sight". *Arch Neural*, *40*, 548-551
- Palermo, L., Di Vita, A., Piccardi, L., Traballese, M., & Guariglia, C. (2014). Bottom-up and top-down processes in body representation: A study of brain-damaged and amputee patients. *Neuropsychology*, *28*(5), 772-781. <https://doi.org/10.1037/neu0000086>
- Paqueron, X. (2003). The phenomenology of body image distortions induced by regional anaesthesia. *Brain*, *126*(3), 702-712. <https://doi.org/10.1093/brain/awg063>
- Paré, M., Behets, C., & Cornu, O. (2003). Paucity of presumptive ruffini corpuscles in the index finger pad of humans. *Journal of Comparative Neurology*, *456*(3), 260-266. <https://doi.org/10.1002/cne.10519>
- Parianen Lesemann, F. H., Reuter, E.-M., & Godde, B. (2015). Tactile stimulation interventions: Influence of stimulation parameters on sensorimotor behavior and neurophysiological correlates in healthy and clinical samples. *Neuroscience & Biobehavioral Reviews*, *51*, 126-137. <https://doi.org/10.1016/j.neubiorev.2015.01.005>
- Parsons, L.M., Fox, P.R., Downs, J.H., Glass, T., Hirsch, T.B., Martin, C.C, Jerabek, P.A., Lancaster, J.L. (1995). Use of implicit motor imagery for visual shape discrimination as revealed by PET. *Nature*, *375*
- Parvizi-Fard, A., Amiri, M., Kumar, D., Iskarous, M. M., & Thakor, N. V. (2021). A functional spiking neuronal network for tactile sensing pathway to process edge orientation. *Scientific Reports*, *11*(1), 1320. <https://doi.org/10.1038/s41598-020-80132-4>
- Patel, A. T., Duncan, P. W., Lai, S.-M., & Studenski, S. (2000). The relation between impairments and functional outcomes poststroke. *Archives of Physical Medicine and Rehabilitation*, *81*(10), 1357-1363. <https://doi.org/10.1053/apmr.2000.9397>

- Paul RL, Merzenich M, Goodman H (1972) Representation of slowly and rapidly adapting cutaneous mechanoreceptors of the hand in Brodmann's areas 3 and 1 of Macaca Mulatta. *Brain Res* 36:229-249.
- Paullus, J. R., & Hickmott, P. W. (2011). Diverse excitatory and inhibitory synaptic plasticity outcomes in complex horizontal circuits near a functional border of adult neocortex. *Brain Research*, 1416, 10-25. <https://doi.org/10.1016/j.brainres.2011.07.062>
- Pawela, C. P., Biswal, B. B., Hudetz, A. G., Li, R., Jones, S. R., Cho, Y. R., Matloub, H. S., & Hyde, J. S. (2010). Interhemispheric neuroplasticity following limb deafferentation detected by resting-state functional connectivity magnetic resonance imaging (fcMRI) and functional magnetic resonance imaging (fMRI). *NeuroImage*, 49(3), 2467-2478. <https://doi.org/10.1016/j.neuroimage.2009.09.054>
- Pei, Y.-C., Denchev, P. V., Hsiao, S. S., Craig, J. C., & Bensmaia, S. J. (2009). Convergence of Submodality-Specific Input Onto Neurons in Primary Somatosensory Cortex. *Journal of Neurophysiology*, 102(3), 1843-1853. <https://doi.org/10.1152/jn.00235.2009>
- Pellijeff, A., Bonilha, L., Morgan, P. S., McKenzie, K., & Jackson, S. R. (2006). Parietal updating of limb posture : An event-related fMRI study. *Neuropsychologia*, 44(13), 2685-2690. <https://doi.org/10.1016/j.neuropsychologia.2006.01.009>
- Penfield W, Boldrey E (1937) Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation. *Brain* 60:389-443
- Perez, C. A., Holzmann, C. A., & Jaeschke, H. E. (2000). Two-point vibrotactile discrimination related to parameters of pulse burst stimulus. *Medical and Biological Engineering and Computing*, 38(1), 74-79. <https://doi.org/10.1007/BF02344692>
- Peters, R. M., Hackeman, E., & Goldreich, D. (2009). Diminutive Digits Discern Delicate Details : Fingertip Size and the Sex Difference in Tactile Spatial Acuity. *The Journal of Neuroscience*, 29(50), 15756-15761. <https://doi.org/10.1523/JNEUROSCI.3684-09.2009>
- Petoe, M. A., Jaque, F. A. M., Byblow, W. D., & Stinear, C. M. (2013). Cutaneous anesthesia of the forearm enhances sensorimotor function of the hand. *Journal of Neurophysiology*, 109(4), 1091-1096. <https://doi.org/10.1152/jn.00813.2012>
- Petrus, E., Dembling, S., Usdin, T., Isaac, J. T. R., & Koretsky, A. P. (2020). Circuit-Specific Plasticity of Callosal Inputs Underlies Cortical Takeover. *The Journal of Neuroscience*, 40(40), 7714-7723. <https://doi.org/10.1523/JNEUROSCI.1056-20.2020>
- Pettit., M.J., Schwark, H.D. (1993). Receptive Field Reorganization in Dorsal Column Nuclei During Temporary Denervation. *Science*, 262.
- Peviani, V. C., Miller, L. E., & Medendorp, W. P. (2024). Biases in hand perception are driven by somatosensory computations, not a distorted hand model. *Current Biology*, 34(10), 2238-2246.e5. <https://doi.org/10.1016/j.cub.2024.04.010>
- Peviani, V., & Bottini, G. (2018). The distorted hand metric representation serves both perception and action. *Journal of Cognitive Psychology*, 30(8), 880-893. <https://doi.org/10.1080/20445911.2018.1538154>
- Peviani, V., Liotta, J., & Bottini, G. (2020). The motor system (partially) deceives body representation biases in absence of visual correcting cues. *Acta Psychologica*, 203, 103003. <https://doi.org/10.1016/j.actpsy.2020.103003>
- Philip, B. A., & Frey, S. H. (2014). Compensatory Changes Accompanying Chronic Forced Use of the Nondominant Hand by Unilateral Amputees. *The Journal of Neuroscience*, 34(10), 3622-3631. <https://doi.org/10.1523/JNEUROSCI.3770-13.2014>
- Phillips, J. R., & Johnson, K. O. (1981). Tactile spatial resolution. II. Neural representation of Bars, edges, and gratings in monkey primary afferents. *Journal of Neurophysiology*, 46(6), 1192-1203. <https://doi.org/10.1152/jn.1981.46.6.1192>
- Phillips, J. R., Johansson, R. S., & Johnson, K. O. (1990). Representation of braille characters in human nerve fibres. *Experimental Brain Research*, 81(3), 589-592. <https://doi.org/10.1007/BF02423508>
- Phillips, J. R., Johnson, K. O., & Hsiao, S. S. (1988). Spatial pattern representation and transformation in monkey somatosensory cortex. *Proceedings of the National Academy of Sciences*, 85(4), 1317-1321. <https://doi.org/10.1073/pnas.85.4.1317>
- Pilz K, Veit R, Braun C, Godde B (2004) Effects of co-activation on cortical organization and discrimination performance. *Neuroreport* 15:2669-2672.
