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Cross-sensory perception and deprivation

by

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Declaration

I hereby declare that except where specific reference is made to the work of others, the contents of this dissertation are original and have not been submitted in whole or in part for consideration for any other degree or qualification in this, or any other university. This dissertation is my own work and contains nothing which is the outcome of work done in collaboration with others, except as specified in the text and Acknowledgements. This dissertation contains fewer than 65,000 words including appendices, bibliography, footnotes, tables and equations and has fewer than 150 figures.

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Abstract

Tactile information is crucial for interacting with our environment; however, its interaction with other sensory modalities and inter-sensory processes is a topic that remains underexplored. The present doctoral thesis aims to i) explore the effects of active touch on tactile perception and the role of visual calibration; ii) define the role of active and passive touch in sensory integration; iii) investigate cross-modal interactions between audio-tactile cues that could enhance tactile perception; iv) provide the neuroscientific basis for developing technology aimed at assessing tactile perception in situations of sensory impairment or in sensory-deprived children.

To achieve these objectives, we developed experiments involving sighted and blind adult participants, as well as children with hemiparesis and typically neurodeveloping ones. These experiments employed psychophysics methods and modelling. Experiments 1-2 particularly consisted on tasks involving passive and active tactile perceptions tasks, in unisensory settings (Experiment 1) or combined with acoustic feedback (Experiment 2), using a dynamic stimulus consisting of a moving wheel with a sinusoidal grid. Additionally, in Experiment 3, we involved active exploration with a haptic display capable of independently producing transient changes in both fingertip-surface friction (tactile stimulus) and transient sounds (auditory stimulus). In Experiment 4, we explored passive tactile perception on the forearm of children with hemiparesis and a control group, elicited by a haptic device (MSI Caterpillar). This could be presented alone or in addition to visual or auditory cues, in either a congruent or incongruent manner. i) Results from active and passive touch conditions revealed significantly lower precision in the blind group during active movements compared to passive perception, while no difference was observed in sighted participants. The reduced reliability of tactile feedback during active touch in blind individuals suggests that the lack of visual calibration might impact inter-sensory and motor-sensory processes required during an action. This further supports the role of visual calibration in active touch perception and highlights the need for intervention in this population. ii) When audio feedback was introduced, blind participants did not exhibit any differences between the unisensory and bimodal conditions, indicating a reduced interaction between senses. In

contrast, sighted individuals were significantly negatively affected by the auditory cue in the active condition. This suggests that movement might introduce noise to the signal, making sighted participants more susceptible to auditory interference, spotlighting the importance of auditory features in tasks involving active exploration. iii) When typical participants engaged in tactile explorations of a haptic display with different pitched sounds, the high-pitched one was found to modulate the bias in the perceived localization of a tactile stimulus. This suggests that frequency can modulate the perceived location of a tactile stimulus in active touch conditions. Finally, iv) in the detection and localization of a tactile stimulus, there was a significant worse performance between the more affected arm of children with hemiparesis and the non-dominant one of the control group. Our results also suggest the presence of interaction between tactile and visual feedback in both groups. This finding supports the use of multimodal technology as an effective approach in the evaluation and potential rehabilitation of somatosensory impairments.

Overall, the findings arising from my Ph.D. project provide new insights into the scientific understanding of tactile perception in active touch conditions, both in unisensory and multisensory contexts, delving into the role of visual calibration in this process. Furthermore, it expands knowledge of the impact of motor deficits on somatosensory perception and suggest new approaches for its evaluation and rehabilitation. The findings discussed here should be taken into consideration in the development of new haptic devices aimed at enhancing or substituting sensory information.

Key-words: active touch, blind, hemiparesis, multisensory, passive touch, vision.

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Chapter 1

Introduction

Our senses are the gate to the world. While hearing and vision allow us to share sensory events, our engagement with these events are driven by the somatosensory perception. Nevertheless, the somatosensory system seems more complex compared to the visual and auditory ones, as well as not as thoroughly understood in many aspects. This might be explained by the wide range of receptor types and stimuli that are processed within this system (Jacobs, 2011).

Furthermore, it is important to note that the perception of stimuli is not an isolated experience, as multisensory cues are typically present in real-world scenarios. Despite certain dimensions are dominated by a particular sensory modality, such as audition for time perception (Burr et al., 2009), and vision for spatial one (Alais and Burr, 2004), no information-processing system can be accurate under all conditions. Due to this, our brain tries to minimize variance and enhance the reliability of our percept by merging and integrating different sensory sources across and within modalities (Ernst and Bülthoff, 2004). In fact, it has been suggested that, even at early levels of the processing, the different sensory pathways might impact each other (Shams et al., 2000). At the neurophysiological level, the presentation of spatiotemporal congruent stimuli has been suggested to increase neural responses (Miller et al., 2015; Stein et al., 1989), the event-related potentials (ERPs) (Talsma et al., 2007) and blood oxygen-level dependent (BOLD) activation (Stevenson et al., 2006). At the behavioral level, the interactions between sensory modalities has been suggest to contribute to a more robust perception, for instance, multisensory stimulati has been shown to yield a more accurate and faster responses (e.g. Lunn et al., 2019; Sperdin, 2009) than unisensory one, as well as enhanced precision (e.g. Martolini et al., 2021). However, multisensory cues do not always imply a benefit, as the perceptual load, which is the amount of information processed, might also play a role in the perception (Macdonald and Lavie,

2011). Nonetheless, the majority of research in multisensory or cross-modal processing is developed between visual and auditory modalities, neglecting the somatosensory system, particularly when the tactile feedback is experienced under active touch conditions.

1.1 Multitouch project

The research presented in this thesis should be viewed within the context of the Marie Curie ITN multiTOUCH project (https://multitouch-itn.eu/). This project focused on the integration between different modalities with tactile cues, with the aim to contribute to the design of the next-generation of multisensory human-computer interfaces (HCI). To this end, the project attempts to develop interfaces that provide a richer user experience for individual's with sensory impairments. The central concept focuses on fostering the integration of haptics into HCI to enhanced acceptability of applications and technological devices. In order to do so, a cohort of experts in neuroscience, psychophysics, computer science, HCIs, haptics, and medical rehabilitation conformed the consortium. Hence, the multidisciliary network of multiTOUCH involved 5 academic partners:

- Université de Lille, France.
- Universita Degli Studi di Genova, Italy.
- Fondazione Istituto Italiano di Tecnologia, Italy.
- Université Catholique de Louvain, Belgium.
- Universitatea Stefan cel Mare Suceava, Romania.

In addition, the multitouch consortium comprised of three non-academic partners, specifically, two Start-ups; GoTouch VR and Hap2u in France, and a neuropediatric hospital, Verbund Katholischer Kliniken in Düsseldorf, Germany. 6 early-stage researchers (ESRs), with a background in neuroscience or engineering were recruited within the different institutions. All ESRs underwent an intensive training and participated in international scientific collaborations among the partners. This effort was aimed to broaden the ESR's knowledge and promote a comprehensive perspective on haptics.

Within multiTOUCH, this PhD project had the aim to deepen into our understanding of somatosensory processing and its interactions with motor function, in both unimodal and multimodal sensory conditions, in situations of sensory impairment or sensory deprivation. The research in this thesis has the goal to ultimately contribute to the development of new

haptic technologies. The following sections of this first chapter will be dedicated to a general description of the somatosensory system and mechanoreceptors, the integration between motor and somatosensory information and finally multimodal interactions. Chapter 2, as a necessary first experimental approach, explores the role of movement in tactile and cross-modal interactions in both blind and sighted individuals. Subsequently, in Chapter 3, we explained the impact of the frequency of a sound on tactile perception in active touch condition. In chapter 4, we deepen into the knowledge about the intricate interplay between tactile and motor function, and how additional sensory cues could foster tactile perception in typically and atypically developing children, as well as set new scenarios to use technology in the clinical field. Finally, in Chapter 5 we present the general discussion of the presented results, and highlight its clinical, technological and scientific implications.

1.2 Somatosensory system

Somatosensory perception is the heart of our interactions with the world, for example it has a fundamental role in survival, such as recognizing the heat of a fireplace, or the presence of a wound in our body. But somatosensory perception also allows us to experience the caress of a loved one, as well as make possible to locate an annoying insect on our skin and to guide us to reach the target with our hand to shoo it away. Hence, we could divide the somatosensory system into five different modalities: temperature, pain, proprioception (i.e. position of our own body in space), kinesthesia (i.e. movement of our own body or proprioception in motion), and touch. While the primary somatosensory receptor surface is the skin, we also have receptors located in internal organs, tendons and muscles (Jacobs, 2011), where we can find a majority of neurons that responds to mechanical stimuli (Handler and Ginty, 2021). As the main focus of this thesis is non-painful mechanical stimuli, this section will particularly aim to address these types of receptors and its pathways.

In the skin, we find different types of mechanoreceptors that respond diverse physical changes, such as vibration, stretch, pressure, light touch, texture and noxious pressure. Some of them are known as low-threshold mechanoreceptors (LTMs), as they respond to innocuous stimuli, while others respond to noxious stimuli and are classified as high-threshold receptors (HTMs) (Delmas et al., 2011). There are six types of LTMs mechanoreceptors in the skin that might be capable of detecting the innocuous feedback (Delmas et al., 2011). (i) Meissner corpuscles are encapsulated rapidly adapting (RA) mechanoreceptors, located in the dermal papillae, that transmit information regarding dynamic deformations and indentation (Johnson, 2001). (ii) Pacinian corpuscles are encapsulated RA receptors, that signal vibrations (Brisben

et al., 1999; Sato, 1961). (iii) Merkel complexes are groups of 50-70 slowly adapting type I (SAI) cells, located at the base of the epidermis (Iggo and Muir, 1969), sensitive to textures (Delmas et al., 2011). (iv) Ruffini corpuscles are located in the dermis, constitute slowly adapting type II (SAII) receptors and transmit information about skin stretch, indicating motion direction (Chambers et al., 1972). (v) C-fibers, located at the subepidermal corium, signal innocuous and social touch (Löken et al., 2009). (vi) Hair follicles epithelial cells are also able to release different neurotransmitters to communicate with the diverse neurons around the follicle, being able to conduct a variety of information (Agramunt et al., 2023). The LTMs receptors are connected to β-type A-fibres (Aβ nerve fibres), with the exception of hair follicles, which are connected also to Aδ fibres, and the C-fibres. Aβ nerve endings have higher velocity of conduction and lower thresholds to signaling, while Aδ and C-fibers have conduct at lower velocities and present higher thresholds (Delmas et al., 2011). The differences in speed are due to the higher myelinization and diameter of the axons (Jacobs, 2011).

Proprioceptors are mechanoreceptors that monitor joints position, the tension in ligaments and tendons, and inform about the muscular contraction. Structurally, those mechanoreceptors represent the highest level of complexity. Between the find the Golgi tendon organs monitor strain. Each of these receptors lie between tendons and muscles (Tuthill and Azim, 2018), and contain the sensory endings from motor neurons (Proske, 1979; Proske and Gandevia, 2012). Another receptor are muscle spindles, that perceive muscle length (i.e. contractions and stretches) and their velocity (Delmas et al., 2011; Kröger and Watkins, 2021; Prochazka and Wand, 1980; Proske and Gandevia, 2012), these are encapsulated receptors consisting on specialized muscle fibers, or intrafusal fibers. Different neurons innervate said intrafusal fibers: proprioceptive neurons, and efferent projections coming from motoneurons (For more detailed information see Kröger and Watkins, 2021; Proske, 1997). Finally, we have the receptors found in the joint capsules, which are Paciniform corpuscles, responding to compressions, and Ruffini-like endings similar to the ones found in the skin, perceiving changes in stretch (Grigg, 1994). However, also some of the mechanoreceptors located in the skin can provide relevant proprioceptive information about body posture, joints motion and direction and speed of the own body. Between them we found Pacinian corpuscles, Merkel complexes and Ruffini corpuscles (Jacobs, 2011).

Through different neural pathways, the somatosensory information goes from these receptors to the central nervous system. The soma of the somatosensory neurons are located in the trigeminal and dorsal root ganglia, receiving information about the face and body respectively (Capra and Dessem, 1992; Devor, 1999). A group of pathways conduct noncon-

scious proprioception, while other conscious somatosensory information. For nonconscious proprioception, the feedback about the body and limbs movement and location start in the receptors located in tendons and muscles, and project to the ipsilateral side of the cerebellum. The group that conduct conscious information, starts in the skin, tendons and muscles, and finish in the contralateral cortex. While the information from the face is conveyed by the trigeminal system, dorsal column–medial lemniscus pathway, carries proprioceptive information and tactile cues from the body. The information travels then contralaterally to the thalamus, where feedback coming from the body synapses in the ventral posterior lateral nucleus, while the one coming from the head in the ventral posterior medial nucleus (Jacobs, 2011). From the thalamus, the information synapses to the ipsilateral somatosensory cortex (i.e. Brodmann's areas 3a, 3b, 1, and 2), located in the postcentral gyrus. In particular, areas 3a (Fling et al., 2014) and 2 (Kaas, 1993), receive projections from muscles and deep proprioceptive inputs. Projections from the thalamus regarding cutaneous perception reach 3b and 1, and less extensively other somatosensory areas. In 3b we find the primary cutaneous map, representing in topographic order the contralateral part of the face and body (Kaas, 1993), known as "homunculus" (Penfield and Rasmussen, 1950). From 3b, the information reach area 1 (Garraghty et al., 1990; Kaas, 1993), yielding a second cutaneous map. A third map can be found in area 2, that receives projections from both areas, 3b and 1 (For a review see Harding-Forrester and Feldman, 2018). Interestingly, somatotopic maps representing, in some cases in a magnified manner (e.g. head, mouth and hands), each part of the body, can already be found at the level of the brainstem in animal models (Qi and Kaas, 2006). Subsequently, the information reaches the secondary somatosensory cortex (SII) (Disbrow et al., 2001; Ruben et al., 2001),and the area parietal ventral (Disbrow et al., 2000), that inherited a less precise somatosensory representations (Disbrow et al., 2001).

The same stimulus can trigger different types of mechanoreceptors of touch and proprioception, contributing both to control body positions, with evidences of integration already in the spinal cord (Tuthill and Azim, 2018). Behavioral studies offers further evidence of how cutaneous perception influences proprioception (Proske and Gandevia, 2012), which in turn can impact kinesthetic perceptions, as vibration applied to muscle tendons in static participants' hands elicited the illusion of movement (Tardy-Gervet et al., 1986).

By delving into the world of mechanoreceptors, proprioceptors, their neural pathways, as well as in their interplay, these studies uncover the rich complexity of the somatosensory system. They reveal the depth and sophistication with which we navigate our environment, setting the base of the research carried out in this doctoral thesis.

1.3 Somatosensory and motor integration

The complexity of the somatosensory perception becomes even greater when we consider the motor information. The motor system, similarly exhibits somatotopic organization (Leyton and Sherrington, 1917; Penfield and Boldrey, 1937), and it is closely interconnected with the somatosensory system. These connections, that are already reported at the level of the mechanoreceptors (Tuthill and Azim, 2018), span broadly across cortical somatosensory and motor areas. They go beyond merely linking primary cortices, also bridging the prefrontal and premotor cortex with secondary somatosensory (SII) and parietal cortices, illustrating a complex network of neural pathways (For further details see Ostry and Gribble, 2016). Interestingly, somatosensory receptive fields are also found in primary motor cortex, as well as in the dorsal and ventral premotor cortices (Rosén and Asanuma, 1972; Wong et al., 1978). Figure 1.1 illustrate the bidirectional interactions between regions.

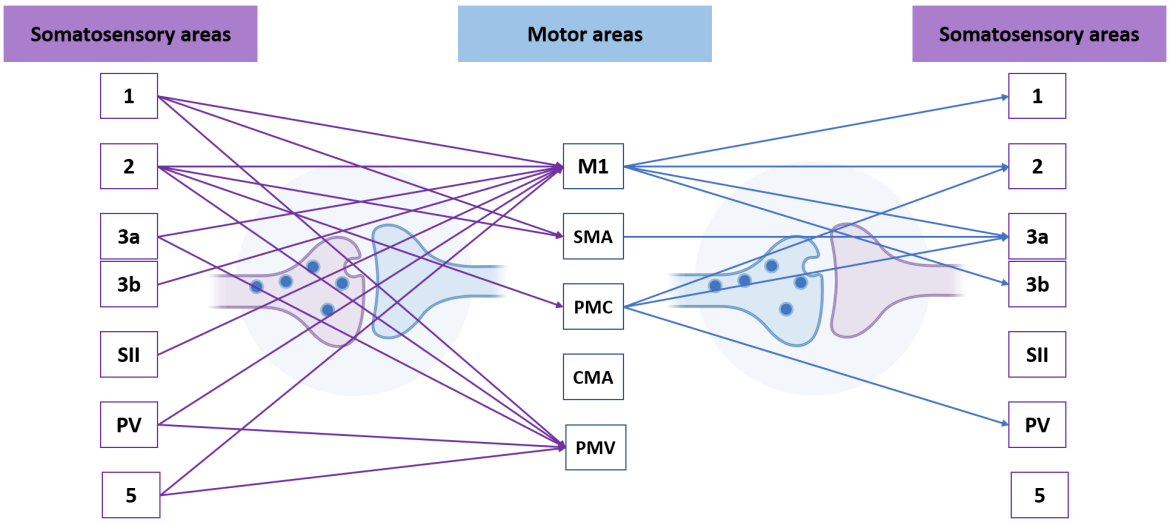

Figure 1.1 Interactions reported in previous literature between sensory and motor cortices, showing a bilateral exchange of information between them. Primary somatosensory cortex (Brodmann's areas 1, 2, 3a and 3b); secondary somatosensory cortex (SII); Parietal ventral area (PV); association somatosensory area (5); primary motor cortex (M1); supplemental motor area (SMA); premotor cortex (PMC); cingulate motor area (CMA); ventral premotor cortex (PMV). Diagram based on Ostry and Gribble (2016). Neurons created with BioRender.com.

The study of individuals who have suffered a brain injury best exemplifies the tight connection between motor and somatosensory function, as individuals who report motor impairments also exhibit somatosensory deficits. For instance, (Tyson et al., 2008) explored a cohort of 102 adults with hemiparesis after a stroke, showing that somatosensory impairments

were prevalent. In particular, tactile deficits occurred more commonly than proprioceptive losses. These impairments were linked to the level of weakness and the severity of the stroke. Furthermore, they reported significant impact on mobility, autonomy, and the overall recovery process (Tyson et al., 2008). Despite, the prevalence rate of these deficits vary between studies (Carey et al., 2018; Tyson et al., 2008; Zandvliet et al., 2020), it has been suggested that full motor recovery of patients with upper-limb paresis depend on the spontaneous recovery of the somatosensory function (Zandvliet et al., 2020). This supports previous literature that suggested a relationship between sensory and motor functions for motion recovery (de Diego et al., 2013). However, there is a progressive formation of the motor cortex over time, development linked to the refinement of fine motor skills (Cech and Martin, 2012; Säisänen et al., 2021). Indeed, the brain's maturity at the moment of the injury can also impact its expression (Cooper et al., 1995). How motor symptomatology impact children's somatosensory function is an underexplored topic, that also face challenges due to methodological inconsistences. Chapter 4, deepen into this topic, where I explore somatosensory perception in children with hemiparesis using a technological solution.

As previously stated, the relationship between motor and somatosensory areas is bidirectional. It has been suggested that motor control utilizes sensory and proprioceptive feedback to refine movements towards an objective, despite the presence of variability and noise in sensory inputs and motor outputs (Todorov and Jordan, 2002). In fact, in typically developed individuals, it has been reported that tactile input act as an additional proprioceptive cue, that can consistently bias by the reaching movements. They suggest that touch dynamically lead reaching movements towards intended targets (Bettelani et al., 2020; Moscatelli et al., 2019). On the contrary, the creation of the "efference copy" is an example of the modulations that the motor system has on somatosensory perception. The "efference copy" is the internal model of our movement which sets up our sensory feedback expectations (Wolpert et al., 1995). The "efference copy" aims to explain why there is reduced tactile perception in the presence of self-generated movement (e.g. Fuehrer et al., 2022). This internal model sets up our expectations for the sensory feedback we anticipate receiving as a result of our movement. The actual sensory feedback, termed "reafference", is then compared to the "efference copy". Through this comparison, our brain distinguishes relevant external information that requires further processing from self-generated information, which may be irrelevant and therefore suppressed or gate. The discrepancy, or "exafference", between these two types of information represents the information that further processed (e.g. Angelaki and Cullen, 2008; Saradjian, 2015). This phenomenon is known as movement-related tactile gating.

In conclusion, the literature abovementioned imply that somatosensory and motor information are intertwined at a multiple level of their pathways, engaging in constant integration and interaction, showing even certain degree of overlap in their representations (Harrison and Murphy, 2014). However, due to the high degree of plasticity between motor and sensory systems (For a review see Ostry and Gribble, 2016), and the role of somatosensory and visual feedback in sensorimotor control (Tardy-Gervet et al., 1986), it might be possible that the success of their integration are mediated by vision. However, this phenomenon has only been explored in sighted individuals. According the cross-modal theory, before integration of multimodal cues is possible, a continue re-calibration between senses plays a fundamental role until 8-10 years old. During this process, the most reliable sense helps to calibrate the others. Until that milestone is achieved, one sense dominates the perception (Gori et al., 2008). This mechanism facilitates optimal integration by enabling appropriate weighting of the available sensory signals (Nardini et al., 2013; Petrini et al., 2014). Due to the higher reliability of vision in space perception (Alais and Burr, 2004), the long-lasting lack of visual feedback might impact proper integration between sensory cues during a movement. However, despite ongoing efforts to develop solutions enabling blind individuals to experience perception akin to that of their sighted peers by the use of haptics, the aspect of sensory-motor integration has remained underexplored. Chapter 2, seeks to delve deeper into this topic by studying movement-related tactile gating in blind and sighted individuals.

1.4 Multimodal interactions

Somatosensory and motor information are never isolated. For instance, when we tie our shoes before going out home, multisensory cues are guiding our movement. The interaction between the different modalities occurs at different levels of the processing flow. As mentioned previously, multisensory cues are use to detect the same environmental information. It has been suggested that somatosensory and auditory modalities are already interacting at the level of the inferior colliculus external nuclei, located in the midbrain, as it encodes somatotopic map and auditory localization (Aitkin et al., 1981). These projections would be subsequently directed towards the superior colliculus (Van Buskirk, 1983). The superior colliculus, is another well explored structure involved in multimodal processing (Wallace et al., 1996). This structure, has been suggested to contain space maps from the visual, auditory and somatosensory modalities (Meredith and Stein, 1986), mediating multimodal integration and motor actions (Benavidez et al., 2021). In addition, there is a body of literature suggesting that the primary sensory areas are also involved in multisensory processing (e.g. Fishman

and Michael, 1973; Foxe et al., 2000; Kayser et al., 2005; Murray et al., 2016; Ranieri et al., 2022). However, traditionally, the areas identified (besides the superior colliculus) as responsible for the convergence of feedback from multiple senses are the association cortices. For example, the superior temporal sulcus, the prefrontal cortex (Driver and Noesselt, 2008), and the intraparietal area (Andersen et al., 1997), which is the area where multimodal information also interacts with motor feedback. The efficient integration of information is crucial for creating an optimal motor plan. Furthermore, continuous sensory feedback during the execution of a task fine-tunes the motor plan, enhancing both current and future performance (Edwards et al., 2019). When information is spatially and temporally coherent, in typical individuals this has been translated into generally better accuracy, precision in several cognitive tasks (e.g. Lunn et al., 2019; Martolini et al., 2021; Sperdin, 2009; Vizcay et al., 2023). For instance, research indicates that people react more quickly to stimuli that engage multiple senses simultaneously than to the fastest individual sensory stimulus (Van der Stoep et al., 2015). This phenomenon is understood through a model suggesting the nervous system optimally blends visual, auditory, and tactile inputs. It assesses the variability in these sensory inputs and assigns their weight, based on how reliable they are (Alais and Burr, 2004; Ernst and Banks, 2002). Process has been also suggest to contribute to learning (Edwards et al., 2019; Lehmann and Murray, 2005; Murray et al., 2004). However, multisensory interaction can sometimes have negative effects when the information provided by one sense acts a distractor (Mozolic et al., 2007) or when there is a conflict between the different feedback, inducing illusions (Keil, 2020). Interestingly, multisensory integration is also influenced by higher cognitive processes, such as cross-modal associations (Parise and Spence, 2009). For instance, the frequency of a sound has been associated with multiple physical features, such as brightness (Marks, 1974), size (Marks et al., 1987), and spatial elevation during visual (Parise et al., 2014) and static touch (Occelli et al., 2009). Chapter 3 further explores the impact of cross-modal interaction in our perception, focusing in particular in the effect of the sound frequency on touch perception, investigating potentials contributions of pitch in the localization of a tactile stimulus in the presence of a motor component (i.e. active touch).

In typical individuals, the developmental trajectories of multisensory integration and interactions seem to depend on the particular tasks. For instance, faster latencies in 8 months old infants' eye and head movements were seen in the presence of audio-visual targets compared to the unimodal conditions (Neil et al., 2006). Despite a larger temporal binding window (i.e. the interval of time in which two stimuli can be perceived as one) has been found in children compared to adults (Hillock-Dunn and Wallace, 2012), several

studies reported that multisensory processing might be a milestone acquired with age. For instance, Petrini et al. (2014) found, in a auditory-haptic tasks, that while adults integrated information in an optimal fashion children did not, suggesting that multisensory integration develops late in the discrimination of size. Barutchu et al. (2019) further support these findings, reporting that the impact of somatosensory information on sound categorization was more pronounced in adults compared to children, implying that the integration of auditory and somatosensory information develops progressively over time. In this line, it has been suggested a lack of optimal multisensory integration until the age of 8-10 in many tasks (Gori et al., 2008, 2012b,c), with younger children presenting unisensory dominance in a visual-haptic experiment, which changed according to the particular task they had to performed: vision dominated bimodal perception when judging orientation (Gori et al., 2008), while touch dominated size perception (Gori et al., 2008; Scheller et al., 2019). The explanation of this might be found in the sensory modalities development, which maturate at different speed (Gottlieb, 1971). This gradual development of the unisensory systems might be what support multisensory processes, allowing the statistical relationships among multiple sensory inputs encountered in daily life (Brandwein et al., 2010). In this scenario, as reported in the previous section, the cross-modal calibration theory states that before integration is possible, children use the most reliable sense to calibrate the others (Gori et al., 2008). This process is especially crucial during the early years of life, a period marked by rapid changes in the body, needing ongoing recalibration among the senses to adapt effectively. In agreement with this theory, these mechanisms can be disrupted in the presence of sensory impairments. The lack of visual calibration, the most reliable sense in space perception (Alais and Burr, 2004), has been suggested to be the cause of an alteration in multisensory processing found in blind individuals in spatial tasks, with numerous studies suggesting the presence of a reduced audio-tactile interactions in this population (e.g. Collignon et al., 2009; Hamilton-Fletcher et al., 2018; Hötting and Röder, 2004; Röder et al., 2004). It is important to mentioned, that this has been mainly explore in passive touch conditions. Since motor information might modulate perception, in Chapter 2, particularly in Study 2, I address the impact of an absent visual feedback in the cross-modal calibrations during active touch conditions.

Multisensory processes might also be disrupted in neurological patients, population that tend to experience a unisensory deficit that can contribute to motor deficits (For a review see Bolognini et al., 2016). The ability to properly integrate multimodal cues has been also suggested to be impaired. For instance, it has been reported that after a stroke, the 33% of the individuals experience a multisensory deficit. This is more likely to occur when the lesion is in the left hemisphere and in the cerebellar/brainstem (Van der Stoep et al., 2019). In

adults after a traumatic brain injury, it has been reported higher cognitive demands in the presence of multimodal information (Mayer et al., 2015), as well as an increased deficit in the integration between the somatosensory system and the visual or auditory one, compared to the integration of visual and auditory feedback (Sarno et al., 2003). Despite the significant impact that sensory function and its integration have on cognitive and motor deficits, this area remains underexplored, especially in children. Chapter 4 presents existing literature in the pediatric population, exploring cross-modal interactions in children with hemiparesis.

To summarize, in this section I delve into multisensory and motor integration, and how the different sensory systems, interact at different neurophysiological levels and structures, contributing to our understanding of environmental cues. Spatial and temporal binding has been suggested as key in multisensory integration (e.g. Slutsky and Recanzone, 2001; Stevenson et al., 2012) however, recent studies explore the impact of cross-modal correspondence in this multisensory processing (e.g. Parise et al., 2014; Parise and Spence, 2009; Spence, 2011). The spatial elevation of a tactile feedback and the frequency of the sound, despite his potential contribution to the development of haptic devices, has only been explored in passive touch condition (Deroy et al., 2016; Occelli et al., 2009). Chapter 3 tries fills this gap in the literature by exploring the impact of pitch on tactile localization during active explorations. I also highlight the developmental aspect of multisensory integration (Gori et al., 2008, 2012b,c; Petrini et al., 2012, 2014), by noting its gradual maturation and the significant impact of experience on this process, disrupted by a long-lasting sensory deficit (Collignon et al., 2009; Hamilton-Fletcher et al., 2018; Hötting and Röder, 2004; Röder et al., 2004). Since motor information might modulate perception, Chapter 2, particularly in Study 2, addresses the impact of an absent visual feedback in the cross-modal calibrations during active touch conditions. Finally, in this section I point out how multisensory integration can be affected by neurological conditions, leading to deficits in both, motor control and sensory processing (Bolognini et al., 2016). I particularly emphasize the need for further exploration on multisensory integration in children with sensory impairments, which is one of the aims of the Chapter 4.

1.5 Objectives of the thesis

Within the multiTOUCH framework, the goal of my Ph.D. project is to delve into how the brain processes somatosensory inputs and their interactions with motor function across both unimodal and multimodal conditions. This research aims to provide new insights that could contribute to the development of new haptic technologies tailored for situations involving

sensory impairment or sensory deprivation. To achieve this general objective, this thesis aims to:

I. Examine how active touch influences tactile perception and the modulation of visual calibration (See Section 2.1).

II. Determine the contributions of both active and passive touch to cross-modal interactions (See Section 2.2).

III. Explore audio-tactile interactions that could contribute to enhance tactile perception (See Chapter 3).

IV. Provide neuroscientific foundation for the creation of technologies designed to evaluate tactile perception in situations of impairment or sensory deprivation (See Chapters 4 and 5).

Chapter 1 illustrates the intricate nature of somatosensory and motor system, as well as draws the multisensory scenario in which we interact and the disruptions it might suffer in the presence of brain injury or sensory impairment. Chapter 2 sheds light into the modulations of the motor system over somatosensory perception in sighted and blind individuals. By using psychophysics, I reveal a reduced tactile reliability in blind participants due to the lack of visual calibration over the years (Section 2.1). Furthermore, when exposed to non-informative auditory feedback, I observed a diminished interaction between modalities in this population. On the contrary, for their sighted counterparts, the presence of movement increases their susceptibility to auditory interference (Section 2.2). Building on from Chapter 2, which suggests the importance of auditory cue features during self-elicited movements, and with the aim of investigating auditory feedback that could enhance tactile perception, Chapter 3 delves into whether pitch can influence the perceived location of a tactile stimulus in conditions of active touch. The psychophysical experiment presented suggests that high pitched sounds can bias the location of a tactile stimulus during exploration. In Chapter 4, through the use of a technological device and psychophysics, I contribute to the understanding of the intricate interplay between sensory and motor function by exploring the somatosensory perception, as well as visual-tactile and audio-tactile interactions, in children with hemiparesis and typically developing peers. Our results indicate somatosensory impairment in children with hemiparesis, and the presence of visuo-tactile interactions. Moreover, I identified developmental changes in the schemes of arm joints in typically developing children that are disrupted in the presence of hemiparesis. This research highlights the benefits of technological tools in clinical evaluation. Chapter 5, the concluding chapter of this doctoral thesis discusses

the findings within the state-of-art framework and highlights the potential applications of these results. Overall, this project deepens our understanding of the interplay between motor and somatosensory function. The results obtained offer valuable guidance for developing more effective rehabilitation approaches and technological aids tailored to meet the needs of those with sensory and motor impairment, as well as visually deprived individuals.

Chapter 2

Active touch in blindness

In Chapter 1, I introduced how interrelated are sensory perception and motor function, as well as the role of vision in space perception. Starting from this evidence, we can expect that long-lasting absence of vision might have an effect on the integration required during motor actions in blind individuals. Thus far, no study has been developed to trace the effect of visual loss on active touch perception.

As stated in the previous chapter, we interact with our environment through actions, which necessitate the integration of sensory feedback and motor execution (Gori et al., 2012b). This process is exemplified in the coordination between sensory inputs and motor outputs in the hand area (Jones et al., 1978), where inputs from the primary somatosensory cortex are essential for motor planning. Active touch, defined as self-generated movements by the participant, depends on the integration of tactile, proprioceptive, and kinesthetic information (Lederman and Klatzky, 1993; Robles-De-La-Torre and Hayward, 2001; Saal and Bensmaia, 2014), highlighting the complex interplay between different sensory modalities and motor control. On the contrary, passive touch is based predominantly on cutaneous perception (Elaine Chapman et al., 1996; Gori et al., 2012b).

Several studies have found that tactile sensitivity to a stimulus is enhanced when there's movement between the stimulus and the skin, rather than when the stimulus is stationary (Chapman, 1994; Cybulska-Klosowicz et al., 2011). Interestingly, when this movement is generated by our own body, research indicates that the somatosensory cortex actually reduces the processing of incoming sensory signals (Elaine Chapman et al., 1996; Kurz et al., 2018; Williams et al., 1998). This reduction, known as tactile suppression or movement-related tactile gating, is thought to help decrease the amount of sensory feedback processed by the cortex (Elaine Chapman et al., 1996; Kurz et al., 2018). It is proposed to be a mechanism by which the central nervous system (CNS) manages sensory input through various levels of

the somatosensory pathway (Elaine Chapman et al., 1996; Fuehrer et al., 2022; Voudouris and Fiehler, 2022). It is under debate whether tactile gating imply an overall diminished tactile perception or is a result of the brain's prediction (Bays et al., 2005; Kilteni and Ehrsson, 2020; Kilteni et al., 2020; Shergill et al., 2003), with some researchers arguing that tactile gating operates independently from any form of sensory prediction (Kilteni and Ehrsson, 2022). However, strong evidence supports the forward model as explanation for the phenomenon of tactile gating (Fuehrer et al., 2022).

This theory suggests that whenever we move, our brain not only sends out the command for that movement but also creates a mental representation of it, known as an "efference copy." This copy acts as an internal prediction of what sensory feedback we should expect from the movement. Our brain then compares this predicted feedback with the actual sensory information it receives, the "reafference." If the predicted feedback matches the actual sensory input, the brain uses sensory gating to filter out this information, considering it as generated by our own body. The discrepancies, or the sensory information that doesn't match the prediction, are identified as new external inputs, termed "exafference." This new information is then prioritized for further processing (Angelaki and Cullen, 2008; Saradjian, 2015). For example, when you run your fingertip over the edge of an object, your brain anticipates certain tactile sensations. It focuses on the important sensations that help identify the object's shape or texture and filters out the less important background ones. For an accurate exafference, a precise internal prediction (efference copy) and effective integration of sensory feedback from our skin, muscles, and joints are essential. This means that sensations from touch, awareness of body position (proprioception), movement (kinesthesia), and motor commands must be combined to distinguish between self-generated and externally generated information. Interestingly, the effectiveness of these cognitive processes can be influenced by the absence of a sensory modality. For example, in goal-directed movements, research indicates that the absence of vision is responsible of individuals relying more on their sense of muscle movement (Yoshimura et al., 2010). Furthermore, it has been suggested that without visual calibration over the auditory and haptic modalities, the spatial representation provided by proprioception is either delayed or significantly reduced (Cappagli et al., 2017a; Fiehler et al., 2009). Proprioceptive and tactile integration has been also suggested to be impaired after by the loss of vision. Studies focusing on blind individuals have found that they do not experience the rubber hand illusion, a phenomenon where sighted people feel that a rubber hand is their own when it is touched in synchrony with their hidden real hand (Ehrsson et al., 2005; Petkova et al., 2012). This inability among blind participants to undergo the illusion suggests a fundamental difference in how multisensory information is integrated at

central levels. Researchers propose that blind individuals may not be able to re-map tactile sensations onto an external reference frame, a process that sighted people do naturally. This effect, already present in visually impaired infants (Gori et al., 2021), it is believed to be the cause of the difficulties seen in individuals who are blind to merge the sensations of touch experienced simultaneously on a rubber hand and their own hand. This integration is what allows sighted individuals to undergo the rubber hand illusion (Nava et al., 2014; Petkova et al., 2012).

The diminished interaction between touch and hearing in individuals with visual impairments has also been well-documented. To illustrate this, Hötting and Röder (2004) noted that individuals who are congenitally blind showed less susceptibility to irrelevant stimuli during an auditory-tactile illusion task, unlike sighted participants. Similar results were obtained by Occelli et al. (2012) in a ventriloquist effect experiment. This illusion occurs when conflicting spatial information from one sensory modality influences the perception of a stimulus from another modality, typically leading to a mislocalization of sounds based on visual cues. The congenitally blind participants demonstrated a decreased ventriloquist effect, indicating a weaker integration between hearing and touch in the absence of visual input from early life (Occelli et al., 2012). As already introduced in Chapter 1, a possible explanation for these findings is provided by the cross-modal calibration theory (Gori, 2015). This theory states that developing of multisensory integration, which require interpreting cues from distinct reference frames and combining them into a single percept (Nardini et al., 2008), its needed a continuous recalibration process among the different sensory systems during the development. This recalibration process is guided by cross-sensory comparisons, where the most reliable or informative sense at a given time helps calibrate the others, leading to more accurate multisensory integration (Gori, 2015). This dynamic adjustment process is crucial for forming a comprehensive multisensory representation of our environment. For instance, in tasks requiring spatial awareness, vision is typically the most dependable sense for providing accurate spatial information (Alais and Burr, 2004). Consequently, the absence of visual information can result in multisensory alterations (Gori et al., 2012a; Hötting and Röder, 2004; Vercillo et al., 2017, 2018), potentially leading to spatial development deficits or delays (Cappagli et al., 2017b; Occelli et al., 2014).

Taken together, the previous research suggests the importance of motor-sensory and inter-sensory integration in the movement-related tactile gating, as well as integration as a developmental achievement in which vision has a leading role, at least in spatial tasks. Intriguingly, although the significance of active touch is well recognized in the everyday experiences of blind individuals, the impact of their voluntary movements on tactile perception

has been neglected. In the next sections, I explore the impact of blindness over motor-sensory integration and the modulation of motor information on cross-modal interactions. Specifically, first I focus on tactile perception in conditions of active touch. This is with the aim to explore whether and to what extend tactile precision is affected by self-elicited movement, and how visual experience might be mediating this process in blind individuals (Section 2.1). Subsequently, I focus on cross-modal audio-tactile interactions during active touch. This is in order to understand whether active touch can impact cross-modal processing, and how this process might be affected by the loss of vision in blind participants (Section 2.2). Results suggest that the lack of visual calibration is responsible of a reduced reliability of touch in blind people, with 10 years of blindness being enough for this effect to arise. In addition, it increases the internal noise of their sighted peers, making them vulnerable to auditory interference. Results of Chapter 2 offer important insights on the role of vision in somatosensory-motor integration, and the relevance of auditory features when apply to active touch conditions.

2.1 Exp. 1: Movement-related tactile gating in blindness

When an action is performed, self-elicited movement evokes a suppression of afferent information to the somatosensory cortex (Elaine Chapman et al., 1996; Kurz et al., 2018; Williams et al., 1998). For optimal functioning, this process requires proper integration of motor-sensory and inter-sensory systems (i.e., cutaneous perception, kinesthesia, and proprioception) (Chapman, 1994), as well as reliable information (Gori et al., 2012c). However, it has been reported that blindness might modulate said processes. For instance, some authors suggest a reduced integration between senses in this population (Nava et al., 2014; Petkova et al., 2012), as well as altered proprioceptive space representation due to the lack of visual calibration (Cappagli et al., 2017a; Fiehler et al., 2009). It remains unclear whether the absence of visual input can also modulate tactile perception during movements.

With this experiment, our aim is to explore the impact of movement on tactile perception, and the role of vision, using dynamic stimuli. As previously mentioned, the presence of movement between the skin and the stimulus foster tactile perception (Chapman, 1994; Cybulska-Klosowicz et al., 2011). By using a dynamic stimulus, we are able to provided movement also in passive touch condition, allowing us to explore the effects of voluntary movements. Comparing tactile performance in passive and active touch conditions, it is possible to disentangle the impact of movement in tactile perception, while by comparing sighted and blind individuals give us the chance to explore how sensory and motor integration

might be affected by visual long-lasting loss. To this end, we developed a psychophysics experiment to measure the precision of blind and sighted participants in two-alternative-force-choice (2AFC) velocity discrimination tasks.

Our hypotheses were (i) that sighted individuals would exhibit similar precision in both passive and active touch due to compensatory mechanisms displayed during movement (Elaine Chapman et al., 1996), while (ii) blind counterparts would show worse performance during active touch, due to an impaired integration of the different signals.

2.1.1 Method

Participants

The sample size for our experiment was determined through a power analysis. This analysis used the mean and standard deviation (SD) from a touch-based event-time perception study on passive and active conditions (Tomassini et al., 2012). The selection of said work was based on the utilization of the same device used in our experiment and the finding of a significant difference between active and passive tactile perception. The power analysis was computed via the function "pwr.t.test" (package "pwr") in RStudio (Version 1.4.1106; 2021), using the Cohen d value calculated from the abovementioned work to predict the sample size required, given the desired alpha and power. The Cohen's d value, computed as 1.48 from Tomassini's experiment (which had a sample size of 8), led to a power analysis suggesting 11 participants, based on an alpha of .05 and a power of .9. Because our target sample was blind individuals, a population that presents a lack of homogeneity in terms of blindness duration, we decided to increase the number of participants to 18 per group. Hence, 18 blind individuals (10 women; mean age ± SD: 41.67 ± 11.9 years) and 18 age-matched sighted controls (12 women; mean age ± SD: 35.11 ± 11.72) participated in our study. There was no significant age difference between the two groups ($t(34)=1.67$, $p=0.105$). The blindness onset ranges from 0 to 46 years (mean ± SD: 11.11 ± 15.76 years). Table 2.1 shows the clinical details of the blind individuals who participated in our study. Besides blindness, participants reported no history of motor-sensory or cognitive deficits.

In line with the Declaration of Helsinki, the research protocol was approved by the local health service's ethics committee (Comitato Etico Regione Liguria, Genoa, Italy; Prot. IIT_UVIP_COMP_2019 N. 02/2020, 4 July 2020). An informed consent form was signed by every participant.

Table 2.1 Blind participants' clinical details. The table shows participants' gender, their age at the moment of testing, pathology, blindness onset, visual perception and their braille reading frequency.

Participant	**Gender**	**Age**	**Blindness onset**	**Pathology**	**Visual perception**	**Braille reading frequency**
S1	F	22	0	Retinopathy of prematurity	Lights and shadows	Rarely
S2	F	34	0	Retinopathy of prematurity	No	Often
S3	F	50	0	Retinopathy of prematurity	Lights and shadows	Always
S4	F	32	0	Hereditary retinal dystrophies Retinitis pigmentosa	Lights and shadows	Rarely
S5	F	32	0	Retinopathy of prematurity	No	Occasionally
S6	M	49	0	Congenital atrophy of the optic nerve	No	Occasionally
S7	M	52	40	Optic nerve subatrophy for a benign tumor	Lights and shadows	Never learnt
S8	M	29	0	Leber Amaurosis	No Rarely	
S9	F	56	35	Retinitis pigmentosa	Lights and shadows	Never learnt
S10	M	49	6	Congenital glaucoma	No	Often
S11	M	33	17	Corneal opacity	No	Often
S12	M	43	26	Leber Amaurosis and Retinitis pigmentosa	Lights and shadows	Rarely
S13	F	43	0	Atrophy of the optic nerve	No	Rarely
S14	F	54	0	Retinitis pigmentosa	No	Rarely
S15	M	59	0	Glaucoma	No	Never
S16	F	56	46	Dystrophies involving the retinal pigment epithelium and Leber's congenital amaurosis	No	Occasionally
S17	M	33	20	Degenerative oculopathy of both eyes	Light and shadows, with strong contrast even colors. Field of view <1	Never
S18	F	24	10	Alstrom syndrome and Retinitis pigmentosa	Lights and shadows	Rarely

Design and procedure

A tactile stimulation was provided by a custom-made device (Figure 2.1), which was operated by a custom Matlab code (R2020b, The MathWorks, USA). The device consisted of a physical wheel with a 10 cycles/cm grating that could rotate at different velocities.

For the experiment, participants sat in a chair, aligning their body's midline with the center of the wheel. The index finger of their right hand was the area stimulated (see Figure 2.1 for an illustration of the finger's position on the wheel). Both blind and sighted participants were blindfolded to ensure the lack of visual input. Participants were instructed to detect and verbally report which stimulus was faster in a sequence of two movements with different speeds. The first one was presented always at 3cm/s (standard) during 1 second. After 500 ms of pause, the second stimulus (comparison) started during another second with a velocity determined by the adaptive algorithm, QUEST (Watson and Pelli, 1983), for a threshold estimation that could guarantee a well-sampled psychometric function.

We had two experimental conditions, with 30 trials each: (1) passive touch, where participants had to perceive passively the wheel's movement with their finger still; (2) active touch, in which participants were tasked to actively move their finger in the opposite direction of the wheel's rotation. The finger's active movement was controlled according to instructions (Togoli et al., 2020). We trained participants to move at approximately 3 cm/s, our standard velocity, and requested them to maintain this speed. To mitigate the noise created by the device, participants were provided with sound-isolating headphones.