- Pitron, V., & De Vignemont, F. (2017). Beyond differences between the body schema and the body image : Insights from body hallucinations. *Consciousness and Cognition*, 53, 115-121. <https://doi.org/10.1016/j.concog.2017.06.006>
- Pitron, V., Alsmith, A., & De Vignemont, F. (2018). How do the body schema and the body image interact? *Consciousness and Cognition*, 65, 352-358. <https://doi.org/10.1016/j.concog.2018.08.007>
- Pleger, B., Dinse, H. R., Ragert, P., Schwenkreis, P., Malin, J. P., & Tegenthoff, M. (2001). Shifts in cortical representations predict human discrimination improvement. *Proceedings of the National Academy of Sciences*, 98(21), 12255-12260. <https://doi.org/10.1073/pnas.191176298>

- Pleger, B., Foerster, A.-F., Ragert, P., Dinse, H. R., Schwenkreis, P., Malin, J.-P., Nicolas, V., & Tegenthoff, M. (2003). Functional Imaging of Perceptual Learning in Human Primary and Secondary Somatosensory Cortex. *Neuron*, 40(3), 643-653. [https://doi.org/10.1016/S0896-6273\(03\)00677-9](https://doi.org/10.1016/S0896-6273(03)00677-9)
- Pleger, B., Tegenthoff, M., Ragert, P., Förster, A., Dinse, H. R., Schwenkreis, P., Nicolas, V., & Maier, C. (2005). Sensorimotor returning in complex regional pain syndrome parallels pain reduction. *Annals of Neurology*, 57(3), 425-429. <https://doi.org/10.1002/ana.20394>
- Poggio, G. F., & Mountcastle, V. B. (1963). THE FUNCTIONAL PROPERTIES OF VENTROBASAL THALAMIC NEURONS STUDIED IN UNANESTHETIZED MONKEYS. *Journal of Neurophysiology*, 26(5), 775-806. <https://doi.org/10.1152/jn.1963.26.5.775>
- Pons TP, Garraghty PE, Friedman DP, Mishkin M (1987) Physiological evidence for serial processing in somatosensory cortex. *Science* (80- ) 237:417–20.
- Pons TP, Garraghty PE, Mishkin M (1992) Serial and parallel processing of tactual information in somatosensory cortex of rhesus monkeys. *J Neurophysiol* 68:518–27
- Pons, T. P., Garraghty, P. E., Cusick, C. G., & Kaas, J. H. (1985). The somatotopic organization of area 2 in macaque monkeys. *Journal of Comparative Neurology*, 241(4), 445-466. <https://doi.org/10.1002/cne.902410405>
- Porro, C., Martinig, M., Facchin, P., Maieron, M., Jones, A., & Fadiga, L. (2007). Parietal cortex involvement in the localization of tactile and noxious mechanical stimuli : A transcranial magnetic stimulation study. *Behavioural Brain Research*, 178(2), 183-189. <https://doi.org/10.1016/j.bbr.2006.11.011>
- Powell TPS, Mountcastle VB (1959) Some aspects of the functional organization of the cortex of the postcentral gyrus of the monkey: a correlation of findings obtained in a single unit analysis with cytoarchitecture. *Bull Johns Hopkins Hosp* 105:133–162.
- Pratt, S., Wand, B. M., Hince, D. A., Travers, M. J., Schneider, L., Kelly, S., & Gibson, W. (2024). Tactile localization accuracy at the low back. *Attention, Perception, & Psychophysics*, 86(3), 1008-1021. <https://doi.org/10.3758/s13414-024-02843-4>
- Pruszynski, J. A., & Johansson, R. S. (2014). Edge-orientation processing in first-order tactile neurons. *Nature Neuroscience*, 17(10), 1404-1409. <https://doi.org/10.1038/nn.3804>
- Pruszynski, J. A., Flanagan, J. R., & Johansson, R. S. (2018). Fast and accurate edge orientation processing during object manipulation. *eLife*, 7, e31200. <https://doi.org/10.7554/eLife.31200>
- Puckett, A. M., Bollmann, S., Junday, K., Barth, M., & Cunnington, R. (2020). Bayesian population receptive field modeling in human somatosensory cortex. *NeuroImage*, 208, 116465. <https://doi.org/10.1016/j.neuroimage.2019.116465>
- Qi, H., & Kaas, J. H. (2004). Myelin stains reveal an anatomical framework for the representation of the digits in somatosensory area 3b of macaque monkeys. *Journal of Comparative Neurology*, 477(2), 172-187. <https://doi.org/10.1002/cne.20247>
- Qi, H., & Kaas, J. H. (2006). Organization of primary afferent projections to the gracile nucleus of the dorsal column system of primates. *Journal of Comparative Neurology*, 499(2), 183-217. <https://doi.org/10.1002/cne.21061>
- Qi, H., Gharbawie, O. A., Wong, P., & Kaas, J. H. (2011). Cell-poor septa separate representations of digits in the ventroposterior nucleus of the thalamus in monkeys and prosimian galagos. *Journal of Comparative Neurology*, 519(4), 738-758. <https://doi.org/10.1002/cne.22545>
- Ragert, P., Kalisch, T., Bliem, B., Franzkowiak, S., & Dinse, H. R. (2008). Differential effects of tactile high- and low-frequency stimulation on tactile discrimination in human subjects. *BMC Neuroscience*, 9(1), 9. <https://doi.org/10.1186/1471-2202-9-9>
- Ramachandran, V. S. (1993). Behavioral and magnetoencephalographic correlates of plasticity in the adult human brain. *Proceedings of the National Academy of Sciences*, 90(22), 10413-10420. <https://doi.org/10.1073/pnas.90.22.10413>
- Rapp, B., Hendel, S. K., & Medina, J. (2002). Remodeling of somatosensory hand representations following cerebral lesions in humans: *Neuroreport*, 13(2), 207-211. <https://doi.org/10.1097/00001756-200202110-00007>
- Rasmussen, A. T., & Peyton, W. T. (1948). The course and termination of the medial lemniscus in man. *Journal of Comparative Neurology*, 88(3), 411-424. <https://doi.org/10.1002/cne.900880304>
- Rasmusson, D. D. (1982). Reorganization of raccoon somatosensory cortex following removal of the fifth digit. *Journal of Comparative Neurology*, 205(4), 313-326. <https://doi.org/10.1002/cne.902050402>
- Recanzone, G. H., Merzenich, M. M., & Dinse, H. R. (1992d). Expansion of the Cortical Representation of a Specific Skin Field in Primary Somatosensory Cortex by Intracortical Microstimulation. *Cerebral Cortex*, 2(3), 181-196. <https://doi.org/10.1093/cercor/2.3.181>
- Recanzone, G. H., Merzenich, M. M., & Jenkins, W. M. (1992a). Frequency discrimination training engaging a restricted skin surface results in an emergence of a cutaneous response zone in cortical area 3a. *Journal of Neurophysiology*, 67(5), 1057-1070. <https://doi.org/10.1152/jn.1992.67.5.1057>

- Recanzone, G. H., Merzenich, M. M., & Schreiner, C. E. (1992b). Changes in the distributed temporal response properties of SI cortical neurons reflect improvements in performance on a temporally based tactile discrimination task. *Journal of Neurophysiology*, *67*(5), 1071-1091. <https://doi.org/10.1152/jn.1992.67.5.1071>
- Recanzone, H., Merzenich, M., Jenkins, M., Grajski, A., & Dinse, R. (1992c). Topographic Reorganization of the Hand Representation in Cortical Area 3b of Owl Monkeys Trained in a Frequency-Discrimination Task.
- Reddy, N. A., Clements, R. G., Brooks, J. C. W., & Bright, M. G. (s. d.). *Simultaneous cortical, subcortical, and brainstem mapping of sensory activation*.