Design and procedure

Each condition's data were fitted with Cumulative Gaussians, deriving the point of subjective equality (PSE) and just noticeable difference (JND) from the mean and standard deviation, respectively, of the best-fitting function. By bootstrapping (Efron and Tibshirani, 1993), we calculated the standard errors for both the JND and PSE estimates. For this work, we used the JND as the dependent variable, representing the minimum velocity needed to discriminate accurately the faster stimulus in 75% of the trials. First, we proceeded with the detection of outliers, defined as participants whose JND values were more than 1.5 times the interquartile range below the 1st quartile or above the 3rd quartile. This operation was done using JASP 0.16.0.0. A higher JND, meaning worse performance, was detected in four outliers: one in the sighted control group, and three in the blind one. The sighted participant was an outlier in the passive condition. One blind individual was an outlier in the passive condition as well, another in the active one, and a third in both passive and active conditions. Visual inspection

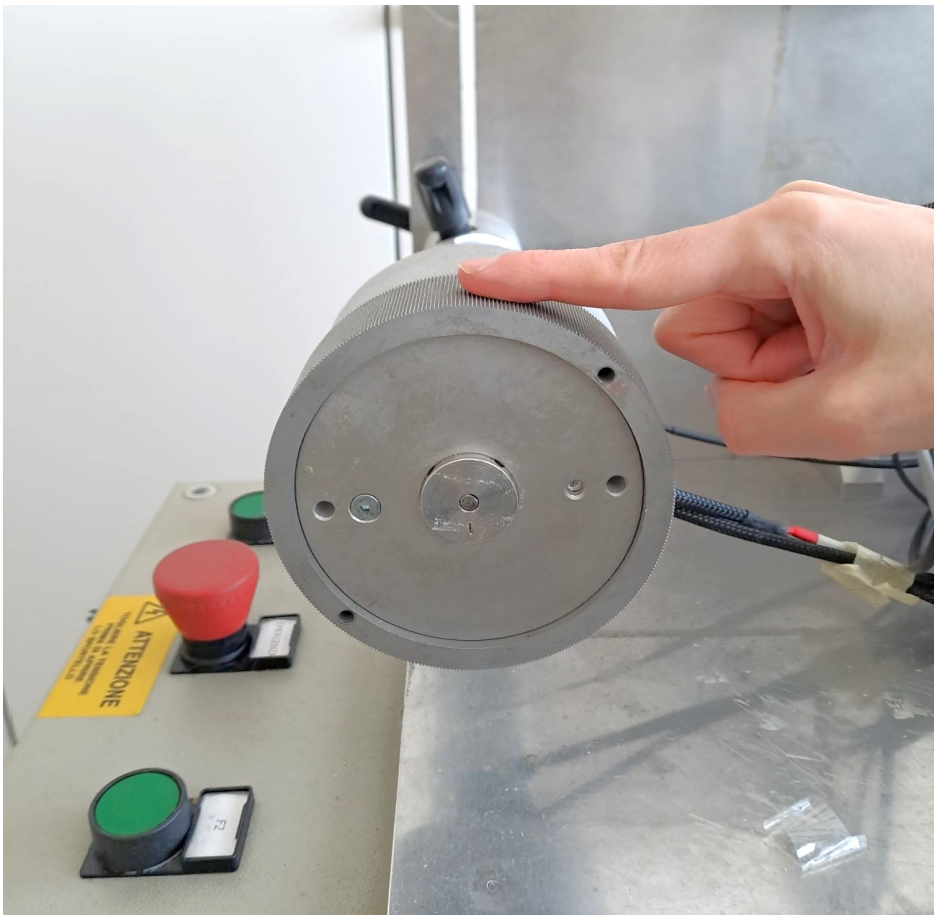

Figure 2.1 Experimental Setup, representing the position of the finger in the wheel.

of the data validated their poorer performance. Hence, in the analysis, 32 participants (17 sighted and 15 blind) were included.

Due to the inconsistency in the blindness duration, we calculated a Pearson correlation analysis, with the "cor.test" in R (package "stats"), between years of blindness and the JND for each condition (Passive, Active) in order to determine whether to split the blind sample.

The normality of the data was assessed using the Jarque Bera test. A mixed two-way ANOVA was performed, considering group (Blind, Sighted) as a between-subject factor and condition (Passive, Active) as a within-subject factor. Partial eta squared (h2P) was used to calculate the effect size. Unpaired t-tests for the between-subject factors and paired t-tests for the within-subject factors were used for the post-hoc comparisons. Cohen's d was calculated using the "cohensD" (package "lsr") in R as effect size. Values lower than .05 after Bonferroni correction were considered significant.

Although the average age of the blind group was not significantly higher than that of the controls, it was slightly higher. Therefore, to explore a possible linear relationship between

the participants' performance and age, we computed a linear model (LM) using the lm function (Package "stats"). This was done to ensure the validity of our results. First, for each condition (Passive, Active) separately, we performed an LM using the JND as the response variable and the group (Blind, Sighted) and age of the participants as between-subject fixed effects. The next step was to apply this model independently for each group (Blind, Sighted), with age as the only between-subject effect. To estimate the model's significance, we used ANOVA. To evaluate the goodness of fit of the data to the regression line we used the R2 value.

The potential effects of braille reading on tactile perception were controlled by computing an LM including the JND as response variable and the frequency of braille reading ("Always", "Often", "Occasionally", "Rarely", "Never" and "Never Learnt"), as the between-subject effect. To estimate the significance of the model's effect, as before, we used ANOVA. R2 value was used to indicate the goodness of fit of the data to the regression line.

2.1.2 Results

Regarding the effects of the blindness duration on the JND, no correlations were found for the active condition (t(13)= -.056, p = .956, r= -.015) or the passive one (t(13)= -1.443, p=.173, r= -.371). This suggests that a lack of vision, regardless of its duration, was responsible of the performance in the blind group. Because of that, all blind participants were included in the same group.

The Mixed ANOVA exhibited a significant main effect of condition (Passive, Active) on the JND (F(1,30)= 19.969, p<.001, η2P = .40), with a reduced precision (i.e. higher values of the JND) during active touch compared to its passive form. However, it also showed a significant interaction effect between the condition (Passive, Active) and the group (Blind, Sighted) (F(1,30)= 4.879, p =.035, η2P = .14). In particular, the post-hoc comparison revealed a significant difference between the active and passive conditions in the blind group (t(20.241)= -3.467, p=.005, Cohen's d= 1.266), while no significant difference was present for the sighted participants (t(31.981)= -1.337, p=.381, Cohen's d= .459), meaning that a significant decrease in precision during active touch was only evident in the blind group (Figure 2.2). Interestingly, when comparing the precision of both groups, there were no significant differences either in the passive (t(27.303)= 1.236, p=.454, Cohen's d= .426), nor the active condition (t(25.833)= -1.163, p=.511, Cohen's d= .419). This suggests that the difference found between active and passive touch conditions in the blind group was not due to their significantly higher precision during passive touch compared to controls, or a

significantly worse performance during the active, but rather due to the significant impact on their precision caused by the movement.

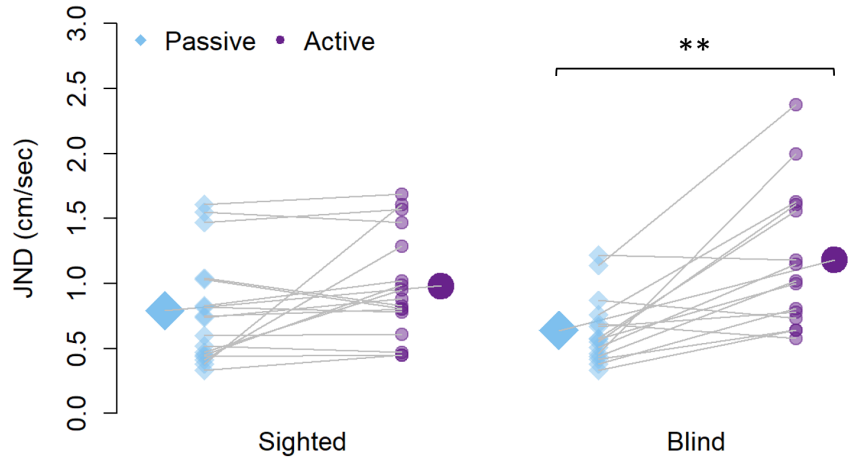

Figure 2.2 Just noticeable difference, or JND, obtained from sighted and blind participants for the passive (blue diamonds) and active (purple circles) touch condition. Although the JND in the active condition is generally higher than in the passive, only the blind group shows significantly worse performance in the active compared to the passive one. *p < 0.05. **p < 0.01.

To control for a possible impact of age on performance, we computed an LM for each condition, considering the group and age as fixed effects. This revealed no significant effect for the passive condition (R2=.148, p= .206), but the model showed a trend towards significance in the active one (R2=.231, p= .058). Therefore, we performed two additional LMs, one for each group in the active condition (see Figure 2.3), considering age as a fixed effect. While no significant effect was present for the blind group (R2=.055, p= .401), the sighted group showed a significant main effect of age (R2=.413, p=.005), with increased JND values in older participants. Our results suggest that tactile precision during active movements does not depend on age in the blind group, although it is affected by aging in their sighted counterparts.

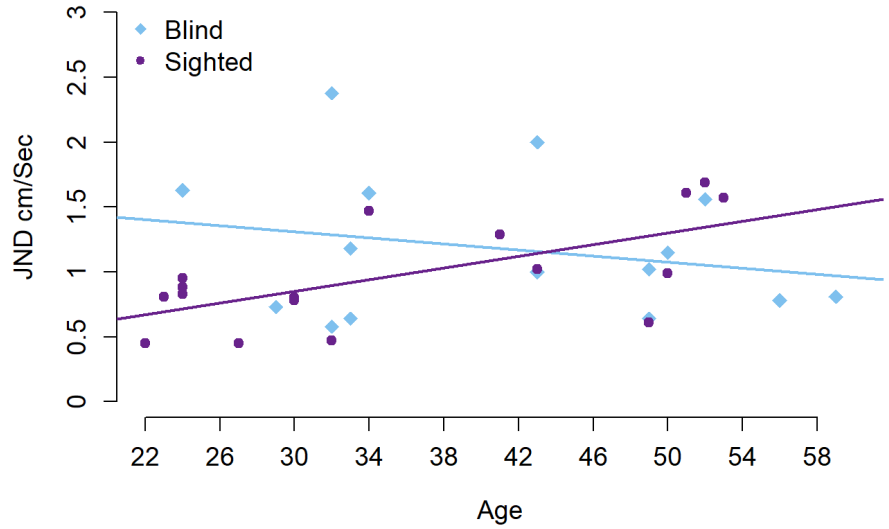

Figure 2.3 Linear Model (LM) analysis for each group (blind – blue diamonds, sighted – purple circles) between their age and JND in the active condition. The blue line corresponds to the regression line of blind participants, while the purple one represents the regression line of sighted individuals. Age had a significant effect in the sighted group, with an increased JND values in older participants.

To explore the possible effects of braille usage frequency on the performance of our blind participants, a Linear Model (LM) was applied for each condition. There was no significant effect for the active touch condition (R2=.096, p= .958) or for the passive one (R2=.153, p= .886), suggesting that the frequency of braille usage by our participants did not determine their precision.

2.1.3 Discussion

Perception and action are linked through sensory-motor and inter-sensory integration. The expression of this process is active touch, crucial in the interaction with the environment (Gori et al., 2012b). However, the role of vision in these processes has been a neglected topic. We hypothesized that sighted individuals would exhibit similar precision in both passive and active touch due to compensatory mechanisms displayed during movement (Elaine Chapman et al., 1996). Conversely, we predicted reduced precision in the blind group during active touch, attributing this to a lack of visual calibration (Cappagli et al., 2017a). Despite this, our main findings were: (1) a generalized reduction in precision in the active touch condition, and

(2) a more pronounced decrease in precision within the blind group. This study explores the precision in velocity discrimination using tactile feedback in passive and active conditions, as well as how the lack of vision might modulate tactile perception in active touch. A physical wheel was used to provide dynamic tactile stimulation that could be perceived passively, with the finger fixed in a certain position, or actively, in which participants had to perform a movement in the opposite direction of the wheel's rotation.

The generally lower precision during active touch, compared to passive touch, might be explained by the alleged movement-related tactile gating. This phenomenon refers to the reduction in somatosensory information processed by the cortex due to a body movement, which can lead to a worse encoding (Elaine Chapman et al., 1996; Gori et al., 2012b; Holst-Wolf et al., 2016), that has been associated with higher detection thresholds (Gertz et al., 2017; Voudouris et al., 2019) or lower detection rates during movements (Chapman and Beauchamp, 2006). Surprisingly, a clear general higher precision during passive touch compared to active has not been reported. Previous research suggests that motor strategy might be behind this, responsible for an enhancement of performance during active touch, for instance, by the adaptation of the movement's speed, the orientation of the digits while exploring, and the gating. Moreover, the enhanced activation of central components, such as motor set and attention, might contribute to fostering performance (For a review see Chapman, 1994). These two components might partially or wholly compensate for the effect of the gating, thus conveying a similar perceptual experience in most tasks. Some motor strategies could not be applied in our experiment, as the finger's orientation and speed were predetermined. This might have impacted the compensatory mechanisms, resulting in generally lower precision during active touch.

Our most interesting results refers to the differential behavior observed in the blind and sighted participants. Specifically, precision during the active condition is significantly worse compared to the passive one in the blind group, not in the sighted one. It has been suggested that the mechanism underlying the gating of somatosensory information, experienced during self-generated movements, could be linked to the creation of the efference copy (Blakemore et al., 1999; Kelso, 1977; von Holst, 1954; von Holst and Mittelstaedt, 1950). As mentioned above, the efference copy corresponds to the internal representation of the motor command generated during a self-generated movement. This representation, which allows us to predict the sensory information that would be generated by the movement, is compared to the actual sensory feedback perceived. The difference represents the relevant information from the external stimulus that needs to be further processed (Fuehrer et al., 2022; Voudouris and Fiehler, 2022). The functional role of this process is to enable us to distinguish between

afferents originating from our own movements and those originating from the external world (Saradjian, 2015). Therefore, haptic performance might be compromised if the anticipated sensory feedback is imprecise due to a noisy efference copy mechanism (Gori et al., 2012b). This is evident in children, a population whose ability to integrate sensory information and motor development does not reach adult-like levels until 8-12 years old (Gori et al., 2012b), spotlighting that reliable integration and information are necessary requirements for the success of this process. Since these processes has been suggested to be impaired in the blind population (Cappagli et al., 2017b; Champoux et al., 2011; Collignon et al., 2009; Petkova et al., 2012), our results imply, for the very first time, that motor-sensory and inter-sensory integration might also be affected, causing a non-specific gating of somatosensory information in the cortex during voluntary movements. Thus, the neural computations needed for the processing and comparison of tactile inputs during active movements might be affected, negatively impacting the precision. Interestingly, blindness duration did not influence blind participants' performance. This support that visual input is necessary for maintaining certain cognitive processes (Amadeo et al., 2019, 2020). Finally, in line with Legge et al. (2008), the findings of our work revealed that tactile precision remains unaltered, despite aging, in blind individuals during active touch perception, while in sighted participants experience a decline over the years, which might due to higher use of active touch in the blind group. In Chapter 5, these results will be further discussed.

Although the decrease in precision found here aligns with the results of Kilteni and Ehrsson (2022), who identified movement-related tactile gating as the responsible, one possible limitation of our paradigm is that it could have triggered both gating (i.e. external touch experienced while moving) and sensory attenuation (i.e. tactile feedback created by our own body). Further research is needed to determine whether the diminished tactile reliability in the blind group was due to more robust suppression by higher cortical levels, or due to a reduction in its strength. It should be mentioned that sensory gating has been suggested to be modulated by the relevance of the task and the context (Juravle et al., 2013), with some authors even reporting a movement-related sensory facilitation (Mouchnino et al., 2015). Given that the movement displayed during our experiment was irrelevant for the task, further research is needed in more ecological contexts.

To summarize, our work suggests that, as seen in children, due to the lack of visual calibration over the tactile modality, active touch can make tactile signal less reliable in blind individuals. This effect is already present after 10 years of blindness. These findings should be considered in the development of sensory substitution and sensory enhancement

technology tailoring this population, as well as stress the need of intervention. Further discussion is provided in Chapter 5, particularly Section 5.2.1.

In Section 2.1., text and images are adapted from Casado-Palacios, M., Tonelli, A., Campus, C., & Gori, M. (2023). Movement related tactile gating in blindness. Scientific Reports, 1–8. https://doi.org/10.1038/s41598-023-43526-8 https://creativecommons.org/licenses/by/4.0/

2.2 Exp. 2: Cross-modal interactions and movement-related tactile gating in blindness

In the previous section, I showed that active touch can impact the reliability of tactile feedback, particularly in blind individuals. However, in real world scenarios, the same environmental event is typically perceived by multiple sensory modalities. For instance, the tactile sensation and sound when our fingers tap a table, or the tactile, visual and auditory feedback from splashing our feet in the sea. Our brains are tasked with merging these inputs from different sensory channels into a single, unified percept, enabling us to perceive our surroundings in a cohesive manner. However, when multiple senses provide information about the same event, one sense may predominate in our perception due to its greater reliability (Ernst et al., 2000; Parise and Ernst, 2017). On the other hand, in situations where sensory information is uncertain or ambiguous, our brain combines cues from multiple senses to deduce the most plausible interpretation of the sensory feedback (Parise and Ernst, 2017). Research has highlighted the advantages of this multisensory integration, such as improved reaction times when responding to stimuli that are presented through more than one sensory modality (Pomper et al., 2014). However, in the presence of conflicting information between two sensory systems, one modality can negatively impact the other (Keil, 2020), or be a distractor (Mozolic et al., 2007). As previously stated, when vision is absent, and thus not able to calibrate the different sensory systems during development, there is a reduced interaction between different sensory information in blind individuals (e.g. Cappagli et al., 2017b; Champoux et al., 2011; Collignon et al., 2009; Petkova et al., 2012).

However, even in sighted individuals, the interactions between audio and touch has been an underexplored topic in multisensory research. This gap is even greater when tactile perception is elicited by active movements. Despite the modulations that movement has on somatosensory perception, inducing a gate of information processed (Chapman,

1994; Elaine Chapman et al., 1996; Kurz et al., 2018), the influence of this phenomenon on multisensory processing, as well as the effect of vision on these interactions, remains unexplored. In this section I aim to shed light into this topic following the same paradigm previously presented: dynamic stimuli was used to yield a better perception (Elaine Chapman et al., 1996) in a two-alternative force choice task (2AFC) aimed at assessing the precision in velocity discrimination. In this study, we compared the data from the unimodal tactile conditions (active, passive), with a new bimodal audio-tactile stimuli active and passive conditions. In the latter, we introduced auditory feedback that accompanied it, despite not being informative about the tactile sensation. By comparing the precision obtained in the audio-tactile to the unimodal tactile in both active and passive conditions, our goal was to defined how active movement influences multisensory processing. Moreover, by involving participants with and without blindness, we aim to explore the potential impact of visual experiences on these multisensory integration processes.

Our hypotheses were (i) a non-significant difference between bimodal and unimodal sensory stimulation in the passive condition for both groups, as tactile feedback might be reliable enough to not require additional sensory information in its estimation, as well as (ii) for the blind group in the active touch, due to the reduced interaction between multimodal information. On the contrary, we predict (iii) significant differences in the precision of the sighted participants in the bimodal, compared to the unimodal stimulus, due to the interaction between the non-informative auditory signal and the tactile one.

2.2.1 Method

Participants

This study builds upon data gathered in our previous experiment (Section 2.1), utilizing the tactile conditions (both passive and active) as a foundation for evaluating participants' ability to discriminate speed with bimodal audio-tactile stimulation, used in the current work. In this phase, we recalled the same participants to performed the audio-tactile conditions specifically designed for this research.

Our participant group included 18 individuals with blindness (10 women; mean age ± SD: 41.67 ± 11.9 years) and an aged-matched group of 18 sighted individuals (12 women; mean age ± SD: 35.11 ± 11.72). Statistical analysis confirmed that the age difference between the two groups was not significant ($t(34) = 1.67$, $p = 0.105$). The clinical characteristics of the participants with blindness are detailed in Table 2.1. All participants reported no history of sensory-motor (other than blindness) or cognitive deficits.

The research protocol, in line with the Declaration of Helsinki, was approved by the local health service's ethics committee (Comitato Etico Regione Liguria, Genoa, Italy; Prot. IIT_UVIP_COMP_2019 N. 02/2020, 4 July 2020). All participants signed an informed consent form.

Design and procedure

The tactile stimulation was provided by the same device presented previously: a physical wheel with 10 cycles/cm greeting which velocity could be programmed (Gori et al., 2011; Tomassini et al., 2012). For auditory stimulation, we employed a 927 Hz tone generated by a component of the MSI Caterpillar system (Gori et al., 2019), which was linked to the wheel, as illustrated in Figure 2.4. The operation of both devices was controlled through a Matlab custom script (R2020b, The MathWorks, USA).

Following the same procedure of the previous experiment, participants were seated with their body's midline aligned with the wheel apparatus. The orientation of the finger is shown in 2.4. The tactile stimulation was applied to the index finger's fingertip of the right hand. To ensure that vision did not influence the results, all participants, both blind and sighted, wore blindfolds. The experimental task involved participants perceiving two sequential tactile stimulations at different speeds, each lasting one second, with a 500ms pause between them. The first stimulus was always set at a standard speed of 3cm/s, while the second speed was determined by the adaptive QUEST algorithm (Watson and Pelli, 1983). Participants' task was to identify the faster stimulus and to verbally report it to the experimenter. Overall, this study included two type of stimuli: tactile (T) – from the previous work – and audio-tactile (AT). The tactile perception could be either passive, where the participant's finger remained stationary, or active, where the participant moved their finger in the opposite direction to the wheel's movement. There were 30 trials per condition, 120 trials in total. While in the tactile-only condition, participants were provided with sound-isolating headphones to prevent the device's noise from affecting the results, no headphones were employed in the bimodal one.