- Reed, J. L., Pouget, P., Qi, H.-X., Zhou, Z., Bernard, M. R., Burish, M. J., Haitas, J., Bonds, A. B., & Kaas, J. H. (2008). Widespread spatial integration in primary somatosensory cortex. *Proceedings of the National Academy of Sciences*, *105*(29), 10233-10237. <https://doi.org/10.1073/pnas.0803800105>
- Reed, J. L., Qi, H.-X., Zhou, Z., Bernard, M. R., Burish, M. J., Bonds, A. B., & Kaas, J. H. (2010). Response Properties of Neurons in Primary Somatosensory Cortex of Owl Monkeys Reflect Widespread Spatiotemporal Integration. *Journal of Neurophysiology*, *103*(4), 2139-2157. <https://doi.org/10.1152/jn.00709.2009>
- Reinersmann, A., Skinner, I. W., Lücke, T., Massy-Westropp, N., Rudolf, H., Moseley, G. L., & Stanton, T. R. (2021). Intact tactile anisotropy despite altered hand perception in complex regional pain syndrome : Rethinking the role of the primary sensory cortex in tactile and perceptual dysfunction. *PeerJ*, *9*, e11156. <https://doi.org/10.7717/peerj.11156>
- Reuter, E., Voelcker-Rehage, C., Vieluf, S., & Godde, B. (2014). Effects of age and expertise on tactile learning in humans. *European Journal of Neuroscience*, *40*(3), 2589-2599. <https://doi.org/10.1111/ejn.12629>
- Riemer, M., Wolbers, T., & Kuehn, E. (2019). Preserved multisensory body representations in advanced age. *Scientific Reports*, *9*(1), 2663. <https://doi.org/10.1038/s41598-019-39270-7>
- Rifi, Z., Remore, L. G., Tolossa, M., Wei, W., Sun, X. R., & Bari, A. A. (2024). Somatotopic organization of the ventral nuclear group of the dorsal thalamus : Deep brain stimulation for neuropathic pain reveals new insights into the facial homunculus. *Brain Structure and Function*, *229*(2), 349-358. <https://doi.org/10.1007/s00429-023-02733-9>
- Risso, G., Martoni, R. M., Erzegovesi, S., Bellodi, L., & Baud-Bovy, G. (2020). Visuo-tactile shape perception in women with Anorexia Nervosa and healthy women with and without body concerns. *Neuropsychologia*, *149*, 107635. <https://doi.org/10.1016/j.neuropsychologia.2020.107635>
- Ro, T., & Koenig, L. (2021). Unconscious Touch Perception After Disruption of the Primary Somatosensory Cortex. *Psychological Science*, *32*(4), 549-557. <https://doi.org/10.1177/0956797620970551>
- Rocchi, L., Erro, R., Antelmi, E., Berardelli, A., Tinazzi, M., Liguori, R., Bhatia, K., & Rothwell, J. (2017). High frequency somatosensory stimulation increases sensori-motor inhibition and leads to perceptual improvement in healthy subjects. *Clinical Neurophysiology*, *128*(6), 1015-1025. <https://doi.org/10.1016/j.clinph.2017.03.046>
- Roland PE, O'Sullivan B, Kawashima R (1998) Shape and roughness activate different somatosensory areas in the human brain. *PNAS* *95*:3295–3300.
- Romo, R., & De Lafuente, V. (2013). Conversion of sensory signals into perceptual decisions. *Progress in Neurobiology*, *103*, 41-75. <https://doi.org/10.1016/j.pneurobio.2012.03.007>
- Romo, R., Hernández, A., Zainos, A., Lemus, L., & Brody, C. D. (2002). Neuronal correlates of decision-making in secondary somatosensory cortex. *Nature Neuroscience*, *5*(11), 1217-1225. <https://doi.org/10.1038/nn950>
- Rongala, U. B., Spanne, A., Mazzoni, A., Bengtsson, F., Oddo, C. M., & Jörntell, H. (2018). Intracellular Dynamics in Cuneate Nucleus Neurons Support Self-Stabilizing Learning of Generalizable Tactile Representations. *Frontiers in Cellular Neuroscience*, *12*, 210. <https://doi.org/10.3389/fncel.2018.00210>
- Root, V., Muret, D., Arribas, M., Amoroso, E., Thornton, J., Tarall-Jozwiak, A., Tracey, I., & Makin, T. R. (2022). Complex pattern of facial remapping in somatosensory cortex following congenital but not acquired hand loss. *eLife*, *11*, e76158. <https://doi.org/10.7554/eLife.76158>
- Ross, B., Dobri, S., Jamali, S., & Bartel, L. (2022). Entrainment of somatosensory beta and gamma oscillations accompany improvement in tactile acuity after periodic and aperiodic repetitive sensory stimulation. *International Journal of Psychophysiology*, *177*, 11-26. <https://doi.org/10.1016/j.ijpsycho.2022.04.007>
- Rossetti, Y., Rode, G., Boisson, D. (1995). Implicit processing of somaesthetic information: a dissociation between where and how? *NeuroReport*, *6*, 506-510
- Rowe, M., Turman, A., Murray, G., & Zhang, H. (1996). Parallel organization of somatosensory cortical areas i and ii for tactile processing. *Clinical and Experimental Pharmacology and Physiology*, *23*(10-11), 931-938. <https://doi.org/10.1111/j.1440-1681.1996.tb01145.x>
- Rubén J, Krause T, Taskin B, Blankenburg F, Moosmann M, Villringer A (2006) Subarea-specific suppressive interaction in the BOLD responses to simultaneous finger stimulation in human primary somatosensory cortex: evidence for increasing rostral-to-caudal convergence. *Cereb cortex* *16*:819–826

- Rusconi, E., Kwan, B., Giordano, B., Umiltà, C., & Butterworth, B. (2006). Spatial representation of pitch height : The SMARC effect. *Cognition*, *99*(2), 113-129. <https://doi.org/10.1016/j.cognition.2005.01.004>
- Rusconi, E., Tame, L., Furlan, M., Haggard, P., Demarchi, G., Adriani, M., Ferrari, P., Braun, C., & Schwarzbach, J. (2014). Neural Correlates of Finger Gnosis. *Journal of Neuroscience*, *34*(27), 9012-9023. <https://doi.org/10.1523/JNEUROSCI.3119-13.2014>
- Saal, H. P., & Bensmaia, S. J. (2014). Touch is a team effort : Interplay of submodalities in cutaneous sensibility. *Trends in Neurosciences*, *37*(12), 689-697. <https://doi.org/10.1016/j.tins.2014.08.012>
- Saito, K., Otsuru, N., Inukai, Y., Kojima, S., Miyaguchi, S., Tsuiki, S., Sasaki, R., & Onishi, H. (2018). Inhibitory Mechanisms in Primary Somatosensory Cortex Mediate the Effects of Peripheral Electrical Stimulation on Tactile Spatial Discrimination. *Neuroscience*, *384*, 262-274. <https://doi.org/10.1016/j.neuroscience.2018.05.032>
- Sakata, H., Takaoka, Y., Kawarasaki, A., & Shibutani, H. (1973). Somatosensory properties of neurons in the superior parietal cortex (area 5) of the rhesus monkey. *Brain Research*, *64*, 85-102. [https://doi.org/10.1016/0006-8993\(73\)90172-8](https://doi.org/10.1016/0006-8993(73)90172-8)
- Sanchez Panchuelo, R. M., Besle, J., Schluppeck, D., Humberstone, M., & Francis, S. (2018). Somatotopy in the Human Somatosensory System. *Frontiers in Human Neuroscience*, *12*, 235. <https://doi.org/10.3389/fnhum.2018.00235>
- Sanchez-Panchuelo, R. M., Besle, J., Beckett, A., Bowtell, R., Schluppeck, D., & Francis, S. (2012). Within-Digit Functional Parcellation of Brodmann Areas of the Human Primary Somatosensory Cortex Using Functional Magnetic Resonance Imaging at 7 Tesla. *The Journal of Neuroscience*, *32*(45), 15815-15822. <https://doi.org/10.1523/JNEUROSCI.2501-12.2012>
- Sasaki, R., Kojima, S., Otsuru, N., Yokota, H., Saito, K., Shirozu, H., & Onishi, H. (2023). Beta resting-state functional connectivity predicts tactile spatial acuity. *Cerebral Cortex*, *33*(16), 9514-9523. <https://doi.org/10.1093/cercor/bhad221>
- Sathian, K., & Zangaladze, A. (1998). Perceptual learning in tactile hyperacuity : Complete intermanual transfer but limited retention. *Experimental Brain Research*, *118*(1), 131-134. <https://doi.org/10.1007/s002210050263>
- Sathian, K., & Zangaladze, A. (2002). Feeling with the mind's eye : Contribution of visual cortex to tactile perception. *Behavioural Brain Research*, *135*(1-2), 127-132. [https://doi.org/10.1016/S0166-4328\(02\)00141-9](https://doi.org/10.1016/S0166-4328(02)00141-9)
- Sathian, K., Zangaladze, A., Hoffman, J.M., Grafton, S.T. (1997). Feeling the mind's eye. *NeuroReport*, *8*, 3877-3881.