Data analysis

Each condition's data were fitted with Cumulative Gaussians. From the best-fitting function we obtained the PSE and JND estimates, derived, respectively, from the mean and standard deviations. By bootstrapping (Efron and Tibshirani, 1993), we calculated the standard errors

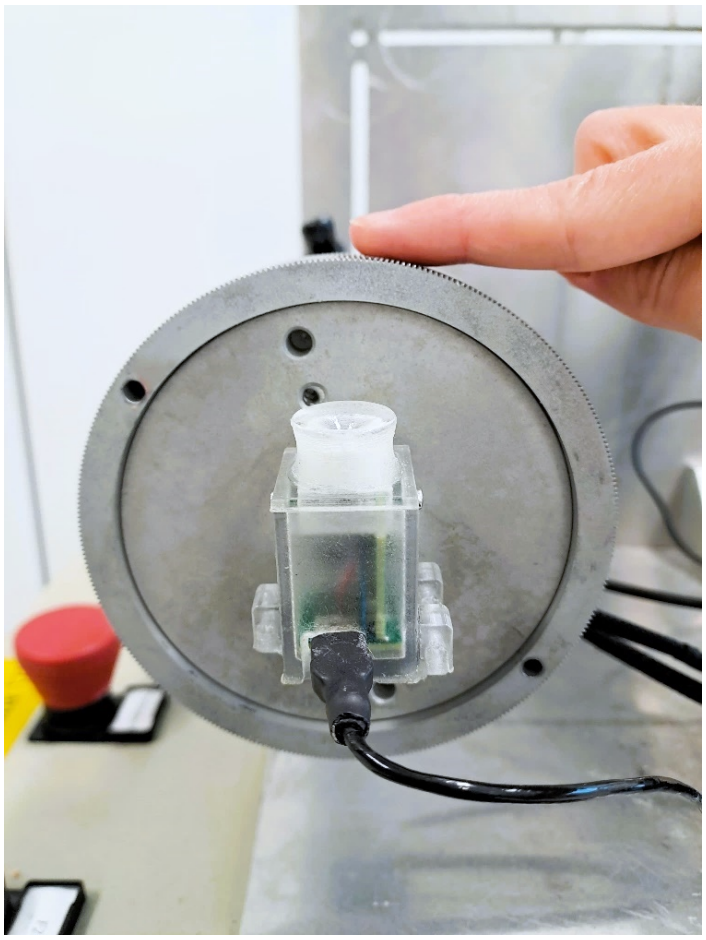

Figure 2.4 Experimental setup consisting a wheel with a greeting of 10 cycles/cm and a module of MSI Caterpillar.

for both PSE and JND estimates. Again for this work, the dependent variable used was the JND.

During our analysis, each participant's psychometric curve was carefully examined to identify those presenting and inverted pattern, indicating a negative JND. To handle these case conservatively, any negative JND identified was substituted with the highest possible JND value, which, in our study, was set at 6 cm/s. This adjustment was necessary for two blind participants: one presetting a negative JND during the audio-tactile active touch condition, while the other in the audio-tactile in passive touch condition.

Further analysis involved identifying outliers within all conditions. An outlier was defined as a JND value either below the first quartile minus three times the interquartile range (IQR) or above the third quartile plus three times the IQR. The larger variability allowed in this study compared to the previous experiment was due the introduction of the bimodal condition,

which added another level of noise. Following this criteria, one outlier was found within the blind group for the audio-tactile stimulation in the passive condition. After removing this outlier, the final participant count for the analysis included 18 sighted individuals and 17 blind participants.

To address the variability in the onset of blindness among the participants, a Pearson correlation analysis was conducted to assess if it was necessary to categorize the blind participants based on the duration of their blindness. This analysis aimed to explore potential correlations between the blindness duration of the participant and their JND values across different sensory stimulations (Tactile and Audio-Tactile) and conditions (Passive and Active). For this purpose, the "cor.test" function from the "stats" package within the R programming environment (R Core Team, 2013) was used.

The normality of the data was assessed using the Jarque Bera test. Instead of t-test, when normality assumptions were not followed, Wilcoxon tests were applied ("wilcox.test" function, package "stats") (R Core Team, 2013). Planned comparisons were done, separately for active and passive touch, between the two sensory stimulations (Tactile and Audio-Tactile). In addition, to further support our findings, we calculated the delta from the audio-tactile and the tactile modalities (SensoryDelta), by subtracting the JND values of the latter from those of the former. We then conducted planned comparisons of these Delta scores against zero to assess the significance of the differences between sensory modalities.

Additionally, we computed the delta (ConditionDelta) representing the difference between active and passive conditions—again by subtracting the JND of the passive condition from the active one. This calculation allowed us to specifically examine the effect of movement on sensory perception within the two sensory stimulation, providing a nuanced understanding of how active touch influences multisensory processing.

2.2.2 Results

No correlations were found between JND and blindness duration for either passive (Tactile: r= .04, t(15)= .156, p=.8785; Audio-Tactile: r= -.153, t(15)= -.598, p=.559) or active conditions (Tactile: r= -.227, t(15)= -.901, p=.382; Audio-Tactile: r= -.108, t(15)= -.419, p=.681). For this reason, again in this study we merged all blind participants in a single group.

For the sighted individuals the statistical analysis revealed a significant worse precision in the audio-tactile compared to tactile (Z= 0.446, p=.046) (Figure 2.5.a), while this was not true for the passive condition (Z= .046, p= .837) (Figure 2.5.b), or for their blind peers (Active: Z= 0.146, p= .513; Passive: Z=.166, p= .459). These findings suggest that the

non-informative sound only affected the performance of the sighted participants during self-elicited movements.

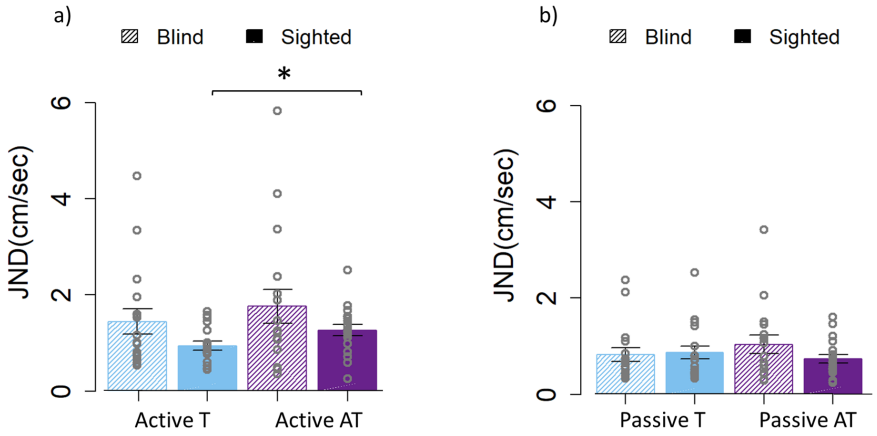

Figure 2.5 Just Noticeable Difference (JND) scores for both blind and sighted participants across the two sensory modalities. 45° lined boxes mark the JND values for the blind group, while full colored boxes the JND values for sighted one. Blue color represents the unimodal tactile (T) modality, and purple the audio-tactile (AT) sensory stimulation. Panel 2.5.a include the results for the active conditions, Panel 2.5.b for the passive condition. A significant worse performance was only shown in for the AT sensory stimulus during active touch in the sighted group. *$p < 0.05$.

The SensoryDelta (i.e. differences in the JND between audio-tactile and tactile sensory stimulation) for both active and passive touch condition can be seen in Figure 2.6. As predicted, when compared to zero, the only significance observed was in the active condition in the sighted participants ($t(17)= 2.363$, $p =.03$). This group presented a positive value of the SensoryDelta, indicating a higher values in the JND in the audio-tactile sensory stimulation compared to the tactile one. That imply that, within each condition (i.e. passive, active), the difference between unimodal and bimodal sensory stimulation is only significantly difference in sighed participants in the presence of movement (Figure 2.6)

Subsequently, ConditionDelta (i.e. difference in JND between active and passive conditions) was calculated to further explore the implications of movement in perception. This calculation was done separately for both sensory stimulations (Tactile, Audio-Tactile). A significant difference from zero was found in the blind group for both sensory stimulations (Tactile: $t(16)= 2.599$, $p =.019$, $p =.013$; Audio-Tactile: $t(16)= 2.804$, $p =.013$). This difference presented always a positive delta value, indicating that the active condition had a higher JND value than the passive. A significant difference from zero only emerged in the

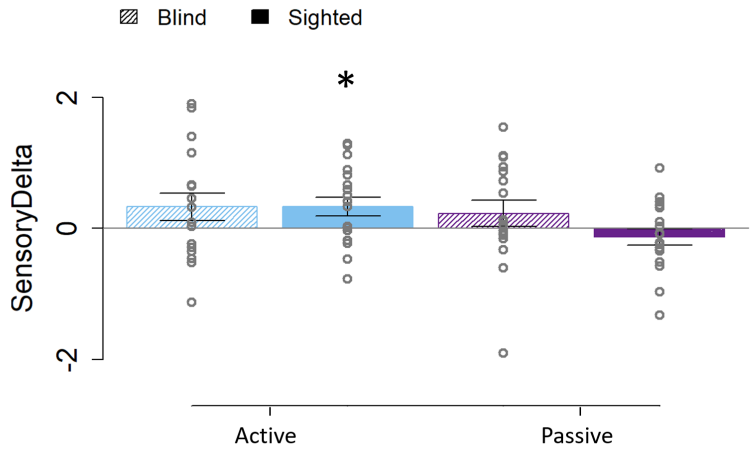

Figure 2.6 Values of the SensoryDelta. The blind group is represented by 45° lined boxes, and the sighted participants, represented by the full colored boxes. Blue color represents the active condition, while purple the passive one. A significant difference, when compared against zero, appeared in the sighted group for the active condition. *p < 0.05.

sighted group in the presence of audio-tactile stimuli ($t(17)= 3.31$, $p =.004$), showing also a positive delta. These findings suggest that the movement always diminish precision in blind individuals, while in their sighted peers only when coupled with a non-informative cue (Figure 2.7.).

2.2.3 Discussion

In the presence of ambiguation, humans integrate information conveyed by different modalities to generate a more reliable percept of the environmental event (Parise and Ernst, 2017). Despite knowing that body movements can alter how tactile information is encoded (Elaine Chapman et al., 1996; Fuehrer et al., 2022; Voudouris and Fiehler, 2022), the impact of active movement on multisensory processing and the potential modulatory effect of vision have been neglected. Our findings revealed three key points: (i) there was no significant difference in performance between unimodal and bimodal stimulation for both groups in passive conditions, (ii) this non-significance also applied to blind participants in active conditions, but (iii) sighted participants showed significantly different responses between unimodal tactile and bimodal audio-tactile stimulation during active touch. In addition, the results imply that, while movement is the responsible of a worse precision in blind individuals, in

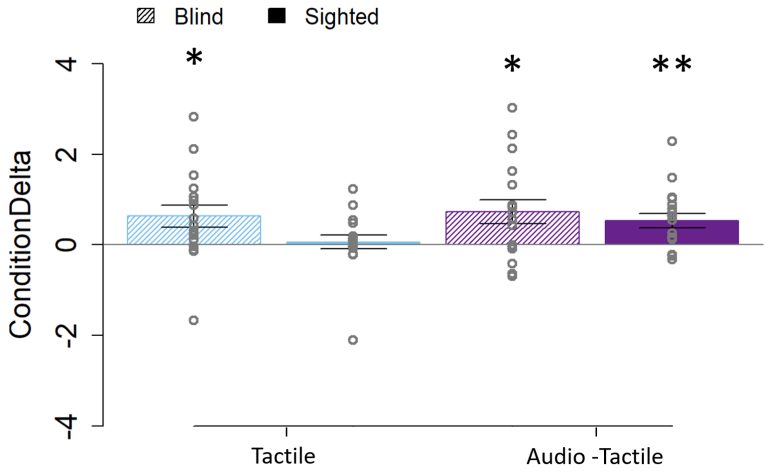

Figure 2.7 Values of the ConditionDelta. The blind group is represented by 45° lined boxes, and the sighted participants, represented by the full colored boxes. Blue color represents the tactile stimuli, while purple the audio-tactile one. A significant difference, when compared against zero, appeared in the blind group for tactile and audio-tactile stimuli, as well as for the sighted group in the presence of bimodal sensory stimulation. *p < 0.05. **p < 0.01 .

sighted is the interaction between the motor component and the non-informative sound. Thus, the outcomes of this experiment supported our initial hypotheses.

Our goal was to investigate how multisensory interactions, specifically the combination of tactile and auditory feedback, are influenced by participant movements and how vision might impact this interplay. To achieve this, we provided dynamic tactile and auditory feedback using a custom-made auditory device, and a physical wheel. By instructing participants to discriminate speed differences, we assessed precision in a unisensory tactile modality (using data from reported in Section 2.1), and in a bimodal audio-tactile modality. Tactile perception was categorized as passive, where the finger remained stationary while sensing the wheel's rotation, or active, where participants moved their finger against the wheel's motion. This design allowed us to closely examine how motor action impact audio-tactile interactions and the role of visual calibration.

The initial finding of our study highlighted that sighted participants exhibited decreased precision in the active touch condition in the presence of bimodal audio-tactile sensory stimulation compared to when they received only tactile input. This reduction in precision was not observed during passive perception, suggesting that the presence of auditory information specifically impacts the precision of tactile perception when an active movement is involved. In contrast, the blind participants did not show any significant difference in

precision between unimodal and bimodal sensory stimulation within conditions. To further analyze and corroborate these observations, we calculated the SensoryDelta, which represents the difference in precision between bimodal (audio-tactile) and unimodal (tactile only) conditions for both passive and active touch. This was done separately for the blind and sighted participants. Consistent with the initial results, a significant positive SensoryDelta was observed for the sighted group in the active condition alone, signifying a worse precision when there were the bimodal stimuli. One possible explanation for this phenomenon is movement-related tactile gating, a process where the brain selectively filters the sensory information being processed during active touch (Chapman, 1994; Kurz et al., 2018). This gating could increase the ambiguity of tactile signals, rendering sighted participants more susceptible to interference from auditory "noise" during movement. This finding underscores the complex interplay between sensory modalities and highlights the particular vulnerability of the sighted population to auditory distractions during tactile tasks that involve movement. In Chapter 5 I further discuss this topic.

Nevertheless, the same effect was not seen in the blind participants, as they were not affected by the presence of the tone regardless the presence of movement. These findings aligns with prior research indicating a diminished interaction between touch and hearing within this group (Champoux et al., 2011; Collignon et al., 2009; Hötting and Röder, 2004; Occelli et al., 2012). For an effective multisensory integration, we need to be able to decode information generated in different references frames, identifying which cues can be integrated into a unified percept (Nardini et al., 2008). As we previously mentioned, vision the most reliable sense in space perception (Alais and Burr, 2004), calibrate other senses in spatial tasks according to the cross-modal calibration theory (Gori, 2015), being responsible of multisensory integration in the spatial domain. Hence, when this calibration is missing, it can lead to a weakened multisensory processing and a reduced ability to automatically merge sensory inputs into a common spatial frame of reference (Collignon et al., 2009; Occelli et al., 2012; Vercillo et al., 2018).

To further explore the effects of self-generated movement on sensory processing, we computed the ConditionDelta, which represents the difference in precision between active and passive conditions across both sensory stimulation (i.e. tactile and audio-tactile). In sighted participants, a significant difference was observed in the bimodal condition but not in the unimodal condition. This indicates that the inclusion of movement worsened precision only when combined with the effect of non-informative auditory feedback. In contrast, blind participants exhibited significant differences in both, tactile and audio-tactile sensory stimulation, consistently showing decreased precision during active conditions. This finding

are in line with the findings reported in Section 2.1, extending our previous results to bimodal scenarios. These findings suggest that the presence of proprioceptive inputs and anticipated sensory feedback play a crucial role in the reduced tactile sensitivity observed. In the previous section, I argued that in the absence of vision, there may be an inefficient integration of tactile, proprioceptive, kinesthetic, and motor information, leading to a decrease in the reliability of tactile perception during active movements. This phenomenon also aligns with the previously reported diminished interaction between touch and hearing in blind individuals, supporting the notion that multisensory integration is compromised without the calibrating influence of vision.

In conclusion, our findings suggest that movements alone are responsible for decreased precision in blind individuals, indicating a reduced interaction between touch and hearing. Conversely, in sighted participants, active touch can increase the noise of the sensory signal, thereby modulating multisensory interaction and rendering them vulnerable to interference from auditory feedback. These results have significant implications for the development of new haptic devices and support the importance of multisensory training, in the spatial domain, in blind individuals. Further discussion is provided in Chapter 5, Sections 5.2.1 and 5.2.2

In Section 2.2., text and images are adapted from Casado-Palacios, M., Tonelli, A., Campus, C., & Gori, M. (2023). Cross-modal interactions and movement-related tactile gating: the role of vision. BioRxiv, 2023.10.30.564759. https://doi.org/10.1101/2023.10.30.564759. https://creativecommons.org/licenses/by-nc-nd/4.0/

Chapter 3

Auditory pitch modulates the localization of audio-tactile stimuli during active touch

In Chapter 1 I introduced that, in the study of multisensory processing, most studies focus on the role of temporal and spatial parameters. This research suggest, in general terms, that multisensory information is more likely to be integrated when it is closer in space (e.g. Frens et al., 1995; Slutsky and Recanzone, 2001) and time (e.g. Shore et al., 2006; Slutsky and Recanzone, 2001). However, priors due to systematic correlations among different sensory signal that might be based on our daily experience, known as cross-modal correspondences (Ernst, 2007; Kanaya et al., 2016), can also have a meaningful effect on multisensory processing (Chiou and Rich, 2012; Spence and Deroy, 2012).

These correspondences, that are non-arbitrary and shared by a population, have been suggested to increase the likelihood of two stimuli being bound together (Spence, 2011). Between them, we can find the association between frequency of a sound and the tactile spatial location (Deroy et al., 2016; Occelli et al., 2009). The spatial connotation of the frequency of an auditory signal is known: in the localization of an auditory source location, humans consistently map high pitch tones to high positions in space (Parise et al., 2014) in a wide range of functions, from perceptual (Pratt, 1930), to attentional (Chiou and Rich, 2012), to cognitive (Rusconi et al., 2006). In fact, some studies suggest that the frequency is the main driver of the perceived spatial elevation in spatial hearing (Pratt, 1930). Parise et al. (2014) suggested that this perceptual association reflects the natural environmental statistics. Moreover, they imply that the ear-filtering properties mirror this natural statistics mapping (Parise et al., 2014). In order to explore the effects of pitch on tactile perception,

Occelli et al. (2009) explored this associations using high and low-frequency tones coming from speakers, and vibratory stimulus generated by two vibromotors embedded in a foam cube, one in the upper part and the other at the bottom. They studied the inverse efficiency (IE) scores in two conditions: compatible, in which participants had to press the same pedal when they perceived a high frequency sound and the vibration in the upper part of the cube, and incompatible, in which different pedals were associated with high frequency sound and the upper vibrator. Their results show an association between the relative elevation of a tactile stimulus and the frequency of a sound in passive touch condition (Occelli et al., 2009). These results are also supported by Deroy et al. (2016), who also found a significant congruency effect between changes in the direction of tactile movements and changes in pitch during passive touch. Interestingly, this cross-modal correspondence has been applied in the sensory enhancement research field for cochlear implant (CI) users. Fletcher et al. (2020) showed that tactile stimulation provided by 12 motors organized in ascending pitch in the forearm were able to equalized the performance of normal-hearing participants listening to CI simulated audio to normal-hearing listeners.

In the experiments described above, the interactions with tactile cues are based on spatial tactile discrimination (i.e. the location of the tactile cue in the body) during passive touch, and the frequency on the sound. When instead the tactile feedback is perceived during movement (i.e. tactile exploration), there are certain factors that can modulate our sensory perceptions. On one hand, while passive touch relies on cutaneous perception solely, in active touch cutaneous information, kinesthetic, proprioceptive and motor information need to be integrated (Chapman, 1994; Elaine Chapman et al., 1996). On the other hand, self-elicited movements are also responsible of a gating of somatosensory information, that might limit the amount of information processed by the cortex (Kurz et al., 2018; Williams et al., 1998). Our previous study (See Chapter 2, Section 2.2), illustrate the impact of active touch on cross-modal interactions. Our findings indicate that active movements may introduce noise into the signal, potentially modulating audio-tactile interactions. This could lead to increased susceptibility among typical individuals to the disruptive effects of auditory feedback noise, adversely affecting their precision. The characteristics of additional sensory signals accompanying the tactile task appear to present a unique influence in active touch scenarios. In addition, during active exploration of a surface there is also a probable temporal discrimination (i.e. the moment in which the stimulus is triggered) guiding our perception. Consequently, it remains unclear whether the abovementioned association between pitch and tactile location also are maintained in the presence of movement, and if it could be used to bias the perceived location of the tactile signal.

The psychophysical experiment presented in this chapter has the aim to explore these questions. To achieve this goal, visually deprived participants had, for each trial, to slide their dominant index finger twice over a haptic display capable of independently producing transient changes in both fingertip-surface friction (tactile stimulus) and transient sounds (auditory stimulus) (Rekik et al., 2017). They were presented with a standard and a comparison stimulus, and asked to discriminate which one was located higher on the plates' y-axis, under three experimental conditions. The standard tactile stimulus was always accompanied by a pink-noise sound. The auditory feedback paired with the tactile feedback in the comparison interval was varied in the three conditions: (i) neutral, in which both the standard and comparison stimulations were accompanied by a pink-noise; (ii) high pitch, in which a 6KHz sound was paired with the comparison tactile stimulation; and (iii) low pitch condition, where the comparison was presented with a 800 Hz sound.

We hypothesized differences in threshold. The high-pitched sound was expected to bias participants' threshold towards lower values, while the low-pitched sound towards higher ones. No hypothesis was made for the slope.

3.1 Method

3.1.1 Participants

21 healthy participants (8 men; mean ± standard deviation (SD) age: 29.33 ± 9.24) participated in our research. All subjects reported no history of psychiatric or neurological disorders, no motor deficits or loss of skin sensitivity in their hands. The research protocol was approved by the UCLouvain Ethics Committee in line with the Declaration of Helsinki. All participants signed informed consent before the beginning of the experiment.

3.1.2 Design and procedure

For the tactile stimulation we used E-VITA tactile display (Rekik et al., 2017) (Figure 3.1). This device renders amplitude-modulated ultrasonic vibrations that reduce the coefficient of friction between the glass plate and the finger during active explorations. The influence of ultrasonic vibration on the display's friction is believed to be facilitated through ultrasonic lubrication and the 'squeeze film' effect. This effect generates a slim layer of compressed air, perceived as a "bump", at the interface between the finger and surface due to the ultrasonic vibrations (Wiertlewski et al., 2016). The tactile stimulus used in this work was a sinusoidal

signal with the device's maximum ultrasonic vibration amplitude and a spatial period of 5000 μm/mm. It was presented on the screen with a height of 10 cm and a width of 2 mm.

A speaker located at the upper part of the device generated the auditory feedback. We employed three types of auditory stimulations, all lasting 200 ms: a burst of pink-noise, a 6KHz, and an 800Hz tone.

In order to present audio and tactile stimuli that could be perceived as synchronous in time and space, we used an external infrared (IR) frame (model TOT104UIR009) of 213x161 mm. This frame could detect the position of the finger and trigger, for the desired finger's location on the haptic display, the auditory cue, creating the perception of an audio-tactile stimulus. The devices were controlled by a custom MATLAB code (R2015b, The MathWorks, USA).

Figure 3.1 Experimental Setup. For each trial, participant slide their fingertip twice on the haptic display, triggering an audio-tactile stimulus that differed in location.

As ensuring that feedback modalities are matched is crucial when implementing bimodal cues (Vizcay et al., 2023), to adjust the perceived intensity of the tactile and auditory stimuli, we performed a staircase procedure (one-up one-down) using pink-noise as auditory stimulus. Participants were instructed to report which of the two stimuli, triggered while they were sliding there finger on the tactile display, was the most salient . The intensity of the tactile stimulus remained constant, while the volume of the auditory one varied. After ten reversals of the staircase, it ended and the average volume of the last nine reversals was returned. This process was repeated for 4 participants, and the final value selected was computed from the average value of all adjustments. In a second step, to avoid an effect of difference in loudness on the results, we used the method of adjustment to equalize the loudness of the three tones. Participants were asked to match the loudness of the 800Hz and the 6kHz tones to the loudness of the adjusted pink noise sound, which was used as a standard. Each tone was adjusted 6 times by 4 different participants (Parise et al., 2014), being the gain factor applied the one resulted for the average of all the values obtained.