- Sattin, D., Parma, C., Lunetta, C., Zulueta, A., Lanzone, J., Giani, L., Vassallo, M., Picozzi, M., & Parati, E. A. (2023). An Overview of the Body Schema and Body Image : Theoretical Models, Methodological Settings and Pitfalls for Rehabilitation of Persons with Neurological Disorders. *Brain Sciences*, *13*(10), 1410. <https://doi.org/10.3390/brainsci13101410>
- Scandola, M., Dodoni, L., Lazzeri, G., Arcangeli, C. A., Avesani, R., Moro, V., & Ionta, S. (2019). Neurocognitive Benefits of Physiotherapy for Spinal Cord Injury. *Journal of Neurotrauma*, *36*(12), 2028-2035. <https://doi.org/10.1089/neu.2018.6123>
- Schluppeck, D., & Francis, S. (2015). Somatosensory Processing. In *Brain Mapping* (p. 549-552). Elsevier. <https://doi.org/10.1016/B978-0-12-397025-1.00045-2>
- Schmidt-Wilcke, T., Wulms, N., Heba, S., Pleger, B., Puts, N. A., Glaubit, B., Kalisch, T., Tegenthoff, M., & Dinse, H. R. (2018). Structural changes in brain morphology induced by brief periods of repetitive sensory stimulation. *NeuroImage*, *165*, 148-157. <https://doi.org/10.1016/j.neuroimage.2017.10.016>
- Schweisfurth, M. A., Frahm, J., & Schweizer, R. (2014). Individual fMRI maps of all phalanges and digit bases of all fingers in human primary somatosensory cortex. *Frontiers in Human Neuroscience*, *8*. <https://doi.org/10.3389/fnhum.2014.00658>
- Schweizer, M., Maier, C., Braun, N. B., R. (2000). Distribution of mislocalizations of tactile stimuli on the fingers of the human hand. *Somatosensory & Motor Research*, *17*(4), 309-316. <https://doi.org/10.1080/08990220020002006>
- Schwenkreis, P., Witscher, K., Janssen, F., Dertwinkel, R., Zenz, M., Malin, J.-P., & Tegenthoff, M. (2000). Changes of cortical excitability in patients with upper limb amputation. *Neuroscience Letters*, *293*(2), 143-146. [https://doi.org/10.1016/S0304-3940\(00\)01517-2](https://doi.org/10.1016/S0304-3940(00)01517-2)
- Schwoebel, J., & Coslett, H. B. (2005). Evidence for Multiple, Distinct Representations of the Human Body. *Journal of Cognitive Neuroscience*, *17*(4), 543-553. <https://doi.org/10.1162/0898929053467587>
- Sehle, A., Büsching, I., Vogt, E., & Liepert, J. (2016). Temporary deafferentation evoked by cutaneous anesthesia : Behavioral and electrophysiological findings in healthy subjects. *Journal of Neural Transmission*, *123*(5), 473-480. <https://doi.org/10.1007/s00702-016-1537-2>
- Serino, A., & Haggard, P. (2010). Touch and the body. *Neuroscience & Biobehavioral Reviews*, *34*(2), 224-236. <https://doi.org/10.1016/j.neubiorev.2009.04.004>

- Severens, M., Farquhar, J., Desain, P., Duysens, J., & Gielen, C. (2010). Transient and steady-state responses to mechanical stimulation of different fingers reveal interactions based on lateral inhibition. *Clinical Neurophysiology*, *121*(12), 2090-2096. <https://doi.org/10.1016/j.clinph.2010.05.016>
- Seyal, M., Siddiqui, I., & Hundal, N. S. (1997). Suppression of spatial localization of a cutaneous stimulus following transcranial magnetic pulse stimulation of the sensorimotor cortex. *Electroencephalography and Clinical Neurophysiology/Electromyography and Motor Control*, *105*(1), 24-28. [https://doi.org/10.1016/S0924-980X\(96\)96090-7](https://doi.org/10.1016/S0924-980X(96)96090-7)
- Shaffer, S. W., & Harrison, A. L. (2007). Aging of the Somatosensory System: A Translational Perspective. *Physical Therapy*, *87*(2), 193-207. <https://doi.org/10.2522/ptj.20060083>
- Shelchikova, N. D., Downey, J. E., Greenspon, C. M., Okorokova, E. V., Sobinov, A. R., Verbaarschot, C., He, Q., Sponheim, C., Tortolani, A. F., Moore, D. D., Kaufman, M. T., Lee, R. C., Satzer, D., Gonzalez-Martinez, J., Warnke, P. C., Miller, L. E., Boninger, M. L., Gaunt, R. A., Collinger, J. L., ... Bensaïma, S. J. (2023). Microstimulation of human somatosensory cortex evokes task-dependent, spatially patterned responses in motor cortex. *Nature Communications*, *14*(1), 7270. <https://doi.org/10.1038/s41467-023-43140-2>
- Shin, H.-C., Park, S., Son, J., Sohn, J.-H. (1995). Responses from new receptive fields of VPL neurons following deafferentation. *NeuroReport*, *7*, 33-36.