The main task was a Two-alternative forced choice (2AFC) localization comparison task. Each trial included two haptic display swipes and participants were asked to report whether the audio-tactile stimulus they experienced during the first or second swipe was located higher on the screen (that is farther away from their body). The haptic display was placed on the table (parallel to its surface) in front of the participant, with its longest dimension aligned with the participant's sagittal axis. Whereas the auditory component of the first swipe was always pink noise, that of the second stimulus was either pink noise, low pitch tone, or high pitch tone (in interleaved pseudorandom order). The first swipe's audio-tactile stimulus was placed at random within a range of ±20 mm from the center of the display. The second swipe's audio-tactile stimulus location was constrained to be within a range of ±60 mm from the center of the display. The psi marginal method (Prins, 2013) (one independent run of the method per auditory condition), executed in the MATLAB Palamedes toolbox (Prins and Kingdom, 2018), was used to place of both standard and comparison, in order to determine the threshold and slope of the psychometric functions. The lapse rate was treated as a marginalized parameter, to minimize the number of stimuli employed for the estimation of this parameter. Possible values for the threshold (α) ranged from - 60 to 60 mm with respect to the center of the display, in steps of 1.5 mm, while slope values (β) between 0.01 and 1. The lapse rate (λ) was ranged from 0 to 0.2 in 0.02 increments. The priors of alpha and beta were uniforms. Lambda prior was a half-normal with a mean of 0 and a standard deviation of 0.5, normalized to sum to 1. The participant went through 3 blocks of the task, each including 70 trials.

3.1.3 Data Analysis

A visual inspection of the raw stimulus-response pairs of every participant was performed to detect possible indiscriminate answers. One participant was excluded for presenting arbitrary ones in every condition. The remaining data was refitted using a hierarchical probit regression model, properly accounting for its structure (conditions within participants and participants within population).

Three parameters defined the relationship between the relative localization of the stimuli and the probability of correctly reporting which one was higher on the screen: the lapse rate (defining the asymptotes of the function), the threshold (localization parameter) and the slope (rate of change parameter). As no systematic lapse rate differences were expected between conditions, it was allowed to vary between participants but not between conditions.

Threshold and slope were allowed to vary between participants and conditions. This gives us the following model:

For i in 1 to I
For k in 1 to K

$$
\begin{aligned}
y_i &\sim Binomial(n_i, \varphi_i) \\
\varphi_i &= \lambda_{k[i]} + (1 - 2\lambda_{k[i]}) \cdot .5 \cdot erfc((-\beta_{k[i],cond[i]} \cdot (x_i - \alpha_{k[i],cond[i]}))/\sqrt{2}) \\
\alpha_{Neutral_k} &= \theta 1_k \\
\alpha_{High_k} &= \theta 1_k + \theta 2_k \\
\alpha_{Low_k} &= \theta 1_k + \theta 3_k \\
\mathrm{Log}_{10}(\beta_{Neutral_k}) &= \theta 4_k \\
\mathrm{Log}_{10}(\beta_{High_k}) &= \theta 4_k + \theta 5_k \\
\mathrm{Log}_{10}(\beta_{Low_k}) &= \theta 4_k + \theta 6_k \\
\lambda_k &= .5/(1+\exp(\theta 7_k)) \\
\theta_{1:7_{1:K}} &\sim MultiNormal(\mu, \Sigma)
\end{aligned}
$$

Where k is the participant's index, K is the total number of participants, i is observation index, I is the total number of observation, n correspond to the number of stimuli presented at a given intensity for a given subject, φ represents the probability to reporting the comparison stimulus as higher than the standard stimulus, λ is the lapse rate, is the threshold (location parameter) of the psychometric function, β is the slope (dispersion parameter) of the psychometric function, x is the stimulus intensity (length of the difference of placement between the standard and comparison stimuli), erfc is the complementary error function, θ are linear predictors of the psychometric function parameters, μ are the group means for each θ, and Σ is the θ covariance matrix

The priors for the mean group parameter selected for intercept was a normal distribution with a mean of 0 and standard deviation (SD) of 20, while for the predictors was a normal distribution with a mean of 0 and SD of 10. The priors for the log10(slope) mean group parameter was -.5 with SD of .5, while for the predictors was a normal distribution with a

mean of 0 and SD of .25. For the lapse, the group mean priors were normal distributions with mean -4 and SD 1. The individual deviations (z) were multiplied by the group-level standard deviations and the Cholesky factor (hyperprior), and added to the group-level means (Stan Development Team, 2024).

Model fitting

We used Stan (Stan Development Team, 2024) using the "Cmdstanr" package (Gabry et al., 2023), within RStudio (Version 2023.12.0) (RStudio Team, 2020) to fit the model using 4 chains of 5000 iterations, with a warm-up period that was discarded of 2500 iterations, resulting in 10000 draws from the posterior distribution.

Model checking

Following the modeling process, we examined the sampler diagnostics to evaluate the adequacy of the posterior distribution sampling using “Cmdstanr” package (Gabry et al., 2023). The diagnostics confirmed the absence of divergent transitions, a never reached maximum treedepth, an E-BFMI larger than .3 (“diagnostic_summary” function). Using "bayesplot" package (Gabry et al., 2019) we verified a reasonably aligned energy diagnostic (“nuts_params” function and “mcmc_nuts_energy” from), $\hat{R}$ values always lower than 1.01 (“rhat” function), and an effective sample size above 10% of the total sample size (“neff_ratio” function).

The effect of the auditory stimulation on the threshold and slope for the different conditions (Neutral, High, Low) was measured by the posterior distribution of the parameters θ_{1_k},θ_{2_k}, θ_{3_k} (threshold), and θ_{4_k},θ_{5_k}, and θ_{6_k} (slope). From these distributions we computed the differences between neutral and high, neutral and low, and between high and low, in threshold and slope, within participants. We estimated the probability of our null hypotheses by comparing 10000 random draws from these posterior distributions with zero. Bilateral tests were used to evaluate differences for the threshold estimates comparisons, as well as for the slope estimates between the different conditions within participants.

For each condition, we constructed an expected psychometric function to better illustrate the posterior distribution. From the 10^4 random draws from the predictive posterior distribution, we plotted the 50th percentile of the probability to detect the comparison as higher for each condition, as well as the points in the percentiles 2.5th and 97.5th (to address the 95% confidence interval), creating a psychometric function that could be anticipated for a new unseen participant from the same population.

3.2 Results

In Figure 3.2 can be seen the difference between conditions for the threshold parameter, showing a significantly reduced threshold for the high condition compared to the neutral one (pHigh≠ Neutral=.008). No significant differences were found between the threshold of the low and neutral conditions (pLow≠ Neutral= .076), or between the high and low conditions (pLow≠High= .491). In terms of Slope, the bilateral tests showed no significances between conditions (pHigh≠Neutral=.19; pLow≠Neutral= .643; pLow≠High= .537).

Figure 3.3 shows the predictive psychometric functions for the posterior distribution of an unobserved participant from the same population.

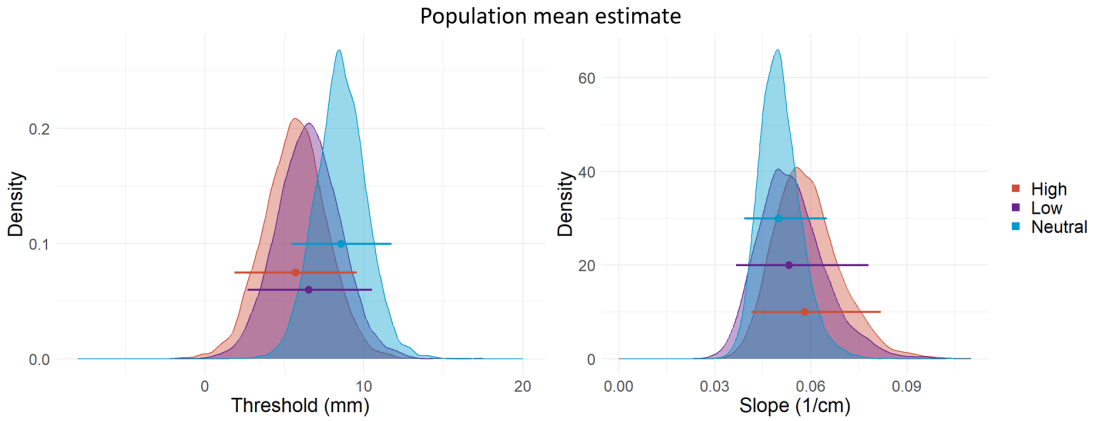

Figure 3.2 Population mean estimates for the threshold (left) and slope (right) parameters for each condition. Red represents the high condition, purple the low condition, and blue the neutral one. For the threshold, in the model these parameters are θ_{1_k} (Neutral), $\theta_{1_k} + \theta_{2_k}$ (High), and $\theta_{1_k} + \theta_{3_k}$ (Low), while for the slope are $10^{\theta_{4_k}}$ (Neutral), $10^{\theta_{4_k}+\theta_{5_k}}$ (High), $10^{\theta_{4_k}+\theta_{6_k}}$ (Low). The horizontal lines indicate the intervals within which the highest 95% of the posterior distribution's probability density is contained, while the dots denote the posterior distributions' median values.

3.3 Discussion

Humans tend to locate high pitched sounds in higher position is space, while low pitched tones are mapped in lower positions (e.g. Parise et al., 2014; Pratt, 1930; Rusconi et al., 2006). This process, that reflects both the natural auditory environments and the filtering effects of the outer ear (Parise et al., 2014), has been scarcely explored in association with touch, and limited to passive touch conditions. To investigate whether sounds with an implicit

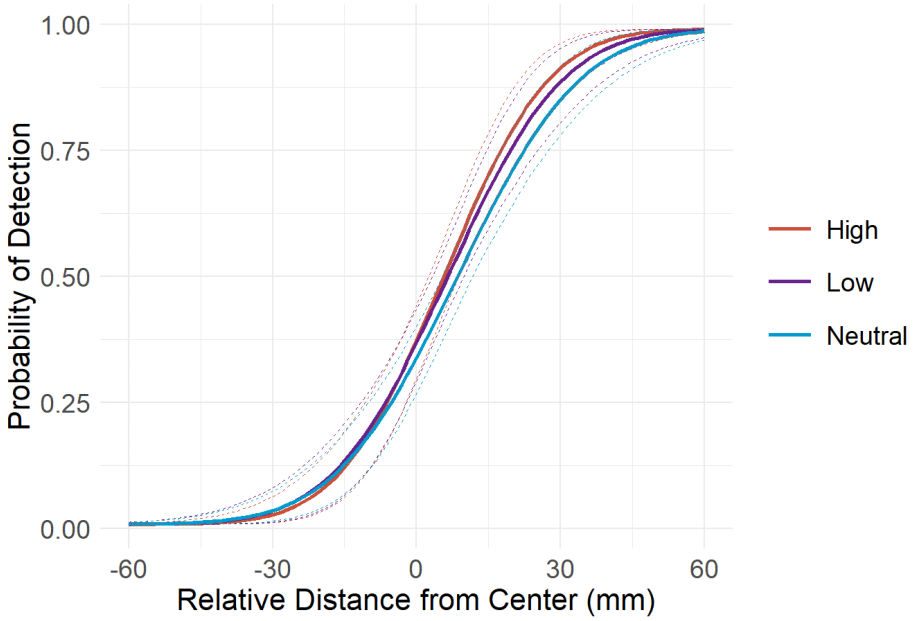

Figure 3.3 Expected psychometric functions derived from the posterior distributions. The bold lines show the psychometric function using the median of 10^4 random draws from the posterior parameter values. The dotted lines indicate the 95% highest probability density intervals range of uncertainty surrounding this expected function.

meaning could contribute to tactile perception during explorations, we studied the effect of frequency-elevation mapping on the localization of tactile stimuli under active touch conditions. We hypothesized that both high and low pitch would have an impact on the threshold with respect to the pink-noise. No hypotheses were made in terms of slope. The results obtained confirmed a significant difference between the threshold of the high pitch condition (i.e. high-pitched sound) and the neutral one (i.e. pink-noise). No significant differences were found with the low-pitched sound, as well in slope between the different conditions.

In this experiment, audio-tactile transient stimuli were provided when the participant slid the index finger of their dominant hand over a haptic display. Participants were instructed to slide their finger twice, and report the stimulus located higher in the plate. We measured the differences in threshold and slope between three different conditions: (i) neutral, using a pink-noise for the standard and the comparison stimulus, (ii) high, in which the standard was associated to the pink-noise and the test to a high-pitched tone, and (iii) low, in which we used a low-pitched tone for the comparison stimuli.

The exploration of the systematic deviations in the answer of the participants reveled a bias towards higher positions in the screen in the neutral condition. This bias could be due to

the dimensions of the fingertip, as the haptic display modulates the friction experienced by the entire surface area of the fingertip (Vezzoli et al., 2016). Furthermore, when localizing dynamic tactile stimuli that move in depth, like in our experiment, it has been reported a forward shift in the perception, which could be contributing to this effect (Merz et al., 2019). Another factor that might be playing a role in this bias is an order effect (García-Pérez and Alcalá-Quintana, 2011; Yeshurun et al., 2008), as the standard stimulus was always presented first than the comparison.

Interestingly, the bias observed in the neutral condition is significantly reduced when the comparison was associated with the high pitch sound. Despite the auditory feedback was always elicited from a speaker located on the top of the haptic display, high-pitched tone could influence participant responses. Specifically, it might heighten the perception of the comparison stimulus being positioned higher than the standard, thus reducing the bias observed in the neutral condition. The cross-modal effects of pitch have been deeply explored in association with the visual modality, with studies suggesting this effect might be due to attentional mechanisms, with high pitch shifting attention towards upper positions (Chiou and Rich, 2012), while others state it can directly affect at the perceptual level (Maeda et al., 2004), due to synesthetic influences among cross-modal stimuli (Parise and Spence, 2009). Despite we cannot contribute to disentangle the reasons with our study, our results suggest that the cross-modal correspondences between frequency and tactile spatial location are not just implicitly associated, as previously reported (Deroy et al., 2016; Occelli et al., 2009), but that they can bias the perceived location of said tactile stimulus in active touch conditions. However, this effect was not seen for the low-pitched tone. Despite the selection of the frequencies was based on the average endpoint of pointing responses found in Parise et al. (2014), the low tone might not be perceived as low enough to yield the effects found in the studies previously mentioned in passive touch (Deroy et al., 2016; Occelli et al., 2009). Our analysis also releveled that the precision was not affected by the frequency of the tone presented. This suggest that the modulation is translated in a shifted threshold towards lower values, while the slope does not vary between conditions. Moreover, our results support that this association is independent of the device's orientation (as in our case, the device is parallel to the table) (Deroy et al., 2016).

To summarize, Chapter 3 shows that high-pitched tones can modulate the perceived location of a tactile stimulus during explorations. However, no effects on precision was found. Our research highlights the importance of the consideration of the cross-modal correspondence in cross-modal binding. It supports previous literature and contribute to create new methods to enhance tactile perception during explorations of an external haptic

display, carrying significant potential for the design of sensory substitution and reinforcement technologies. However, there are potential limitations in our study. Whereas similar effects of the high-pitched tone would be expected with respect to the pink-noise, by intermingling the order of presentation of the standard and comparison stimuli, the bias towards positive values might disappear. Future research should target this question and explore whether a lower-toned pitched could also impact tactile localization during active touch.

Chapter 4

Effective somatosensory and cross-modal evaluation in children with hemiparesis and neurotypically developing children using MSI Caterpillar

In Chapter 1 I reviewed how research in adults after a traumatic brain injury (TBI) or a stroke has contributed to our understanding about sensory impairments (Alwis and Rajan, 2014; Ding et al., 2011; Hall and Lifshitz, 2010), with special focus in the tactile and proprioceptive systems (Carey, 1995; Koh et al., 2021), but also in multisensory processing (Van der Stoep et al., 2019). However, in the pediatric population this topic has been underexplored.

Animal models of pediatric TBI patients revealed atypical neuronal hypoactivity after a lesion in the non-injured somatosensory primary cortex presented (Lu et al., 2015). In humans, it has been suggested that somatosensory evoke potentials (SEPs) can contribute, in both children and adults, to forecast the outcome after acute brain injury (Amantini et al., 2012), assessed by the Torrance Health State (HUI:1) or Glasgow Outcome Scale (GOS) (Carter et al., 1999). In pediatric patients, some of the tools employed for somatosensory assessment are monofilaments, position-matching, tactile threshold and two-point discrimination assessment, having methodological inconsistencies across studies. As a consequence of this inconsistencies, at least partially, emerge variability in results across works, with some authors finding somatosensory impairments in 46-97% of the children with cerebral palsy, percentage that varied according to the modality of somatosensation tested (Van Heest et al., 1993). More recently, Marsico et al. (2023) also reported significant deficit in somatosensory processing in children with upper motor neuron lesion compared to typical

developing children (Marsico et al., 2023). Moreover, there is also a gap in the clinical field in somatosensory assessment. Walmsley et al. (2018), reported that, although 89.7% of the physiotherapists stated to evaluate somatosensory impairments in paediatric patients, only 65.9% of them asses it routinely. This gap is even more pronounced between occupational therapist, going from 91.8% claiming to evaluate it, to 31.6% doing it regularly (Walmsley et al., 2018). Children with hemiparesis, which is generally acquired as a result of cerebral palsy, TBI, strokes, or tumours, introduce a unique set of challenges in rehabilitation. In particular, children with cerebral palsy, common cause of disability and hemiparesis, requires a precise evaluation and intervention (Novak et al., 2017). This includes addressing both the underestimated sensory deficits, in one or more modality, and motor impairments. This stems from the interplay between the sensory function and the motor one, for example, in grip control (Bleyenheuft and Gordon, 2013). This highlights the need of comprehensive approaches to foster the functionality in this population (Cooper et al., 1995). In addition, it has been suggested that the severity of hemiparesis in the upper extremity is usually enhanced in distal muscles than proximal ones in adults (Colebatch and Gandevia, 1989). However, to the best of our knowledge, no studies traced this implication in somatosensory perception in children.

Another crucial and underexplored area in children with brain damage, especially in those with hemiparesis, is the ability to integrate multisensory cues. Galvin et al. (2009) suggested the presence of challenges in children after a TBI in multisensory integration. This assumption was based on parents reports, indicating difficulties in activities that required the integration of multisensory cues, like getting dressed (Galvin et al., 2009). Königs et al. (2017) further explored this topic, suggesting the presence of multisensory deficits after a TBI, with a negative impact in general cognitive function. Despite these findings, remains a lack of studies tracing particularly the cross-modal interactions in children with hemiparesis, with a focus limited to potential benefits in rehabilitation of multisensory training (Kashoo and Ahmad, 2006).

In conclusion, despite motor and cognitive function are often the ones most noticed and attended by the rehabilitator, a neglected comorbid sensory impairment might also impact the general performance of the patient, especially in children. Therefore, understanding the influence of hemiparesis on somatosensory and cross-modal perception, as well as the evaluation of potential impact of technological solutions in clinical settings could significantly contribute to rehabilitation outcomes. With this goal, we designed three tasks using MSI Caterpillar (Gori et al., 2019). We measured the reaction times (RTs) in the detection of a tactile stimulus and their perceived location (that could be presented alone or along

a visual or auditory cue) in the more affected and the less affected arm of children with hemisided sensorimotor symptomatology and in the non-dominant and dominant arm of typically developing children. Results suggest the presence of somatosensory deficits in the more affected arm of the children with hemiparesis, when compared to the non-dominant arm of the control group, a visual dominance in space location and the presence of visual-tactile interactions in both groups. Moreover, our results suggest that the use of the wrist as an anchor point is a developmental achievement, impacted by hemiparesis.

4.1 Method

4.1.1 Participants

11 children with predominant hemisided sensorimotor symptomatology (2 males, mean age 13.55, SD +- 3.86) due to congenital or acquired lesions (e.g. cerebral palsy, traumatic brain injury, hemimegaloencephaly, tumours, cerebrovascular accidents, hydrocephalus) attending the Verbund katholischer Kliniken Düsseldorf, and 8 healthy aged-matched controls (3 males, mean age 12.38, SD +- 3.02) were recruited for this study.

For the clinical population, the inclusion criteria were age 7-19 years and able to remain seated throughout the evaluation and experiment and the presence of paresis emphasized on one hemi-side of the body. Exclusion criteria were not being able to follow instructions, or communicate discomfort or pain or verbally name numbers, injury or surgery involving the upper limbs within the last 6 months. Children and young people verbally agreed to be involved in the study. Parents and children signed the informed consent form. Research protocol approved by Ethics Committee of North Rhine Medical Association (Geschäftsstelle der Ethik-Kommission der Ärztekammer Nordrhein, Germany) adhered to the guidelines of good clinical practice.

The eligibility of the neurotypically developing children tested was to be between 7 and 19 years old, and no history of cognitive or motor-sensory deficits. As with the clinical population, participants verbally agreed to be involved in the study. Informed consents were signed. In line with the Declaration of Helsinki, the research protocol was approved by the local health service's ethics committee (Comitato Etico, ASL3 Genovese, Italy).

4.1.2 Clinical assessment

First, to control for the somatosensory state of the children with hemiparesis, we carried out a clinical evaluation of the visually deprived participants:

- An adaptation of the Nottingham Sensory Assessment was done to evaluate (a) Light touch (gentle touch with a cotton ball) and (b) Pressure (press the skin with the index finger enough to gently deform the skin contour) bilaterally in the hand, wrist and upper forearm of the participants (right and left arm). After 3 repetitions, the score is from 0 (absent sensation: no sensation perceived the three times) to 2 (normal perception: stimulation perceived the 3 times) (Connell et al., 2008).

- From the Semmes Weinstein Monofilament Test we used 4 monofilaments (F3.61, J4.31, K4.56, T6.65) to evaluate the tactile perception of our participants in the hand, wrist and upper forearm of the children bilaterally. We pressed each monofilament to the skin in 90° angle for a maximum of 2 seconds. The monofilaments reported was the one perceived at least once out of two attempts for each test point.

  The score was transformed into a scale from 0 to 4 (0: no sensation using T6.65 monofilament; 1: T6.65 monofilament felt; 2: K4.56 monofilament perceived; 3: J4.31 monofilament perceived; 4: F3.61 monofilament perceived), with higher scores indicating better tactile function.

- Vibration test: The vibration detection threshold was tested using a Rydel-Seiffer 64 Hz graduated (0-8 scale) tuning fork (Medicon) (Panosyan et al., 2016). The threshold was tested bilaterally in the radius and determined by the patients' report when the perceived vibration disappeared. The final value was computed with the mean of two repetition coded from 0 to 8 (Xirou et al., 2020). Values lower than 6.5 were considered a sign of impairment (Martina et al., 1998).