- Simões, C., Mertens, M., Forss, N., Jousmäki, V., Lütkenhöner, B., & Hari, R. (2001). Functional Overlap of Finger Representations in Human SI and SII Cortices. *Journal of Neurophysiology*, *86*(4), 1661-1665. <https://doi.org/10.1152/jn.2001.86.4.1661>
- Simões, E. L., Bramati, I., Rodrigues, E., Franzoi, A., Moll, J., Lent, R., & Tovar-Moll, F. (2012). Functional Expansion of Sensorimotor Representation and Structural Reorganization of Callosal Connections in Lower Limb Amputees. *The Journal of Neuroscience*, *32*(9), 3211-3220. <https://doi.org/10.1523/JNEUROSCI.4592-11.2012>
- Simões-Franklin, C., Whitaker, T. A., & Newell, F. N. (2011). Active and passive touch differentially activate somatosensory cortex in texture perception. *Human Brain Mapping*, *32*(7), 1067-1080. <https://doi.org/10.1002/hbm.21091>
- Sirigu, A., Grafman, J., Bressler, K., & Sunderland, T. (1991). MULTIPLE REPRESENTATIONS CONTRIBUTE TO BODY KNOWLEDGE PROCESSING: EVIDENCE FROM A CASE OF AUTOTOPAGNOSIA. *Brain*, *114*(1), 629-642. <https://doi.org/10.1093/brain/114.1.629>
- Smeets, M. A. M., Smit, F., Panhuysen, G. E. M., & Ingleby, J. D. (1997). The influence of methodological differences on the outcome of body size estimation studies in anorexia nervosa. *British Journal of Clinical Psychology*, *36*(2), 263-277. <https://doi.org/10.1111/j.2044-8260.1997.tb01412.x>
- Smith, M. C., & Deacon, P. (1984). TOPOGRAPHICAL ANATOMY OF THE POSTERIOR COLUMNS OF THE SPINAL CORD IN MAN: THE LONG ASCENDING FIBRES. *Brain*, *107*(3), 671-698. <https://doi.org/10.1093/brain/107.3.671>
- Smith, P. S., Dinse, H. R., Kalisch, T., Johnson, M., & Walker-Batson, D. (2009). Effects of Repetitive Electrical Stimulation to Treat Sensory Loss in Persons Poststroke. *Archives of Physical Medicine and Rehabilitation*, *90*(12), 2108-2111. <https://doi.org/10.1016/j.apmr.2009.07.017>
- Snyder, L. H., Grieve, K. L., Brotchie, P., & Andersen, R. A. (1998). Separate body- and world-referenced representations of visual space in parietal cortex. *Nature*, *394*(6696), 887-891. <https://doi.org/10.1038/29777>
- Song, Y., Su, Q., Yang, Q., Zhao, R., Yin, G., Qin, W., Iannetti, G. D., Yu, C., & Liang, M. (2021). Feedforward and feedback pathways of nociceptive and tactile processing in human somatosensory system: A study of dynamic causal modeling of fMRI data. *NeuroImage*, *234*, 117957. <https://doi.org/10.1016/j.neuroimage.2021.117957>
- Sorrentino, G., Franza, M., Zuber, C., Blanke, O., Serino, A., & Bassolino, M. (2021). How ageing shapes body and space representations: A comparison study between healthy young and older adults. *Cortex*, *136*, 56-76. <https://doi.org/10.1016/j.cortex.2020.11.021>
- Spengler F, Dinse HR (1994) Reversible relocation of representational boundaries of adult rats by intracortical microstimulation. *Neuroreport* *5*:949–953
- Spengler, F., P.L. Roberts, T., Poeppel, D., Byl, N., Wang, X., Rowley, H. A., & Merzenich, M. M. (1997). Learning transfer and neuronal plasticity in humans trained in tactile discrimination. *Neuroscience Letters*, *232*(3), 151-154. [https://doi.org/10.1016/S0304-3940\(97\)00602-2](https://doi.org/10.1016/S0304-3940(97)00602-2)
- Spitoni, G. F., Galati, G., Antonucci, G., Haggard, P., & Pizzamiglio, L. (2010). Two forms of touch perception in the human brain. *Experimental Brain Research*, *207*(3-4), 185-195. <https://doi.org/10.1007/s00221-010-2446-5>
- Spitoni, G. F., Pireddu, G., Cimmino, R. L., Galati, G., Priori, A., Lavidor, M., Jacobson, L., & Pizzamiglio, L. (2013). Right but not left angular gyrus modulates the metric component of the mental body representation: A tDCS study. *Experimental Brain Research*, *228*(1), 63-72. <https://doi.org/10.1007/s00221-013-3538-9>

- Sripati, A. P., Yoshioka, T., Denchev, P., Hsiao, S. S., & Johnson, K. O. (2006). Spatiotemporal Receptive Fields of Peripheral Afferents and Cortical Area 3b and 1 Neurons in the Primate Somatosensory System. *The Journal of Neuroscience*, 26(7), 2101-2114. <https://doi.org/10.1523/JNEUROSCI.3720-05.2006>
- Stavrinou, M. L., Della Penna, S., Pizzella, V., Torquati, K., Cianflone, F., Franciotti, R., Bezerianos, A., Romani, G. L., & Rossini, P. M. (2007). Temporal Dynamics of Plastic Changes in Human Primary Somatosensory Cortex after Finger Webbing. *Cerebral Cortex*, 17(9), 2134-2142. <https://doi.org/10.1093/cercor/bhl120>
- Sterr, A., Müller, M. M., Elbert, T., Rockstroh, B., Pantev, C., & Taub, E. (1998). Perceptual Correlates of Changes in Cortical Representation of Fingers in Blind Multifinger Braille Readers. *The Journal of Neuroscience*, 18(11), 4417-4423. <https://doi.org/10.1523/JNEUROSCI.18-11-04417.1998>
- Sterzi, R., Bottini, G., Celani, M. G., Righetti, E., Lamassa, M., Ricci, S., & Vallar, G. (1993). Hemianopia, hemianaesthesia, and hemiplegia after right and left hemisphere damage. A hemispheric difference. *Journal of Neurology, Neurosurgery & Psychiatry*, 56(3), 308-310. <https://doi.org/10.1136/jnnp.56.3.308>
- Stevens, J. C., & Choo, K. K. (1996). Spatial Acuity of the Body Surface over the Life Span. *Somatosensory & Motor Research*, 13(2), 153-166. <https://doi.org/10.3109/08990229609051403>
- Stevens, J. C., & Patterson, M. Q. (1995). Dimensions of Spatial Acuity in the Touch Sense : Changes over the Life Span. *Somatosensory & Motor Research*, 12(1), 29-47. <https://doi.org/10.3109/08990229509063140>
- Stevens, J. C., Alvarez-Reeves, M., Dipietro, L., Mack, G. W., & Green, B. G. (2003). Decline of tactile acuity in aging : A study of body site, blood flow, and lifetime habits of smoking and physical activity. *Somatosensory & Motor Research*, 20(3-4), 271-279. <https://doi.org/10.1080/08990220310001622997>
- Stilla, R., & Sathian, K. (2008). Selective visuo-haptic processing of shape and texture. *Human Brain Mapping*, 29(10), 1123-1138. <https://doi.org/10.1002/hbm.20456>
- Stilla, R., Deshpande, G., LaConte, S., Hu, X., & Sathian, K. (2007). Posteromedial Parietal Cortical Activity and Inputs Predict Tactile Spatial Acuity. *The Journal of Neuroscience*, 27(41), 11091-11102. <https://doi.org/10.1523/JNEUROSCI.1808-07.2007>
- Stone, K. D., Keizer, A., & Dijkerman, H. C. (2018). The influence of vision, touch, and proprioception on body representation of the lower limbs. *Acta Psychologica*, 185, 22-32. <https://doi.org/10.1016/j.actpsy.2018.01.007>
- Sun, Y., & Tang, R. (2019). Tool-Use Training Induces Changes of the Body Schema in the Limb Without Using Tool. *Frontiers in Human Neuroscience*, 13, 454. <https://doi.org/10.3389/fnhum.2019.00454>
- Sur M (1980) Receptive fields of neurons in areas 3b and 1 of somatosensory cortex in monkeys. *Brain Res* 198:465–471.
- Sur, M., Wall, J. T., & Kaas, J. H. (1981). Modular Segregation of Functional Cell Classes Within the Postcentral Somatosensory Cortex of Monkeys. *Science*, 212(4498), 1059-1061. <https://doi.org/10.1126/science.7233199>
- Sur, M., Wall, J. T., & Kaas, J. H. (1984). Modular distribution of neurons with slowly adapting and rapidly adapting responses in area 3b of somatosensory cortex in monkeys. *Journal of Neurophysiology*, 51(4), 724-744. <https://doi.org/10.1152/jn.1984.51.4.724>
- Suresh, A. K., Greenspon, C. M., He, Q., Rosenow, J. M., Miller, L. E., & Bensmaia, S. J. (2021). Sensory computations in the cuneate nucleus of macaques. *Proceedings of the National Academy of Sciences*, 118(49), e2115772118. <https://doi.org/10.1073/pnas.2115772118>
- Sutherland, M. T., & Tang, A. C. (2006). Reliable detection of bilateral activation in human primary somatosensory cortex by unilateral median nerve stimulation. *NeuroImage*, 33(4), 1042-1054. <https://doi.org/10.1016/j.neuroimage.2006.08.015>
- Suzuki, K., Yamadori, A., & Fuji, T. (1997). Category-specific comprehension deficit restricted to body parts. *Neurocase*, 3(3), 193-200. <https://doi.org/10.1080/13554799708404054>
- Tajadura-Jiménez, A., Cohen, H., & Bianchi-Berthouze, N. (2017a). Bodily Sensory Inputs and Anomalous Bodily Experiences in Complex Regional Pain Syndrome : Evaluation of the Potential Effects of Sound Feedback. *Frontiers in Human Neuroscience*, 11, 379. <https://doi.org/10.3389/fnhum.2017.00379>
- Tajadura-Jiménez, A., Tsakiris, M., Marquardt, T., & Bianchi-Berthouze, N. (2015). Action sounds update the mental representation of arm dimension : Contributions of kinaesthesia and agency. *Frontiers in Psychology*, 6. <https://doi.org/10.3389/fpsyg.2015.00689>
- Tajadura-Jiménez, A., Vakali, M., Fairhurst, M. T., Mandrigin, A., Bianchi-Berthouze, N., & Deroy, O. (2017b). Contingent sounds change the mental representation of one's finger length. *Scientific Reports*, 7(1), 5748. <https://doi.org/10.1038/s41598-017-05870-4>
- Tajadura-Jiménez, A., Väljamäe, A., Toshima, I., Kimura, T., Tsakiris, M., & Kitagawa, N. (2012). Action sounds recalibrate perceived tactile distance. *Current Biology*, 22(13), R516-R517. <https://doi.org/10.1016/j.cub.2012.04.028>
- Tamè, L., & Longo, M. R. (2015). Inter-hemispheric integration of tactile-motor responses across body parts. *Frontiers in Human Neuroscience*, 9. <https://doi.org/10.3389/fnhum.2015.00345>

- Tamè, L., Braun, C., Holmes, N. P., Farnè, A., & Pavani, F. (2016). Bilateral representations of touch in the primary somatosensory cortex. *Cognitive Neuropsychology*, 33(1-2), 48-66. <https://doi.org/10.1080/02643294.2016.1159547>
- Tamè, L., Braun, C., Lingnau, A., Schwarzbach, J., Demarchi, G., Li Hegner, Y., Farnè, A., & Pavani, F. (2012). The Contribution of Primary and Secondary Somatosensory Cortices to the Representation of Body Parts and Body Sides : An fMRI Adaptation Study. *Journal of Cognitive Neuroscience*, 24(12), 2306-2320. [https://doi.org/10.1162/jocn\\_a\\_00272](https://doi.org/10.1162/jocn_a_00272)
- Tamè, L., Pavani, F., Braun, C., Salemme, R., Farnè, A., & Reilly, K. T. (2015b). Somatotopy and temporal dynamics of sensorimotor interactions : Evidence from double afferent inhibition. *European Journal of Neuroscience*, 41(11), 1459-1465. <https://doi.org/10.1111/ejn.12890>
- Tamè, L., Pavani, F., Papadelis, C., Farnè, A., & Braun, C. (2015a). Early integration of bilateral touch in the primary somatosensory cortex. *Human Brain Mapping*, 36(4), 1506-1523. <https://doi.org/10.1002/hbm.22719>
- Tamè, L., Tucciarelli, R., Sadibolova, R., Sereno, M. I., & Longo, M. R. (2021). Reconstructing neural representations of tactile space. *NeuroImage*, 229, 117730. <https://doi.org/10.1016/j.neuroimage.2021.117730>
- Tan, H-R.M., Wühle, A., Braun, C. (2004). Unilaterally applied stimuli in a frequency discrimination task are represented bilaterally in primary somatosensory cortex. *Neurology & Clinical Neurophysiology*, 83.
- Tandon, S., Kambi, N., Lazar, L., Mohammed, H., & Jain, N. (2009). Large-Scale Expansion of the Face Representation in Somatosensory Areas of the Lateral Sulcus after Spinal Cord Injuries in Monkeys. *The Journal of Neuroscience*, 29(38), 12009-12019. <https://doi.org/10.1523/JNEUROSCI.2118-09.2009>
- Tannan, V., Dennis, R., & Tommerdahl, M. (2005). Stimulus-dependent effects on tactile spatial acuity. *Behavioral and Brain Functions*, 1(1), 18. <https://doi.org/10.1186/1744-9081-1-18>
- Tauste Campo, A., Vázquez, Y., Álvarez, M., Zainos, A., Rossi-Pool, R., Deco, G., & Romo, R. (2019). Feed-forward information and zero-lag synchronization in the sensory thalamocortical circuit are modulated during stimulus perception. *Proceedings of the National Academy of Sciences*, 116(15), 7513-7522. <https://doi.org/10.1073/pnas.1819095116>
- Tawney, G. (1895). The perception of two points not the space-threshold. *Psychological Review*, 2(6), 585-593. <https://doi.org/10.1037/h0073251>
- Taylor-Clarke, M., Jacobsen, P., & Haggard, P. (2004). Keeping the world a constant size : Object constancy in human touch. *Nature Neuroscience*, 7(3), 219-220. <https://doi.org/10.1038/nn1199>
- Thakur, P. H., Fitzgerald, P. J., Lane, J. W., & Hsiao, S. S. (2006). Receptive Field Properties of the Macaque Second Somatosensory Cortex : Nonlinear Mechanisms Underlying the Representation of Orientation Within a Finger Pad. *The Journal of Neuroscience*, 26(52), 13567-13575. <https://doi.org/10.1523/JNEUROSCI.3990-06.2006>
- Tibber, M. Elaine, A. Rees, G. Morgan, M. (2008). The neural correlates of the 3-dot vernier task: Visuospatial extrapolation examined within the framework of a duplex model of vision [Abstract]. *Journal of Vision*, 8(6):952, 952a, <http://journalofvision.org/8/6/952/>, doi:10.1167/8.6.952.