To control for the motor function of the children we used the Gross Motor Function Classification System (GMFCS), with 5 levels from 1 (slight limitations) to 5 (severe limitations), as well as the independent finger movement test, with scores transformed into a scale from 0 to 2 (0: no movement; 1: affected finger movement, without reaching target; 2: reaching target) with higher scores indicating better motor function.

4.1.3 Technology: MSI Caterpillar

To induced the tactile, visual and auditory stimulation, we used a novel version of the MSI Caterpillar system (Gori et al., 2019). For our work, we used a modular array of 5 blocks, that are equal, differing only in the logical identifier (Figure 4.1). However, the number of modules can vary according to the specific needs, as well as the shape. They are connected to each other by a USB micro-A connector. The modules can be attached with a joint or present

a varying distance depending of the interconnection cables length. Figure 4.2 shows a block scheme of the system.

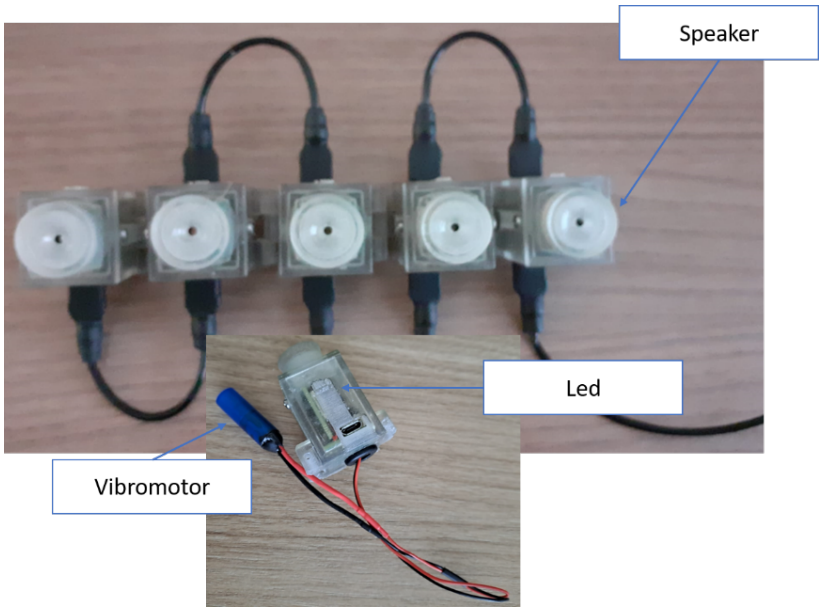

Figure 4.1 MSI Caterpillar system. Array composed by 5 modules, each of them presenting one vibromotor, LEDs, and a buzzer.

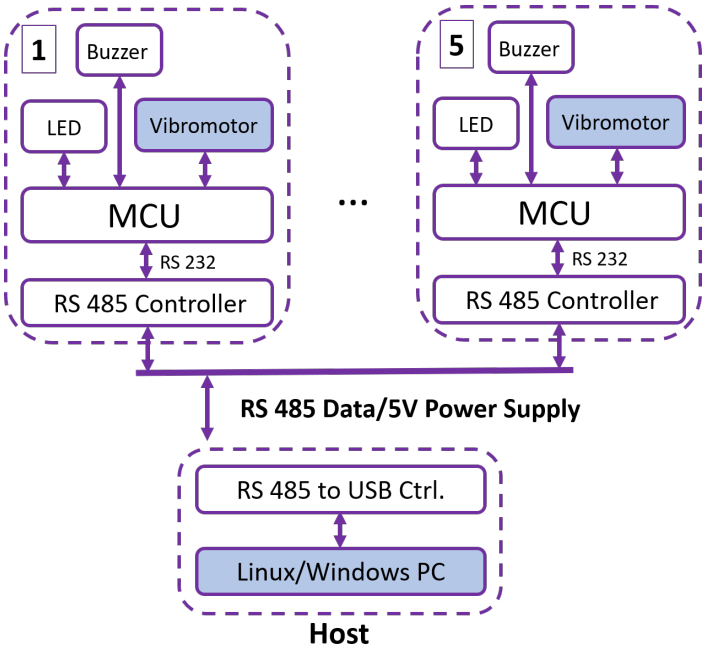

Figure 4.2 Block scheme of MSI Caterpillar.

A single interface (Host), connected to the first or last module of the chain of MSI Caterpillar, power and manage data connection through a multidrop serial bus RS485 with the personal computer (PC). The microprocessor of each element (a PIC 16F628 running at 20MHz) communicates with a RS232 interface with an on-module RS485 controller chip.

The MSI Caterpillar is composed by a vibromotor, LEDs, buffer, stimulus transmission, slave slements and Host control. For more technical details see (Gori et al., 2019). Below are the mentioned features of the stimulation provided and the potential capabilities of the device:

- Haptic stimulation: the stimulator employed in this version of MSI Caterpillar differs to the version employed in (Gori et al., 2019), constituting a novelty of this setup. Each stimulator is a 7 mm of diameter encapsulated cylindrical permanent-magnetic motors direct current (DC). Modifying the duty cycle, it is possible to induced variations in the amplitude of the vibration (2.2$\sim$ 3.6V DC). The vibration is not perceived as painful.

- Visual stimulation: 4 blue high-brightness LEDs are used to provide the visual stimulation. The emission is conveyed through an opaque light guide located at the top of each element.

- Auditory stimulation: a buzzer provides the audio stimulation. The frequency can be controlled by the microprocessor and vary between 300 to 3kHz. 851 Hz was the frequency used in our experiment.

4.1.4 Experimental tasks

During the experiment we allocated MSI Caterpillar in the forearm of the participants. Each of the 5 array's modules were labelled from 1 to 5, with 1 always being positioned closer to the wrist, and 5 closer to the elbow. Children sat in a chair with their tested arm placed as centered as possible with the body midline, and executed three different tasks controlled by a custom MATLAB code (R2020b, The MathWorks, USA).

1. Detection task: tactile stimuli were randomly displayed during 50ms on one of the device's modules. There were 20 trials in total, 4 per module in random order. The intertrial time was randomly chosen between 1 second to 1.5 seconds in steps of 100 ms to avoid automatic answers. The child was instructed to press a button of the computer's mouse with their less affected (dominant) hand as soon as they perceive the stimulus. Their answer was processed by our MATLAB code, registering the reaction times (RTs) of the child. After the answer, the experiment will continue with the next trial.

2. Spatial localization task: unimodal tactile (T) cues were randomly displayed during 100 ms on one of the device's modules. There were 20 trials in total, 4 per module in random order. The child was instructed to verbally report the number of the module generating the tactile stimulation. After the experimenter introduce the answer in the code, the next trial would take place.

3. Spatial localization task with multisensory cues: using audio-tactile (AT) and visual-tactile (VT) stimulation, participants repeated the Spatial localization task. Both multisensory conditions could be congruent (i.e. emitted by the same module of the device) or incongruent (i.e. each sensory stimulation was emitted by a different modules). There was one block per modality (i.e. AT or VT), with 40 trials each (20 trials congruent and 20 incongruent). Again, children were instructed to verbally report the number of the module corresponding to the perceived location of the tactile stimulation.

For discriminative validity, we evaluated differences between the more affected arm of children with hemiparesis and the non-dominant one of typically developing peers. For convergent validity, we will measure the relationship RTs and errors (difference between perceived location and the real one) in the T modality.

4.2 Data analysis

First, as a control for the somatosensory state of the participants from the clinical group, we calculated the percentage of children with scores indicating impairment in the somatosensory evaluation in one or more test.

While task one would allow us to have an estimation of the somatosensory perception by measuring RTs, task two and three would yield the errors in the participants' localization judgments, their precision, and the bias for each particular module. Our independent variables are the group (Children with hemiparesis, controls), modality (T, AT congruent, AT incongruent, VT congruent, VT incongruent), and the arm tested (more affected/non-dominant, less affected/dominant).

The analysis of the data was done using RStudio (Version 2023.12.0) (RStudio Team, 2020). First, we fit the data using Linear Mixed Models (LMM) using "lmer" function from the R package "lme4" (Bates et al., 2015) to examine whether the independent variables (group and arm) can contribute to the prediction of the RTs. The model is specified as follows:

(4.1).

$$\beta 0 + \beta 1 arm + \beta 2 group + \beta 3 arm : group + uP + \varepsilon = RTs \tag{4.1}$$

Where $\beta 0$,$\beta 1$, and $\beta 2$ are the fixed effects coefficients representing the effects of each independent variable on the RTs; $\beta 3$ is the potential interaction between the group and the arm; ε is the error term representing the residual variation not accounted for by the model. Due to the nested structure of the data (conditions within participants), between participants variability is accounted as random effect *(uP)*.

To explore the impact of the independent variables group, modality and arm on the absolute errors (i.e. difference between the perceived and real position), we applied the following LMM:

$$\begin{aligned} \beta 0 + \beta 1 arm + \beta 2 group + \beta 3 modality + \\ \beta 4 arm : group + \beta 5 arm : modality + \\ \beta 6 \cdot group : modality + \beta 7 arm : group : modality + \\ uP + \varepsilon = Errors \end{aligned} \tag{4.2}$$

Where again $\beta 0$,$\beta 1$, $\beta 2$ and, $\beta 3$ are the fixed effects coefficients representing the effects of each independent variable on the errors; $\beta 4$,$\beta 5$, $\beta 6$ and, $\beta 7$ are the potential interactions between them; and the error term representing the residual variation not accounted for by the model is represented by ε. As in the previous LMM, between participants variability is accounted as random effect *(uP)*.

The precision in the participants detection (computed by using the R function "aggregate" to calculate the standard deviation of the answers for each unique combination of the grouping variables – number of the module that induced the stimulation, participant, modality, and arm) was fitted into a third LMM to study the effects of the independent variables group, modality and arm.

$$\begin{aligned} \beta 0 + \beta 1 arm + \beta 2 group + \beta 3 modality + \\ \beta 4 arm : group + \beta 5 group : modality + \\ \beta 6 arm : group : modality + uP + \varepsilon = Precision \end{aligned} \tag{4.3}$$

$\beta 0$,$\beta 1$, $\beta 2$ and, $\beta 3$ are the fixed effects coefficients representing the effects of each independent variable on the errors; $\beta 4$,$\beta 5$, and $\beta 6$ are the potential interactions between them; and the error term representing the residual variation not accounted for by the model is represented by ε. As in the previous LMM, between participants variability is accounted as random effect *(uP)*.

In addition, to explore the effects on the somatosensory bias, the systematic deviation from the real position value in the responses of the participants, of the particular position (i.e. 1-5) of the modules in the forearm of the participants, the group and arm, we executed an LMM for the T modality and also VT congruent. This inclusion was based on the role of vision in space perception (Alais and Burr, 2004). Therefore, we aimed to investigate whether it could rectify potential biases. The distance between the vibro-motors were 2.5 cm, therefore, we multiplied the errors by 2.5 to compute the bias.

$$\begin{aligned} \beta 0 + \beta 1 position + \beta 2 arm + \beta 3 group + \beta 4 position : arm + \\ \beta 5 position : group + \beta 6 arm : group + \\ \beta 5 position : arm : group + uP + \varepsilon = Bias \end{aligned} \tag{4.4}$$

$\beta 0$,$\beta 1$, $\beta 2$ and, $\beta 3$ are the fixed effects coefficients representing the effects of each independent variable on the errors; $\beta 4$,$\beta 5$, $\beta 6$ and $\beta 7$ the potential interactions between them; the error term representing the residual variation not accounted for by the model is represented by . As in the previous LMM, between participants variability is accounted as random effect *(uP)*.

To understand whether the bias found in the module 1 (response variable) presented a linear relationship with age (fixed effect) in the T modality, we performed a Linear Model (LM) for the children with hemiparesis and the neurotypically developing group separately. Another LM was executed between the RTs (response variable) and absolute errors (fixed effects) to assess the presence of convergent validity.

ANOVA was used ("Anova" function from the R package "car") to assess the model's effects significance, with a significance level of α = .05. When significant, pairwise comparisons were applied using the "emmeans" package on R. Values lower than .05 after FDR correction were considered significant.

4.3 Results

The results from the clinical somatosensory evaluation in children with hemiparesis included in the study presented were the following:

- For the light touch test, 7 (63.64%) presented scores lower or equal to 1, predominantly in the more affected arm (6 participants - 85.71%). The areas of stimulation more

affected were the hand and the wrist (6 participants both - 85.71%). In the upper forearm the number was reduced to 4 participants (57.14%).

- In the pressure test, 3 (27.27%) patients showed an impaired tactile perception, all of them in the more affected arm (hand: 1 participant, 57.14%; wrist: 2 participants, 66.67%).

- Using the Semmes Weinstein Monofilament, 6 (54.55%) participants required a superior filament than F3.61. 1 child (16.67%) in the less affected arm, 3 (50%) in both arms, and 2 (33.33%) only in the more affected one. The most common location were the hands (5 participants – 83.33%), and the upper forearm (5 participants – 83.33%), followed by the wrist (4 - 66.67%).

- With the vibration evaluation, 6 (54.55%) participants presented scores inferior to 6. 2 (33.33%) in both arms, while 4 (66.67%) only in the more affected one.

The LMM to study the impact of our dependent variables in the RTs, showed a significant interaction between group and arm ($\chi^2(1)= 10.504$, p=.001). Specifically, the pairwise comparison showed a significant difference between the two groups in the more affected (non-dominant) arm (t(19.28)= -3.88, p=.002), with higher RTs in children with hemiparesis. In addition, there was a significant lower RTs in the dominant compared to the non-dominant arm in the controls (t(3763)= 5.48, p<.001), and in the less affected arm than the more affected one in the children with hemiparesis (t(3763)= -4.52, p<.001) (Figure 4.3).

The statistical analysis of the absolute errors showed a significant interaction between the three fixed effects included in the model ($\chi^2(4)= 18.495$, p=.001) (Figure 4.4). In particular, the pairwise comparisons between the more affected arm in the children with hemiparesis and the non-dominant arm in the typically developing children was significant for the modalities T (t(42.625)=-4.116, p<.001), AT congruent (t(42.625)=-4, p<.001), AT incongruent (t(42.625)=-4.54, p<.001), and VT incongruent (t(42.625)=-3.919, p<.001), with the first group presenting higher errors than the later, suggesting the presence of somatosensory impairment in children with hemiparesis. A significant difference was observed only in the VT incongruent modality (t(42.625)=-3.387, p=.003) when comparing the less affected arm with the dominant arm across both groups, with higher errors in the children with hemiparesis. This suggests a relatively similar perception across the groups in this arm, differing primarily in the increased reliance on visual feedback among the children with hemiparesis. When comparing the less affected arm with the more affected

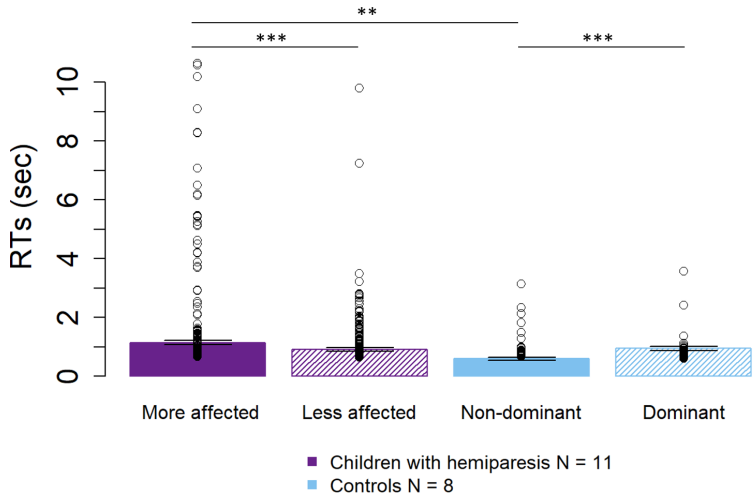

Figure 4.3 RTs in seconds obtained from the children with hemiparesis and the typically developing children (controls). Purple represents the RTs values of the children with hemiparesis in the more affected arm, and less affected arm (45 degrees purple lines). The color blue represents the RTs in the control group in the non-dominant and dominant (45 degrees blue lines). Children with hemiparesis presented significantly higher RTs in their more affected arm compared to the non-dominant arm of their typically developing peers. There were also significant differences between both arms of the participants (more affected vs less affected arm in the clinical group; non-dominant vs dominant in the control one). ** $p < 0.01$, ***$p<.001$.

one in children with hemiparesis, a significant difference raised for the T modality ($t(3763)=-2.977$, $p=.006$), AT congruent ($t(3763)=-2.977$, $p=.006$), and AT incongruent ($t(3763)=-3.97$, $p<.001$). These differences were also present in the control group between the dominant and non-dominant arm (T: $t(3763)= 3.833$, $p<.001$; AT congruent: $t(3763)= 2.67$, $p=.013$; AT incongruent: $t(3763)= 3.56$, $p=.001$). This indicate that in the presence of visual feedback, the differences between arms disappeared. However, while children with hemiparesis presented higher errors for the more affected arm, the control group showed higher errors for the dominant one.

In addition, there were differences between the T and AT modalities with the VT congruent and VT incongruent ones, showing lower errors for VT congruent and higher for the VT incongruent. However, in typically developed children, the differences with the VT condition in the non-dominant arm were only regarding the incongruent presentation: In the more affected arms of children with hemiparesis we found significant differences between T – VT congruent modalities ($t(3763)= 10.391$, $p<.001$), T – VT incongruent ($t(3763)= -5.604$,

p< .001), AT congruent – VT congruent (t(3763)= 10.274, p< .001), AT congruent – VT incongruent (t(3763)= -5.721, p< .001), AT incongruent – VT congruent (t(3763)= 11.675, p< .001), AT incongruent – VT incongruent (t(3763)= -4.32, p< .001), and VT congruent – VT incongruent (t(3763)= -15.995, p< .001), indicating differences with the VT condition. Same differences were present for the less affected arm (T – VT congruent: t(3763)= 8.932, p< .001; T – VT incongruent: t(3763)= -9.924, p< .001; AT congruent – VT congruent: t(3763)= 8.815, p<.001; AT congruent – VT incongruent: t(3763)= -10.041, p< .001; AT incongruent – VT congruent: t(3763)= 9.223, p<.001; AT incongruent – VT incongruent: t(3763)= -9.632, p<.001; VT congruent – VT incongruent: t(3763)= -18.856, p<.001). Interestingly, while the same differences were also present for the dominant hand in the control group (T – VT congruent: t(3763)= 5.476, p< .001; T – VT incongruent: t(3763)= -3.149, p= .024; AT congruent – VT congruent: t(3763)= 4.381, p<.001; AT congruent – VT incongruent: t(3763)= -4.244, p<.001; AT incongruent – VT congruent: t(3763)= 5.682, p<.001; AT incongruent – VT incongruent: t(3763)= -2.943, p=.043; VT congruent – VT incongruent: t(3763)= -8.624, p<.001), in the non-dominant hand only the incongruent VT conditions were significantly different (T – VT incongruent: t(3763)= -5.065, p<.001; AT congruent – VT incongruent: t(3763)= -4.997, p<.001; AT incongruent – VT incongruent: t(3763)= -4.586, p<.001; VT congruent – VT incongruent: t(3763)= -6.982, p< .001).

The statistical analysis of the precision in the localization of the participants showed a significant interaction between the group and the sensory modality ($\chi^2(4)= 159.884$, p<.001). The pairwise comparison revealed a significant lower precision in children with hemiparesis, compared to those typically developing, for the T modality (t(19.724)= -2.526, p=.041), for the AT congruent (t(19.724)= -3.056, p=.032), and AT incongruent (t(19.724)= -2.433, p=.041). There was also significant differences between sensory modalities in clinical group between T – VT congruent (t(3763)= 13.988, p<.001), AT congruent – VT congruent (t(3763)= 16.02, p<.001), AT congruent – VT incongruent (t(3763)= 4.427, p<.001), AT incongruent – VT congruent (t(3763)= 15.649, p<.001), AT incongruent – VT incongruent (t(3763)= 4.056, p<.001) and VT congruent and VT incongruent (t(3763)= -11.592, p<.001). In the control group there were significant differences between T – VT incongruent modalities (t(3763)= -7.096, p<.001), AT congruent – VT incongruent (t(3763)= -7.009, p<.001), AT incongruent – VT incongruent (t(3763)= -5.39, p<.001), and VT congruent and VT incongruent (t(3763)= -7.934, p<.001). There was also a significant interaction between group and arm ($\chi^2(1)= 22.278$, p<.001), with children with hemiparesis showing a significant lower precision in the more affected arm compared to the less affected one (t(3763)= -7.425, p<.001).

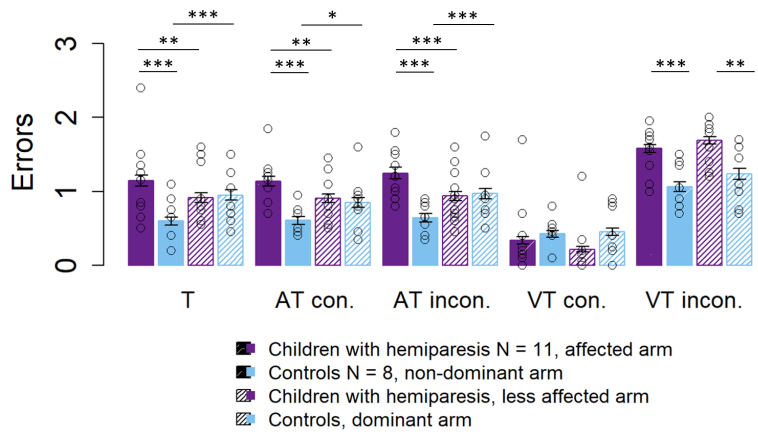

Figure 4.4 Mean absolute errors of the children with hemiparesis and their typically developing peers (controls). The color purple represents the absolute errors for the children with hemiparesis in the more affected arm (purple) and the less affected one (45 degrees purple lines). The color blue represents the absolute errors in the control group for the non-dominant arm and dominant one (45 degrees blue lines). This plot shows the significant differences found between both groups in the more affected (non-dominant) arm, and less affected (dominant) one. Differences between the more affected and less affected arm within the children with hemiparesis group, and between the non-dominant and dominant arm within the control one are also represented. Errors are the difference between perceived and real location, in cm 1=2.5. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

The LMM to explore the bias of the participants according to the specific position of the modules in the forearm (numbered from 1 – closer to the wrist – to 5 – closer to the elbow –) for the T modality showed a significant interaction between the position, group and the arm of the participants ($\chi^2(4)= 18.254$, p=.001). In particular, when comparing both groups, we found differences in the more affected (non-dominant) arm for the module 1 (t(63.936)= -4.265, p<.001), with a higher positive bias in the children with hemiparesis than the control; a trend in the 4 (t(63.936)= 2.232, p=.097), with a negative bias in the first group and a negative one in the typically developing children; and a close trend in the module 5 (t(63.936)= 2.599, p=.058), with children with hemiparesis showing a larger negative bias. No significant differences were found in the less affected (dominant) arm (Figure 4.5). When we compared the arms of the participants, we obtained a significant difference between the more affected and less affected arm of the children with hemiparesis in the module 1 (t(723)= -3.15, p=.017), and the 5 (t(723)= 2.231, p=.026), with larger biases in the more affected arm. In the control group, a significant difference between the dominant and non-dominant arm was found for the module 1 (t(723)= 2.77, p=.006), 2 (t(723)= 2.616, p=.009), and 3 (t(723)= 2.154, p=.032), with larger bias in the dominant arm. Interestingly,

within the clinical group's more affected arm, there was a significant difference between each position, with a reduced bias towards the elbow, except in the last position. Similar differences were observed in the less affected arm, except for positions near the extremes, indicating always lower bias in positions closer to the elbow. Typically developing children presented significant differences for the non-dominant and dominant arm, with always a reduced bias always towards the elbow. These significances can be found in Table 4.1.