- Timm, F., & Kuehn, E. (2020). A Mechanical Stimulation Glove to Induce Hebbian Plasticity at the Fingertip. *Frontiers in Human Neuroscience*, 14, 177. <https://doi.org/10.3389/fnhum.2020.00177>
- Tinazzi, M., Zanette, G., Polo, A., Volpato, D., Manganotti, P., Bonato, C., Testoni, R., & Fiaschi, A. (1997). Transient deafferentation in humans induces rapid modulation of primary sensory cortex not associated with subcortical changes : A somatosensory evoked potential study. *Neuroscience Letters*, 223(1), 21-24. [https://doi.org/10.1016/S0304-3940\(97\)13382-1](https://doi.org/10.1016/S0304-3940(97)13382-1)
- Tommerdahl, M., Favorov, O. V., & Whitsel, B. L. (2005). Effects of high-frequency skin stimulation on SI cortex : Mechanisms and functional implications. *Somatosensory & Motor Research*, 22(3), 151-169. <https://doi.org/10.1080/08990220500084461>
- Tommerdahl, M., Simons, S. B., Chiu, J. S., Favorov, O., & Whitsel, B. L. (2006). Ipsilateral Input Modifies the Primary Somatosensory Cortex Response to Contralateral Skin Flutter. *The Journal of Neuroscience*, 26(22), 5970-5977. <https://doi.org/10.1523/JNEUROSCI.5270-05.2006>
- Tommerdahl, M., Whitsel, B. L., Favorov, O. V., Metz, C. B., & O'Quinn, B. L. (1999). Responses of Contralateral SI and SII in Cat to Same-Site Cutaneous Flutter Versus Vibration. *Journal of Neurophysiology*, 82(4), 1982-1992. <https://doi.org/10.1152/jn.1999.82.4.1982>
- Tong, J., Mao, O., & Goldreich, D. (2013). Two-Point Orientation Discrimination Versus the Traditional Two-Point Test for Tactile Spatial Acuity Assessment. *Frontiers in Human Neuroscience*, 7. <https://doi.org/10.3389/fnhum.2013.00579>
- Tremblay, F., Wong, K., Sanderson, R., & Coté, L. (2003). Tactile spatial acuity in elderly persons : Assessment with grating domes and relationship with manual dexterity. *Somatosensory & Motor Research*, 20(2), 127-132. <https://doi.org/10.1080/0899022031000105154>



- Trzcinski, N. K., Gomez-Ramirez, M., & Hsiao, S. S. (2016). Functional consequences of experience-dependent plasticity on tactile perception following perceptual learning. *European Journal of Neuroscience*, *44*(6), 2375-2386. <https://doi.org/10.1111/ejn.13343>
- Trzcinski, N. K., Hsiao, S. S., Connor, C. E., & Gomez-Ramirez, M. (2023). Multi-finger receptive field properties in primary somatosensory cortex : A revised account of the spatiotemporal integration functions of area 3b. *Cell Reports*, *42*(3), 112176. <https://doi.org/10.1016/j.celrep.2023.112176>
- Tucciarelli, R., Ejaz, N., Wesselink, D. B., Kolli, V., Hodgetts, C. J., Diedrichsen, J., & Makin, T. R. (2024). Does Ipsilateral Remapping Following Hand Loss Impact Motor Control of the Intact Hand? *The Journal of Neuroscience*, *44*(4), e0948232023. <https://doi.org/10.1523/JNEUROSCI.0948-23.2023>
- Turecek, J., Lehnert, B. P., & Ginty, D. D. (2022). The encoding of touch by somatotopically aligned dorsal column subdivisions. *Nature*, *612*(7939), 310-315. <https://doi.org/10.1038/s41586-022-05470-x>
- Türker, K. S., Yeo, P. L. M., & Gandevia, S. C. (2005). Perceptual distortion of face deletion by local anaesthesia of the human lips and teeth. *Experimental Brain Research*, *165*(1), 37-43. <https://doi.org/10.1007/s00221-005-2278-x>
- Tyson, S. F., Hanley, M., Chillala, J., Selley, A. B., & Tallis, R. C. (2008). Sensory Loss in Hospital-Admitted People With Stroke : Characteristics, Associated Factors, and Relationship With Function. *Neurorehabilitation and Neural Repair*, *22*(2), 166-172. <https://doi.org/10.1177/1545968307305523>
- Vallbo, A. B., & Johansson, R. S. (1978). The tactile sensory innervation of the glabrous skin of the human hand. In: "Active Touch, the Mechanism of Recognition of Objects by Manipulation", Gordon, G. (ed.), Pergamon Press Ltd. (Oxford), 1978 pp 29-54.
- Vallbo, B., & Johansson, R. S. (1984). Properties of cutaneous mechanoreceptors in the human hand related to touch sensation. *Human Neurobiology*, *3*, 3-14.
- Valyear, K. F., Philip, B. A., Cirstea, C. M., Chen, P.-W., Baune, N. A., Marchal, N., & Frey, S. H. (2020). Interhemispheric transfer of post-amputation cortical plasticity within the human somatosensory cortex. *NeuroImage*, *206*, 116291. <https://doi.org/10.1016/j.neuroimage.2019.116291>
- Van Boven, R. W., & Johnson, K. O. (1994a). A psychophysical study of the mechanisms of sensory recovery following nerve injury in humans. *Brain*, *117*(1), 149-167. <https://doi.org/10.1093/brain/117.1.149>
- Van Boven, R. W., & Johnson, K. O. (1994b). The limit of tactile spatial resolution in humans : Grating orientation discrimination at the lip, tongue, and finger. *Neurology*, *44*(12), 2361-2361. <https://doi.org/10.1212/WNL.44.12.2361>
- Van Boven, R. W., Ingeholm, J. E., Beauchamp, M. S., Bickle, P. C., & Ungerleider, L. G. (2005). Tactile form and location processing in the human brain. *Proceedings of the National Academy of Sciences*, *102*(35), 12601-12605. <https://doi.org/10.1073/pnas.0505907102>
- Van Der Hoort, B., Guterstam, A., & Ehrsson, H. H. (2011). Being Barbie : The Size of One's Own Body Determines the Perceived Size of the World. *PLoS ONE*, *6*(5), e20195. <https://doi.org/10.1371/journal.pone.0020195>
- Van Der Looven, R., Deschrijver, M., Hermans, L., De Muynck, M., & Vingerhoets, G. (2021). Hand size representation in healthy children and young adults. *Journal of Experimental Child Psychology*, *203*, 105016. <https://doi.org/10.1016/j.jecp.2020.105016>
- Van Nes, S. I., Faber, C. G., Hamers, R. M. T. P., Harschnitz, O., Bakkers, M., Hermans, M. C. E., Meijer, R. J., Van Doorn, P. A., Merckies, I. S. J., & on behalf of the PeriNomS Study Group. (2008). Revising two-point discrimination assessment in normal aging and in patients with polyneuropathies. *Journal of Neurology, Neurosurgery & Psychiatry*, *79*(7), 832-834. <https://doi.org/10.1136/jnnp.2007.139220>
- Vasudevan, M. K., Sadanand, V., Muniyandi, M., & Srinivasan, M. A. (2020). Coding source localization through inter-spike delay : Modelling a cluster of Pacinian Corpuscles using time-division multiplexing approach. *Somatosensory & Motor Research*, *37*(2), 63-73. <https://doi.org/10.1080/08990220.2020.1726739>
- Vega-Bermudez, F., & Johnson, K. O. (1999). SA1 and RA Receptive Fields, Response Variability, and Population Responses Mapped with a Probe Array. *Journal of Neurophysiology*, *81*(6), 2701-2710. <https://doi.org/10.1152/jn.1999.81.6.2701>
- Vega-Bermudez, F., & Johnson, K. O. (1999a). SA1 and RA Receptive Fields, Response Variability, and Population Responses Mapped with a Probe Array. *Journal of Neurophysiology*, *81*(6), 2701-2710. <https://doi.org/10.1152/jn.1999.81.6.2701>
- Vega-Bermudez, F., & Johnson, K. O. (1999b). Surround Suppression in the Responses of Primate SA1 and RA Mechanoreceptive Afferents Mapped with a Probe Array. *Journal of Neurophysiology*, *81*(6), 2711-2719. <https://doi.org/10.1152/jn.1999.81.6.2711>
- Vega-Bermudez, F., & Johnson, K. O. (2004). Fingertip skin conformance accounts, in part, for differences in tactile spatial acuity in young subjects, but not for the decline in spatial acuity with aging. *Perception & Psychophysics*, *66*(1), 60-67. <https://doi.org/10.3758/BF03194861>
- Vega-bermudez, F., Johnson, K.O. (2002). Spatial acuity after digit amputation. *Brain*, *125*, 1256-1264.