Table 4.1 Results of the pairwise comparisons between the different positions of the vibromotors.

Group	**Arm**	**Comparison Position**	**Df**	**t**	**p**
Children with hemiparesis	More affected arm	1-2	723	5.380	<.001
		1-3	723	9.58	<.001
		1-4	723	13.385	<.001
		1-5	723	16.273	<.001
		2-3	723	4.199	<.001
		2-4	723	8.005	<.001
		2-5	723	10.892	<.001
		3-4	723	3.806	.003
		3-5	723	6.693	<.001
		4-5	723	2.887	.05
	Less affected arm	1-3	723	5.643	<.001
		1-4	723	8.398	<.001
		1-5	723	10.892	<.001
		2-3	723	3.674	.004
		2-4	723	6.43	<.001
		2-5	723	8.924	<.001
		3-4	723	2.756	.065
		3-5	723	5.249	<.001
Typically developing children	Non-dominant	1-4	723	3.232	.018
		1-5	723	5.232	<.001
		2-5	723	4.616	<.001
		3-5	723	3.539	.007
	Dominant	1-4	723	5.078	<.001
		1-5	723	7.848	<.001
		2-4	723	4.309	<.001
		2-5	723	7.079	<.001
		3-4	723	2.77	.065
		3-5	723	5.54	<.001
		4-5	723	2.77	.065

For the VT congruent conditions, there was only a main effect of the position ($\chi^2(4)=$ 107.427, $p<.001$), with significant differences between the positions 1-3 ($t(723)=$ 3.301, p=

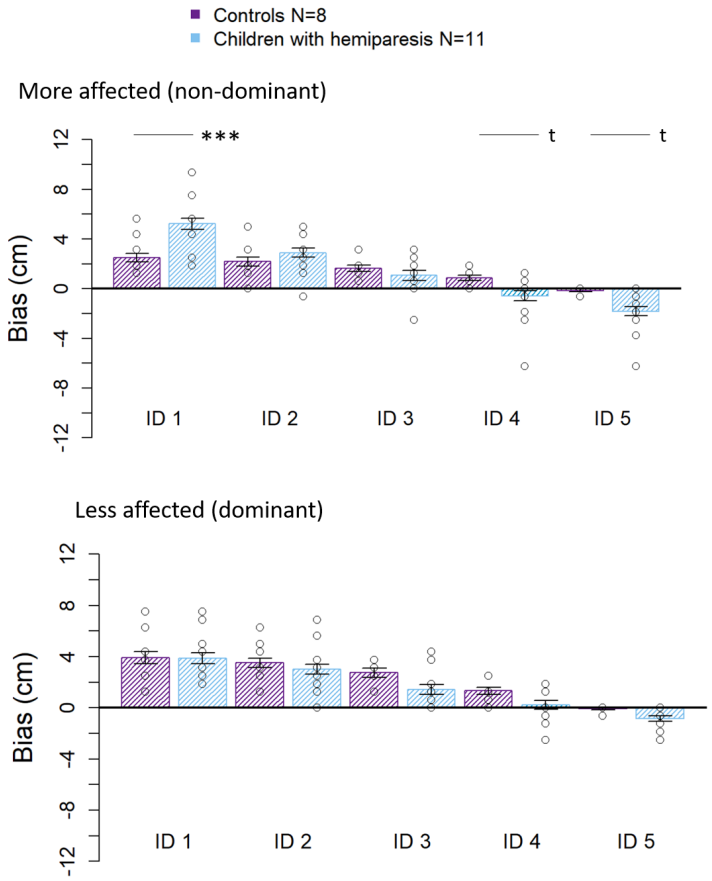

Figure 4.5 Bias expressed in cm presented in the T modality for each position of the modules (ID 1, ID2, ID 3, ID 4, and ID 5) in the forearm of the participants. Children with hemiparesis is represented by the color blue, while children with typical development (controls) is represented by the color purple. Separately for each arm of the participants (i.e. more affected/non-dominant, less affected/dominant), this plot shows the significant differences in the bias between the two groups for each position and between each module within group. In the more affected (non-dominant) arm we found significant differences between groups in the positions 1 (ID 1), 4 (ID 4) and 5 (ID 5), with larger biases in the clinical group. In the less affected arm (dominant) there was a significant difference between the two groups in the position 3 (ID 3). The difference between positions indicate lower bias in positions towards the elbow for both groups. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

.013), 1-4 ($t(723)= 6.594$, $p<.001$), 1-5 ($t(723)= 9.384$, $p<.001$), 2-4 ($t(723)= 3.985$, $p=.001$), 2-5 ($t(723)= 6.776$, $p<.001$), 3-4 ($t(723)= 3.292$, $p=.013$), 3-5 ($t(723)= 6.083$, $p<.001$), 4-5 ($t(723)= 2.791$, $p=.054$), suggesting that despite the visual cue, the pattern is still present (Figure 2.6).

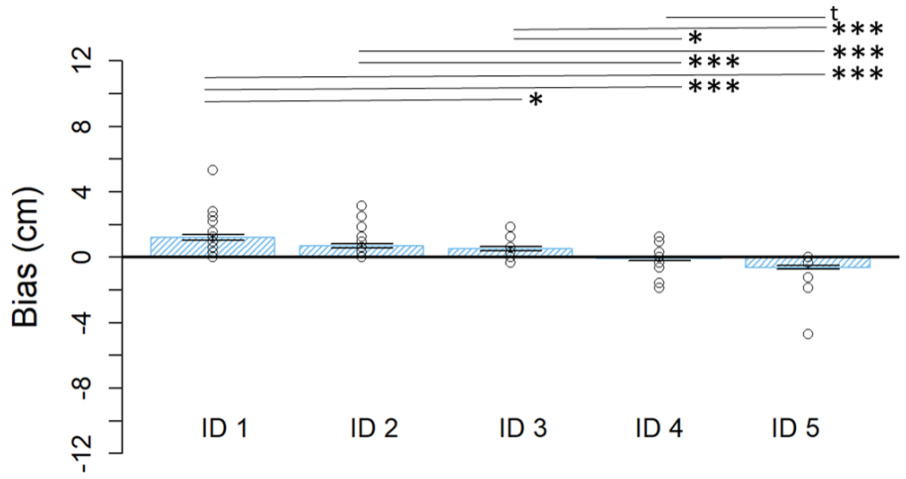

Figure 4.6 Bias expressed in cm presented in the VT congruent modality for each position of the modules (ID 1, ID2, ID 3, ID 4, and ID 5) in the forearm of the participants. Differences between positions indicate a reduced bias in positions towards the elbow in both groups, except for a larger negative bias in the 5 than the 4 position. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

To evaluate the presence of a linear relationship between the bias found in the tactile modality for the position closer to the wrist (ID 1) and the age of the participants, we computed a LM. In the control group there was a significant correlation with age for both arms (non-dominant: R2= .122, p=.0498; dominant: R2= .165, p=.021) (Figure 4.7.a). However, it was not significant for the children with hemiparesis (more affected: R2= .0004, p= .898; less affected: R2= .037, p= .211) (Figure 4.7.b).

Finally, to test the convergence, we applied a LM between the errors and the RTs resulted significant for both arms (more affected: R2= .113, p<.001; less affected: R2= .029, p<.001) (Figure 4.8).

4.4 Discussion

Motor and tactile perception are deeply interconnected. Individuals with paresis serve as an example of this intricate interplay between the motor and the tactile system, by showing that motor recovery depends on improvement in the somatosensory function (Zandvliet et al., 2020). It has been also suggested that some techniques to evaluate the somatosensory state of patients after a stroke, like SEPs, can be used as a tool that contribute in the prediction of the patients' outcome (Amantini et al., 2012), highlighting the importance of its evaluation. However, especially in the pediatric population, somatosensory perception

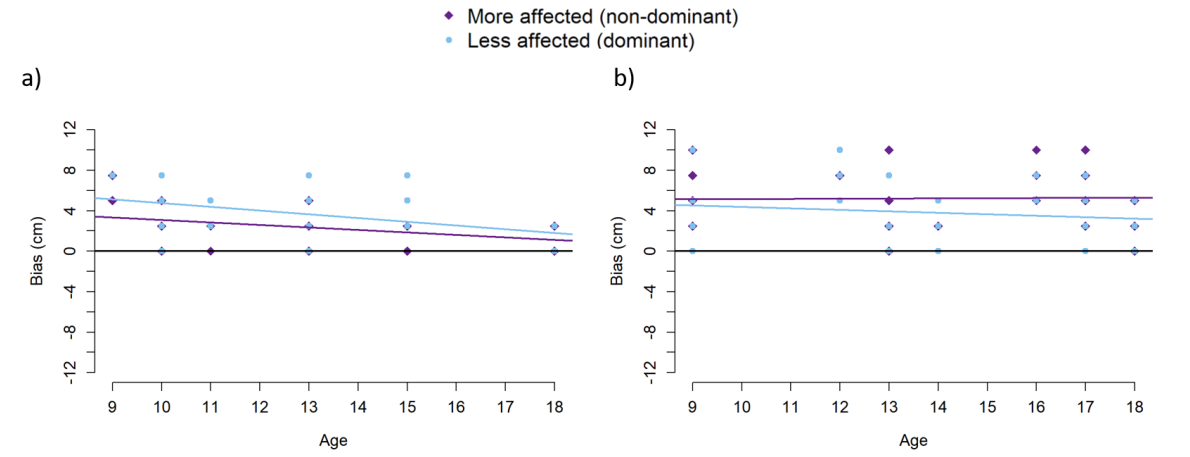

Figure 4.7 Linear Model (LM) analysis in the more affected (non-dominant) and less affected (dominant) arms between the bias in the position 1, for the tactile modality, and age. A LM for each arm was applied (more affected/non-dominant – purple diamonds, less affected/dominant – blue circles), using as a fixed effect the age. The purple line corresponds to the regression line in the more affected (non-dominant), while blue one to the less affected (dominant) arm. a) LM in the control group, showing a significant effect of age for both arms. b) LM in the children with hemiparesis, with no significant effect for neither arm.

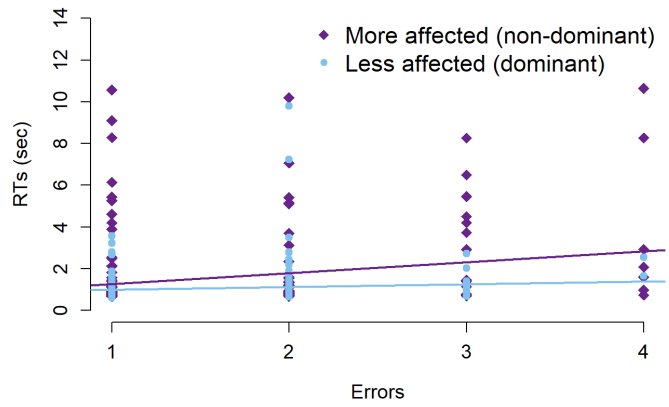

Figure 4.8 Linear Model (LM) analysis in the more affected and less affected arms between the participants' RTs and errors. A LM for each arm was applied (more affected/non-dominant – purple diamonds, less affected/dominant – blue circles), using as a fixed effect the errors. The purple line corresponds to the regression line in the more affected arm (non-dominant), with a significant main effect indicating higher RTs for higher errors. The same effect occurred in the less affected (dominant) arm, being the blue line the regression line. Errors are the difference between perceived and real location, in cm 1=2.5.

is often neglected, and when studied, methodologies and results vary dramatically. With this work, we explored tactile and cross-modal perception in children with hemiparesis, and typically developing peers using a technological solution able to provide multisensory stimuli. Our main hypothesis were (i) higher RTs and errors, as well as less precision, in the more affected arm compared to the non-dominant one of the participants; (ii) better and worse performance in the conditions involving visual feedback in the congruent and incongruent manner, respectively; (iii) a reduced interaction between sensory modalities in children with hemiparesis, (iv) the use of joints (wrist and forearm) as "anchor points", and (v) convergence between our tasks' results. Our results confirmed our hypothesis, except in (iii) a reduced interaction between sensory modalities, and (iv) the use of the wrist as anchor point.

With this goal, we used MSI Caterpillar, a device consisted on a concatenated array of modules able to provide tactile, visual and auditory stimulation. Each module was labelled with a number (1- closer to the wrist, 5- closer to the elbow), and children were instructed to (1) press a laptop's mouse as fast as possible using their less affected (dominant) hand when a tactile stimulus was perceived, and (2) report the perceived location of a tactile, audio-tactile congruent, audio-tactile incongruent, visual-tactile congruent or visual-tactile incongruent stimulus.

Children with hemiparesis had significantly higher RTs in the more affected arm than their neurotypically developing peers in the non-dominant one. The differences between these two sides has been suggested to indicate the presence of somatosensory impairment (Marsico et al., 2023; Sukal-Moulton et al., 2014). When comparing the arms of the participants, we also found higher RTs in the more affected arm than in the less affected one in the clinical group, while in the control one the values were higher for the dominant arm. Previous research about the impact of laterality in typical individuals, shows variability of results. Some works do not report significant differences between dominant and non-dominant hand in tactile pressure (Özcan et al., 2005, 2004), while others suggest a probable superiority of the non-dominant arm in haptic tasks (Squeri et al., 2012) or when applying electrotactile stimulation (Cai et al., 2023). This last line of work is supported by our results using vibrotactile stimulation.

In terms of absolute errors, we saw a significant higher error in the more affected arm in children with hemiparesis than the non-dominant one of their control peers in every condition where tactile sensitivity played a leading role (i.e. T, AT congruent and incongruent, and VT incongruent). This supports our findings in RTs, denoting somatosensory deficits in the first group. Moreover, the localization of a tactile stimulus in the forearm also involves proprioception, which has been also suggested to be impaired in this group (Kuczynski

et al., 2017). For the less affected (dominant) arm we only found a difference between the groups in the VT incongruent condition, with higher errors in the children with hemiparesis. This implies similarities in tactile and proprioceptive perception between groups for this arm, differing only by a stronger guidance by the visual feedback in children with hemiparesis. Further hints of somatosensory and proprioceptive deficits were found when we compared both arms within participants, finding higher errors in the more affected arm compared to the less affected arm of the children with hemiparesis in modalities not including a visual stimulation. However, in the control group higher errors in the same modalities were found for the dominant arm, which is coherent with the findings reported in RTs, suggesting a potential superiority in the non-dominant arm in haptic perception (Cai et al., 2023; Squeri et al., 2012).

The results in precision are perhaps the most informative ones to explore the impact of hemiparesis on cross-modal interactions. First, we should mention that a general lower precision was found in children with hemiparesis, when compared to the control group, in the modalities not including a visual feedback, which further support the presence of somatosensory and proprioceptive deficits in this group. The lack of differences when a visual cue was available, and the findings in absolute errors, would led us to believe that participants are merely following the visual cues, which aligns with previous research showing that vision is the leading sense in space perception (Pasqualotto and Proulx, 2012). Interestingly, the presence of a higher precision in the visuo-tactile congruent than its incongruent form in both groups indicate that participants are not just following vision, but that visual cues and tactile ones are interacting. However, we found certain differences between the two groups. Vision seems to always enhance precision (despite being in its incongruent form), and guide accuracy (higher in the congruent, lower in the incongruent), in children with hemiparesis. In typically developing children only the incongruent VT condition impact precision by diminishing it. On the contrary, in thi group accuracy was compromised by vision (congruent: better accuracy; incongruent: lower accuracy) in the dominant arm, while in the non-dominant significances in accuracy were with respect to the VT incongruent modality. When multisensory information is available, perception is dominated by the most reliable sense. However, in the presence of ambiguity, we are more prone to integrate multisensory signals in an attempt to create the most likely interpretation of the percept (Parise and Ernst, 2017). Our results suggest that, on one hand, when the signal is more ambiguous (i.e. impaired somatosensory perception and proprioception), the visual information has a key role guiding the perception. On the other hand, when the information is reliable enough to yield an optimal estimation (i.e. typical somatosensory and proprioceptive perception in

the non-dominant arm), coherent additional feedback is not required. The dominant arm of typically developing children, while benefits from the higher accuracy provided by the visual feedback, their estimations are equally reliable without the visual cues. Nevertheless, when conflictual information between the tactile and visual modalities is present, the noise generated leads to reduced precision. Thus, these results suggest that multisensory interaction is not impaired in children with hemiparesis.

To have a better understanding of the somatosensory perception of the participants, we also explored the systematic deviations, or bias, for each particular position of the vibromotor in the forearm. Previous literature indicate an enhanced performance in locations close to the joints, as they act as "anchor points" guiding perception (i.e. wrist and elbow) (Cholewiak and Collins, 2003; Cody et al., 2008). Some studies even suggest that the wrist induces a stronger attraction (Cody et al., 2008). Surprisingly, our study does not find said effect. In the typically developing children we saw a significant difference in the bias between different positions of the modules, with an evident drift towards the elbow, where the bias was almost zero in both arms. One possible explanation might be found in the population tested. While the abovementioned studies were done in adults, our work focusses on children between 7-18 years old. Hence, our results suggest that children do not experience the same attraction towards the wrist, which might be a developmental milestone. In fact, we found a linear relationship between the age of the participants and the bias found in the first module (closer to the wrist) for the tactile condition. Säisänen et al. (2021) studied, in participants from 7-33 years old, the motor representation areas of the hand, suggesting that the upper limb muscle of children experience multiple changes during development (Karl et al., 2001; Säisänen et al., 2021). It is possible that this continued improvement and changes in the upper limb muscle representation could play a role in the tendency of adult participants to use both, wrist and elbow as "anchor points". Remarkably, the strength of this pattern might be enough to not be rectifiable by visual cues. In the children with hemiparesis we saw the same pattern, with only a reduced bias in the 3rd and 4th position compared to 5th in the more affected arm. Interestingly, the bias found in the first module do not change with age. Our results imply an interruption of motor and somatosensory typical development, and suggest that in the more affected arm also the attraction towards the elbow is compromised (although less than the wrist). These findings are in line with a stronger weakness found in the hand and wrist in adults with hemiparesis (Colebatch and Gandevia, 1989). Moreover, the clinical evaluation performed in the children with hemiparesis tested further supports our findings, with more affectation in the more affected arm, predominantly in the hand and wrist. Further discussion on this topic can be found in Section 5.2.3.

Finally, for convergent validity, we explore the association between errors and RTs, finding a linear relationship between them.

Overall, our approach enabled us to: (i) detect somatosensory deficits in children with hemiparesis, which support previous research using a technological solution. (ii) Suggest that visual and tactile cues interact in children with hemiparesis fostering somatosensory and proprioceptive perception, with significant repercussions in the rehabilitation process. (iii) Indicate that the use of the wrist as a natural "anchor point" is a developmental milestone, which is affected by the presence of hemiparesis. These findings encourage the implementation of haptic technology clinical evaluations and offer relevant insights of sensory processing in children with hemiparesis, advocating for the development of assessment tools and therapeutic interventions specifically tailored to address the unique sensory profiles observed in these children, which should be considered in pediatric neurorehabilitation.

Chapter 4 is adapted from Casado-Palacios, M., Muller, K., Hömberg, V., Bertonati, G., Campus, C., Crepaldi, M., Maviglia, A., Gori, M. (2024). Effective somatosensory and cross-modal evaluation in children with hemiparesis and neurotypically developing children using MSI Caterpillar. Accepted for publication in IEEE MeMeA.

Chapter 5

General conclusions

The overall aim of this doctoral thesis is to investigate how the brain processes somatosensory inputs and their associations with motor function, both in unimodal and multimodal conditions. By unraveling these mechanisms, the thesis attempt to offer valuable feedback for the development of haptic technology, ultimately advancing the field and contributing to the design of more effective technologies in situations of sensory impairment or deprivation. For this purpose, this project involves the investigation and comparison of different populations, such as blind and sighted individuals, as well as children with typical and atypical development. Following an introductory overview that delves into the complexity of the somatosensory system, its tight connections with the motor system and the multisensory scenario of our world (Chapter 1), I illustrated the impact of blindness over motor-sensory integration and the modulation of motor information on cross-modal interactions (Chapter 2). Subsequently, I explored the interaction between the frequency of the auditory signal and the localization of a tactile stimulus during active explorations (Chapter 3). Finally, I reported the impact of hemiparesis in somatosensory perception (Chapter 4). This final chapter will delve into a comprehensive discussion and interpretation of the research findings outlined throughout this thesis, with a focus on their theoretical foundations and potential clinical applications.

5.1 Summary

Building on the theoretical framework established in Chapter 1, Chapter 2 focused on the influence of lack of vision (i.e. blindness) on motor-sensory integration and how motor information modulates cross-modal interactions. In particular, in Section 2.1, I explore the impact of active touch over tactile perception, and how visual calibration modulate said

perception. Participants were instructed to discriminate the faster velocity between two stimuli elicited by a rotating wheel in passive and active touch conditions. By including sighted and blind individuals, I showed that active touch reduced the reliability of tactile feedback in a velocity discrimination tasks when visual calibration is absent. These findings suggest that visual calibration is fundamental for a proper motor-sensory integration required during actions. In Section 2.2, by introducing a bimodal audio-tactile condition that included a non-informative tone, this study supports that blind individuals' performance is not influenced by an irrelevant audio stimulation. Interestingly, any decrease in performance in this group was attributable purely to the factor of movement. Moreover, a surprising finding emerged among sighted participants, as they were adversely affected by the non-informative tone only during active touch conditions.

Based on the findings obtained from Chapter 2, Chapter 3 aims to explore whether a sound with an implicit meaning can foster tactile perception in typical individuals. Participants were instructed to slide the finger over a haptic display that triggered transient audio-tactile stimuli, and report the stimulus located higher in the Y-axis of the display. By introducing different pitched tones, that have been reported to be associated with implicit spatial features, I showed that high pitch can modulate the bias in the localization of a tactile stimulus in active touch conditions. Particularly, when the tactile stimulus was associated with the high-pitched tone, participants were more likely to perceive it as higher in the plate compared to the previous stimulus, which was paired with a pink-noise.

In Chapter 4, I focused on the impact of motor impairment on somatosensory perception, as well as in cross-modal interactions with auditory and visual signals. Using a novel version of the MSI Caterpillar, neurotypically developing children and children with hemiparesis were instructed to respond as quickly as possible to tactile stimuli applied to their forearms. In addition, they were also asked to report the perceived location of tactile, audio-tactile (congruent or congruent) and visuo-tactile (congruent or congruent) stimuli. Results support the presence of somatosensory deficit in children with hemiparesis, as well as suggest cross-modal interactions between visual-tactile stimuli. Furthermore, I implied that the representation of the joints, and its role guiding perception, is a developmental milestone affected by the presence of hemiparesis.