- Vidyaagar, R., Folger, S. E., & Parkes, L. M. (2014). Re-wiring the brain : Increased functional connectivity within primary somatosensory cortex following synchronous co-activation. *NeuroImage*, *92*, 19-26. <https://doi.org/10.1016/j.neuroimage.2014.01.052>.
- Vogt C, Vogt O (1919) Allgemeinere Ergebnisse unserer Hirnforschung. *J Psychol Neurol Leipzig* *25*:279–462.
- Wahlbom, A., Enander, J. M. D., & Jörntell, H. (2021b). Widespread Decoding of Tactile Input Patterns Among Thalamic Neurons. *Frontiers in Systems Neuroscience*, *15*, 640085. <https://doi.org/10.3389/fnsys.2021.640085>
- Wahlbom, A., Mogensen, H., & Jörntell, H. (2021a). Widely Different Correlation Patterns Between Pairs of Adjacent Thalamic Neurons In vivo. *Frontiers in Neural Circuits*, *15*, 692923. <https://doi.org/10.3389/fncir.2021.692923>
- Wang, L., Zhang, Z., Okada, T., Li, C., Chen, D., Funahashi, S., Wu, J., & Yan, T. (2021). Population Receptive Field Characteristics in the between- and Within-Digit Dimensions of the Undominant Hand in the Primary Somatosensory Cortex. *Cerebral Cortex*, *31*(10), 4427-4438. <https://doi.org/10.1093/cercor/bhab097>
- Wang, Q., Guo, Z.-L., Yu, Y.-B., Yang, W.-Q., & Zhang, L. (2018). Two-Point Discrimination Predicts Pain Relief after Lower Limb Nerve Decompression for Painful Diabetic Peripheral Neuropathy. *Plastic & Reconstructive Surgery*, *141*(3), 397e-403e. <https://doi.org/10.1097/PRS.0000000000004171>
- Wang, X., Merzenich, M.M., Sameshima, K., Jenkins, W.M. (1995). Remodelling of hand representation in adult cortex determined by timing of tactile stimulation. *Nature*, 378.
- Weiss, T., Miltner, W. H. R., Liepert, J., Meissner, W., & Taub, E. (2004). Rapid functional plasticity in the primary somatomotor cortex and perceptual changes after nerve block. *European Journal of Neuroscience*, *20*(12), 3413-3423. <https://doi.org/10.1111/j.1460-9568.2004.03790.x>
- Welker, W. I., & Johnson, J. I. (1965). Correlation between nuclear morphology and somatotopic organization in ventro-basal complex of the raccoon's thalamus. *Journal of Anatomy*, *99*(4), 761-790.
- Werhahn, K. J., Mortensen, J., Kaelin-Lang, A., Boroojerdi, B., & Cohen, L. G. (2002). Cortical excitability changes induced by deafferentation of the contralateral hemisphere. *Brain*, *125*(6), 1402-1413. <https://doi.org/10.1093/brain/awf140>
- Werner, G., & Mountcastle, V. B. (1965). NEURAL ACTIVITY IN MECHANORECEPTIVE CUTANEOUS AFFERENTS : STIMULUS-RESPONSE RELATIONS, WEBER FUNCTIONS, AND INFORMATION TRANSMISSION. *Journal of Neurophysiology*, *28*(2), 359-397. <https://doi.org/10.1152/jn.1965.28.2.359>
- Wheat, H. E., & Goodwin, A. W. (2000). Tactile Discrimination of Gaps by Slowly Adapting Afferents : Effects of Population Parameters and Anisotropy in the Fingerpad. *Journal of Neurophysiology*, *84*(3), 1430-1444. <https://doi.org/10.1152/jn.2000.84.3.1430>
- Wheat, H., Goodwin, A., & Browning, A. (1995). Tactile resolution : Peripheral neural mechanisms underlying the human capacity to determine positions of objects contacting the fingerpad. *The Journal of Neuroscience*, *15*(8), 5582-5595. <https://doi.org/10.1523/JNEUROSCI.15-08-05582.1995>
- Wolpert, D. M., Goodbody, S. J., & Husain, M. (1998). Maintaining internal representations : The role of the human superior parietal lobe. *Nature Neuroscience*, *1*(6), 529-533. <https://doi.org/10.1038/2245>
- Woolsey CN, Fairman D (1946) Contralateral, ipsilateral, and bilateral representation of cutaneous receptors in somatic areas I and II of the cerebral cortex of pig, sheep, and other mammals. *Surgery* *19*:684–702.
- Wu, G., Ekedahl, R., Stark, B., Carlstedt, T., Nilsson, B., & Hallin, R. G. (1999). Clustering of Pacinian corpuscle afferent fibres in the human median nerve. *Experimental Brain Research*, *126*(3), 399-409. <https://doi.org/10.1007/s002210050746>
- Xerri, C. (1999). Representational Plasticity in Cortical Area 3b Paralleling Tactual-motor Skill Acquisition in Adult Monkeys. *Cerebral Cortex*, *9*(3), 264-276. <https://doi.org/10.1093/cercor/9.3.264>
- Xerri, C., Coq, J., Merzenich, M., & Jenkins, W. (1996). Experience-induced plasticity of cutaneous maps in the primary somatosensory cortex of adult monkeys and rats. *Journal of Physiology-Paris*, *90*(3-4), 277-287. [https://doi.org/10.1016/S0928-4257\(97\)81438-6](https://doi.org/10.1016/S0928-4257(97)81438-6)
- Xu, J., & Wall, J. T. (1996). Cutaneous Representations of the Hand and Other Body Parts in the Cuneate Nucleus of a Primate, and Some Relationships to Previously Described Cortical Representations. *Somatosensory & Motor Research*, *13*(3-4), 187-197. <https://doi.org/10.3109/08990229609052575>
- Xu, J., & Wall, J. T. (1999). Functional organization of tactile inputs from the hand in the cuneate nucleus and its relationship to organization in the somatosensory cortex. *The Journal of Comparative Neurology*, *411*(3), 369-389. [https://doi.org/10.1002/\(SICI\)1096-9861\(19990830\)411:3<369::AID-CNE2>3.0.CO;2-F](https://doi.org/10.1002/(SICI)1096-9861(19990830)411:3<369::AID-CNE2>3.0.CO;2-F)
- Yamamotova, A., Bulant, J., Bocek, V., & Papezova, H. (2017). Dissatisfaction with own body makes patients with eating disorders more sensitive to pain. *Journal of Pain Research*, *Volume 10*, 1667-1675. <https://doi.org/10.2147/JPR.S133425>
- Zangaladze, A., Epstein, C. M., Grafton, S. T., & Sathian, K. (1999). Involvement of visual cortex in tactile discrimination of orientation. *Nature*, *401*(6753), 587-590. <https://doi.org/10.1038/44139>

- Zhang, M., Mariola, E., Stilla, R., Stoesz, M., Mao, H., Hu, X., & Sathian, K. (2005). Tactile discrimination of grating orientation: fMRI activation patterns. *Human Brain Mapping*, 25(4), 370-377. <https://doi.org/10.1002/hbm.20107>
- Zhang, Z., Tannan, V., Holden, J. K., Dennis, R. G., & Tommerdahl, M. (2008). A quantitative method for determining spatial discriminative capacity. *BioMedical Engineering OnLine*, 7(1), 12. <https://doi.org/10.1186/1475-925X-7-12>