5.2 Theoretical and clinical implications

The research conducted throughout my Ph.D., as detailed in this thesis, offer insights into tactile perception and the tight relationship with the motor system. In order to achieve this,

I presented different experiment and tasks: velocity judgment task in passive and active tactile conditions (Chapter 2), localization discrimination during explorations (Chapter 3), detection tasks (Chapter 4), and localization tasks in static touch (Chapter 4). Overall, the results emphasize the significance of the motor system's involvement in tactile perception and cross-modal interactions, as well as its modulation.

5.2.1 The role of visual calibration over motor-sensory and multisensory processing: the impact of blindness

In Chapter 2, I focused on motor-sensory integration and the role of vision in spatial tasks. This project used blindness to further disentangle the impact of the visual modality on underlying motor-sensory, inter-sensory, and multimodal processing mechanisms involved in spatial perception. In particular, I aimed to explore the effects of active touch on individuals with visual impairments and those who are visually deprived.

The results agreed with the cross-modal calibration theory (see Gori et al., 2008). Indeed, in Section 2.1, I demonstrated that the consequences of the absence of visual calibration are more extensive than previously reported, implying that it also plays a crucial role in tactile perception during active touch, thereby reducing tactile reliability in the blind population. This might be due to the creation of a noisy efference copy (i.e. brain's predictive models of our motor actions), as it relies on accurate information and integration of the different signals to be successful (Gori et al., 2012b). On one hand, has been suggested that the proprioceptive spatial representation in blind individuals is inaccurate due to the lack of visual calibration (Cappagli et al., 2017a). On the other hand, this absence of calibration is also responsible for reduced interaction and integration between sensory modalities (Cappagli et al., 2017b; Champoux et al., 2011; Collignon et al., 2009; Petkova et al., 2012). This might lead to a non-reliable efference copy. Moreover, the ability to compared between the efference copy and the reafference might also be compromised, resulting in a non-specific gating of somatosensory information. Interestingly, blindness duration did not influence blind participants' performance. Traditionally, research has emphasized the distinction between early and late blind individuals, with some authors describing a similar performance between sighted and late blind participants (Collignon et al., 2009; Hötting and Röder, 2004; Occelli et al., 2012), while others have not observed this similarity (Champoux et al., 2011), and have suggested that visual input is necessary for maintaining certain cognitive processes. This hypothesis has been supported by recent works that found a modulation of neural responses, linked to space representation, over the years following blindness onset (Amadeo et al., 2019,

2020). Given that 10 years was the minimum period of blindness among our participants, our results implied that this duration is sufficient for the absence of visual calibration to alter motor-sensory and inter-sensory integration processes. This work also revealed that tactile precision remains unaltered, despite aging, in blind individuals during active touch perception. However, sighted participants experience a decline in tactile precision over the years. This supports previous findings that reported a negative effect of age on tactile precision in speed judgment among sighted individuals (Norman et al., 2022). Legge et al. (2008) also observed this effect, noting that while aging sighted participants exhibited a 1% decrease in tactile acuity per year, their blind counterparts maintained their acuity over time. They suggested that the increased use of active touch by blind individuals was responsible for their preserved sensitivity throughout their lifespan (Legge et al., 2008). The lack of age impact on precision in the blind group allows us to disregard age differences among our participants in explaining the results for active compared to passive conditions. Research about tactile skills among blind individuals has traditionally involved assessing tactile acuity (Stevens et al., 1996) through various tasks, such as recognizing Braille characters and differentiating grating orientations. Generally, findings suggest that there are no notable differences in sensory thresholds between blind and sighted individuals (Grant et al., 2000; Pascual-Leone and Torres, 1993). Where differences were observed they could often be explained by the enhanced practice from Braille reading or tactile identification of objects, rather than an inherent increase in perceptual sensitivity (Grant et al., 2000; Kauffman et al., 2002; Occelli et al., 2013; Saito et al., 2006; Van Boven et al., 2000). Results obtained in Section 2.1, however, suggested that, when focusing on precision on untrained tasks, active movement are responsible of a reduced reliability of tactile perception, with no effect of braille training in our results. Hence, we suggest that the negative effect on precision found in the blind group when movements are involved might be caused by an altered tactile gating.

In section 2.2, I explored the impact of active touch over multisensory processing. The results indicated that blind individuals do not experience significant differences when the performance obtained during the audio-tactile sensory stimulation is compared to the tactile one within each condition (i.e. passive and active). In this section of the thesis, I discussed these results in light of the previously reported reduced interaction between auditory and tactile information in this population (e.g. Cappagli et al., 2017b; Champoux et al., 2011; Collignon et al., 2009; Petkova et al., 2012). In order to integrate multisensory cues, we need to decode them into a common reference frame (Nardini et al., 2008), however, vision seems to play a relevant role in this achievement. A common paradigm to explore switches in the reference frames is the tactile temporal order judgment (TOJ) in uncrossed-crossed hand

conditions (Shore et al., 2002; Yamamoto and Kitazawa, 2001). For this task, participants are instructed to identify which of their two hands receives a tactile stimulus first, either with their hands positioned uncrossed or crossed over their body's midline, showing that sighted participants experience a cross-hand deficit. Between the possible explanations has been suggested that tactile input might first be represented in skin-based coordinates before being automatically translated into external spatial coordinates (Cadieux et al., 2010; Shore et al., 2002). However, has been reported a lack of cross-hand effect on congenitally blind individuals in TOJ tasks (Crollen et al., 2017; Röder et al., 2004). Initially, these findings were seen as proof that vision is crucial for developing the external coordinate system. However, recent findings suggested that the observed differences between blind and sighted individuals might stem from how each group weight internal versus external coordinate systems (Crollen et al., 2017, 2019). For instance, Schubert et al. (2017) investigated how sighted and blind participants identify the localization of tactile stimuli on the back or palm of one hand, while disregarding simultaneous distracting touches at locations that were either congruent or mismatching on the opposite hand. The setup varied with participants' hands positioned either both facing downwards or one hand facing down and the other facing up. The task required participants to report the location of the touch either based on the hand's anatomy ("palm" or "back") or its external position ("up" or "down" in space). When instructions focused on anatomical location, participants were more precise in identifying anatomically congruent than incongruent target-distractor pairs. On the contrary, with external spatial instructions, participants showed better performance for spatially congruent pairs over incongruent ones. Interestingly, both sighted and blind groups presented this pattern of results, indicating that blind individuals are able of integrating internal (anatomical) and external spatial information for tactile localization. These findings suggest that spatial integration abilities can be modulated by task instructions (top-down information), even in the absence of visual experience from an early age. Indeed, this was farther explored by Crollen et al. (2019) in a TOJ tasks, testing sighted and blind individuals, in uncrossed or crossed positions. By introducing instructions that were designed to either promote the use of an internal frame of reference (left vs. right hand) or an external frame of reference (left vs. right hemispace), these authors showed that, under internal conditions, only sighted participants presented a negative effect cross-hand effect. However, when the instructions emphasized an external reference frame, a decline in performance was noted in both groups. This suggests that blind people engage in external coordinate system under certain conditions. Nonetheless, this activation is not automatic, as they might assign lower weights to information coded in external terms. This specific approach to weighting spatial

information might create challenges in certain contexts, such as when blind individuals need to quickly combine auditory and tactile information. This difficulty could stem from a less integrated default reference frame between these two modalities, as touch is automatically coded in internal terms while audio in external (Collignon et al., 2009). Since participants in the study presented in Section 2.2 were instructed to judge the speed of the rotating wheel, this might have led to an automatic internal frame of reference, completely ignoring the auditory feedback. Indeed, the results on the delta from the active and the passive conditions, indicate that it is the mere presence of movement that diminished tactile precision in the blind participants.

5.2.2 Multisensory interaction during active touch in visually deprived typical individuals

In section 2.2, I also showed the presence of a reduced precision in tactile estimations in sighted individuals in the presence of a non-informative sound during active touch conditions. This effect was not present during passive perception. I discussed the results by suggesting that the movement-related tactile gating might be the responsible of said effects. The reduced amount of somatosensory information processed by the cortex due to the movement-related tactile gating (Chapman, 1994; Kurz et al., 2018), might increase internal noise and ambiguity of the signal. Typically, signals are noisy and ambiguous. However, our brains use multiple ways to try to solve said ambiguity, such as using cues obtained through difference sensory modalities (Sekuler et al., 1997). An example of ambiguous stimulus is found in the stream-bounce illusion. According to this illusion, two identical stimuli move towards each other. After coinciding, they move in different directions. This can be interpreted as (1) the two stimuli collided and then bounced in different directions, or (2) both stimuli simply followed a different path, streaming. Interestingly, the visual stimuli itself do not provide a robust perception of the event, and when a sound is added, the likelihood of perceiving them as bouncing increased (Sekuler et al., 1997). This suggest that in the precedence of ambiguity, multimodal cues are integrated to support perception. In addition, it has been suggested that, internal noise within the brain (i.e. signals random disturbances), can contribute to variability at the behavioral level (Faisal et al., 2008), and be the responsible of alternations in our perceptions. However, Parise and Ernst (2017) show, using the stream-bounce illusion paradigm, that the brain first processes visual and auditory information separately to extract cues for disambiguation. Then, it integrates these cues, by weighted averaging in a Bayesian fashion, to form a coherent perception, demonstrating that noise not only induces perceptual

alternation but also provides systematic biases towards specific interpretations. In our case, the presence of a worse performance in the bimodal condition during active touch might reflect this process. The internal noise created by the movement might be responsible of an interaction with the non-informative auditory signal, as the brain might be expecting extract speed information from temporal patterns of the auditory signal (Schirmer et al., 2016). However, in our experiment, time was kept constant across all stimuli, thus failing to provide any valuable information for estimation. I this line, the results obtained in the delta from the active and the passive conditions, for both tactile and audio-tactile sensory stimulation, imply that the effects of movement were only significantly different from zero in the bimodal condition. These results suggest that, due to the movement, typically developed individuals might be particularly sensitive to the features of the auditory stimulation, relying more on them due to the increased of internal noise. This imply that multisensory information during motor actions, at least under certain conditions, can negatively impact performance (Huntley et al., 2024).

Building on from these findings, in an attempt to find an auditory signal that could contribute to tactile perception, in Chapter 3 I explored the impact of the cross-modal association between pitch and spatial elevation (e.g. Parise et al., 2014; Pratt, 1930) in the detection of a transient audio-tactile stimulus in active touch conditions. Despite no effects on precision was seen, we have significant effects on the bias. Specifically, the introduction of a high-pitched tone resulted in a shift of bias towards lower values. In other words, when the stimulus was paired with the high-pitched tone, the distance needed to perceived it as being higher that the standard (which was associated with pink-noise), was significantly reduced compared to when both stimuli where paired with pink-noise. It has been suggested that the influence of cross-modal correspondences on behavior in multisensory environments may not be innate (Spence and Deroy, 2012). Instead, these effects could rely on explicit strategic considerations. like the prior information given by labeling the pitched tones used, such as high and low pitch. This aligns with earlier research indicating that post-sensory processing, such as semantic labeling or polarity mapping, is essential for cross-modal interactions between auditory pitch and visual features to manifest (Chiou and Rich, 2012; Gallace and Spence, 2006). In our study, despite no information regarding the auditory signal was given to the participants, thus the effect of labels might be reduced, as the presentation of the conditions were intermingled, the bias presented might also be understand in a relative and not absolute way (Gallace and Spence, 2006; Parise and Spence, 2009). This means their manifestation could vary based on the specific range of stimuli employed. However, a study about the effects of pitch on motion, (Maeda et al., 2004) suggested that the impact

of sounds, which are 'metaphorically congruent' with certain motions on visual perception, mainly occurs at the level of perception itself, and that these effects are not attributable to movements of the eyes, suggestive cues, semantic connotations, or biases in responding.

While it has been reported that congruent pitch can reduce the variability of the estimation when congruent to the visual feedback (Parise and Spence, 2009), our results show changes in threshold. This is in line with the effect seen by Maeda et al. (2004). Our findings suggest that, in active touch conditions, while high-pitched tone do not increase the reliability of tactile feedback, can impact the direction of the perception. It is important to mention that, since an unimodal condition was not included in this particular tasks, we cannot disentangle whether, in the localization of transient stimulus, the bimodal condition would led to higher or lower precision compared to the unimodal one.

Overall, we can claim that active touch might increase the noise of the tactile estimations. This could make sighted participants more vulnerable to disturbances stemming from other sensory modalities. In the localization of transient stimulus, when the tactile stimulus is paired with a high-pitched tone, our results suggest that participants tend to perceive the tactile cue as higher. However, no changes in the reliability of the signal is seen across the different conditions included in the experiment. Further research must be done to unveiled how these auditory cues affect precision compared to unimodal tactile conditions following this paradigm. The research findings offer valuable insights in the understanding of multimodal processing during active touch conditions.

5.2.3 Motor impairment, somatosensation, and cross-modal interactions

In Chapter 4, I used MSI Caterpillar to explore the impact of motor impairment on somatosensory perception and cross-modal interactions in the pediatric population. This work suggests an impaired somatosensory perception in the more affected arm of children with hemiparesis compared the non-dominant one of typically developing peers. These deficits were highlighted by a variety of measures: RTs, accuracy and precision. A reduced somatosensory function comorbid to motor impairment has been already suggested in children (Clayton et al., 2003; Kuczynski et al., 2017). Said comorbidity have been suggested to contribute to motor deficits (Auld et al., 2012). The exploration of the bias for each particular position of the vibromotors offered additional insights into the specific nature of the impairment. As reported by previous works in adults, we expected improved performance in areas near joints, as they have suggested to serve as "anchor points" that assist in guiding perception, such as

the wrist and elbow (Cholewiak and Collins, 2003; Cody et al., 2008). However, our data did not fit this pattern. On the contrary, both groups exhibit a larger bias towards the writs, which, in the control group was reduced until almost zero in the position closest the elbow. In the clinical group the minimum bias was reached in the 4th position (module number 1 was located closer to the wrist, 5 closer to the elbow). This difference between the two groups might be due to a decreased somatosensation in the children with hemiparesis, and a higher variability of their responses. More interestingly, we also found a linear relationship between this bias in the closest module to the wrist (i.e. module 1) and the age in typically developing children, but not in children with hemiparesis. These results suggest that the use of the wrist as "anchor point" is a developmental milestone. The explanation might be found in the maturation of the motor cortex and its tight relationship with the somatosensory one. In fact, it has been suggested that the motor representation areas of the upper limb muscle (between 10-12 years of age) experience a great variation and expansion of the motor map representative position (i.e. Centers-of-Gravity) (Karl et al., 2001). As development progresses, the motor map representative position become more concentrated. Starting in preadolescence, there is a shift in the left hemisphere, moving from more lateral positions to medial ones with age. In addition, the forearm and hand's muscle representation ratio increased with age, being associated in the right hemisphere with motor dexterity (Säisänen et al., 2021). This fine-tuning of motor skills has been suggested to last until 30 years of age in humans (Fietzek et al., 2000). It is possible that this continued improvement and changes in the upper limb muscle representation could play a role in the tendency of adult participants to use both, wrist and elbow as "anchor points". Our results suggest that during childhood, the elbow, a joint more involved in gross motor tasks, might have a greater weight and cause the effect reported in this work. The lack of a linear relationship between the bias found in children with hemiparesis, seems to indicate the disruption of the typical maturation process of the motor-sensory cortices. Additionally, this bias was significantly larger in this group for this position in the more affected (non-dominant) arm. Notably, it has been suggested that higher weakness is evident in distal compared to proximal areas (Colebatch and Gandevia, 1989). Some authors reported that the shoulder (proximal region) is less impacted and tends to recover more quickly compared to the hand (distal region) (Jung et al., 2002).

In addition to the somatosensory perception deficits, it was suggested a possible multisensory impairment (Galvin et al., 2009; Königs et al., 2017). However, our data show the presence of visual-tactile interaction in both groups. In children with hemiparesis, visual feedback consistently improved precision, whereas accuracy was influenced by the congruence of the visual cue. Specifically, accuracy was enhanced when the visual cue

was congruent with the task compared to other modalities and diminished when it was incongruent. On the contrary, precision in typically developing children was only affected (negatively), when the visual cue was presented incongruent to the tactile one. Accuracy showed the same pattern as in children with hemiparesis for the dominant arm, but not for the non-dominant arm, where the congruent presentation of visual feedback did not imply a better performance. However, the most relevant finding is that both groups showed a higher precision in the congruent audio-visual condition compared to the incongruent one. During the task, participants were directed to focus solely on tactile (and proprioceptive) cues, disregarding any additonal stimuli. Despite these instructions, given that this activity involves spatial components, and considering the established reliability of vision in spatial perception (Alais and Burr, 2004), it could be anticipated that the reduced tactile perception associated with hemiparesis might result in a total dependency on visual feedback on this group. On the contrary, results suggested that, although vision dominated perception, it still interacted with tactile cues. In typically developing children using the non-dominant arm, which our results suggest may be more sensitive to vibrotactile feedback, tactile input alone was sufficient to create an optimal representation of the event, rendering redundant visual cues unnecessary. However, as ambiguity increases and the estimation becomes less robust or when conflicting information arises, visual and tactile feedback may interact, affecting the accuracy and reducing precision, especially when the visual feedback is incongruent with the tactile input (Parise and Ernst, 2017).

The significance of these findings lies in the potential applications they could inspire based on previous research on sensory-motor plasticity, as the different senses can impact each other. For instance, in typical adults, research has shown the potential to create spatial biases in how bodily information is processed by altering the sensory-motor interaction between stimuli in virtual environments, using visual feedback, without changing the body's actual position in space (Girondini et al., 2024). In this line, recent discussions have highlighted the concept that perceptual and motor learning are interconnected processes, not isolated events. It is suggested that motor learning can lead to modifications within the sensory systems and networks in the brain. Similarly, perceptual learning is believed to influence movements and alter the brain's motor regions (Ostry and Gribble, 2016). For instance, when performing goal-directed reaching movements, training in somatosensory skills, especially when paired with vibrotactile sensory cues offering feedback on movement errors, can notably boost proprioceptive accuracy within a short span of days, which contribute to motor learning. This aid have been suggested to potentially extend to the sensorimotor coordination of unrelated motor tasks (Cuppone et al., 2016). It is also possible, by using motor and visual feedback,

to elicit visuo-motor distortions: in the presence of a new visuomotor environment, such as the one experienced while wearing prism goggles, participants initially make significant directional mistakes during reaching tasks. However, they quickly adjust their movements, returning to near-normal performance within approximately 30-50 reach attempts. This process of visuomotor adaptation involves both sensory and motor adjustments (Simani et al., 2007). The sensory aspect of this adaptation can be evaluated through alignment tests. In these tests, participants are instructed to pinpoint the location of either a visual target or their unseen fingertip with their other unseen fingertip, without allowing their hands to touch. These evaluations demonstrate notable shifts in the perceived positions of both visual and proprioceptive signals after adapting to altered visual feedback, indicating a recalibration of spatial perception in response to the new visuomotor context (Cressman and Henriques, 2009; Haith et al., 2008). Some authors even suggested that these distortions encompassed not only the execution of active hand movements but also are generalized into how passive hand displacements were perceived (Malfait et al., 2008). Interestingly, working on the sensory systems, without motor components, can also lead to greater motor performance. There is a body of research that highlights the significant role of plasticity within sensory systems, which can arise from stimulation, sensory loss, and the consequential changes in movement (Ostry and Gribble, 2016). Recent reviews (e.g. Lametti et al., 2014; Ostry and Gribble, 2016) highlight the dynamic interplay between sensory experiences and motor system adjustments. Proprioceptive (i.e. passive limb movement) training not only enhances motor learning but also amplifies motor cortex excitability, as indicated by changes in Motor Evoked Potentials (MEPs), and augments activity in frontal motor areas during passive movements. When visual and proprioceptive stimuli are combined, it has been found to facilitate the acquisition of complex hand trajectories (Wong et al., 2012). Rosenkranz and Rothwell (2012) suggests that the interaction between proprioceptive input and motor cortex excitability in the hand, particularly in the abductor pollicis brevis muscle, is enhanced as performance on the vibration discrimination task, which correlated with motor learning. In this framework, the presence of interaction between visual and somatosensory cues in children with hemiparesis, support the use of both visual and somatosensory feedback in rehabilitation protocols. This interaction could potentially foster plastic changes with positive contributions to the rehabilitation of the different sensory systems, as well as to motor control.

In conclusion, by using MSI Caterpillar, our results support the presence of somatosensory deficits in children with hemiparesis. In addition, we discussed differences in the developmental representation of the joints, disrupted by the presence of hemiparesis. Finally,

I addressed the presence of visual-tactile interactions, and the potential contributions to rehabilitation based on neural plasticity due to a bidirectional motor-sensory interactions.

5.3 Concluding remarks

The current thesis aimed at understanding how the brain processes somatosensory inputs and its associations with motor function, in unimodal and multimodal conditions, in situations of sensory impairment or deprivation. The goal of the work presented is to provide valuable feedback in the development of haptic technology. I designed different experimental procedures to explore brain's mechanisms in tactile perception due to the movement-related tactile gating, its impact on multisensory processing, and the role of visual calibration, as well its impact on the cross-modal correspondence between auditory pitch and touch. Additionally, I explored how motor impairment affects somatosensory perception, and cross-modal interactions in children. The paradigms designed required the involvement of blind and sighted participants, as well as typically and atypically developing children. Particularly, the methodologies employed included velocity judgment tasks in passive and active tactile conditions, including visually deprived sighted and blind individuals, in unimodal or bimodal audio-tactile conditions using a rotating mechanical wheel (Chapter 2). Based on those findings, using a haptic display, I explored whether modulation in the pitch of a sound could contribute to foster tactile perception in visually deprived sighted participants (Chapter 3). To further explore the interactions between motor and sensory function, we tested children with or without hemiparesis using a technological tool, in the detection and localization of somatosensory and multisensory stimuli (Chapter 4). The diversity in methodologies and techniques employed during my Ph.D. allowed a comprehensive investigation on somatosensory perception in conditions of sensory or motor impairment, and sensory deprivation.

The results presented in this thesis lead to the following conclusions:

I. Tactile perception is commonly acquired trough movements (i.e. active touch), however, our research indicates that perceptions during self-elicited movement are shaped by visual calibration within the tactile modality. The long-lasting absence of visual input might be responsible of an imprecise anticipated sensory feedback and lead to an inaccurate gating of somatosensory cues. Moreover, our results suggest that this process is particularly sensitive to the absence of vision, with 10 years of blindness being enough to elicit this alteration. According to our data, the precision of blind individuals might be compromised when they face unfamiliar tasks involving active explorations.

II. Multisensory cues allow us to create a coherent representation of our environment, with which we relate through our actions. The results presented in this doctoral thesis indicate that active touch can introduce noise to the sensory signal, thereby modulating multisensory interaction in sighted participants and rendering them susceptible to interference from auditory feedback. These findings underscore the importance of carefully selecting auditory stimulation: non-informative auditory signals may interact with tactile cues processed during movement, leading to a detrimental effect on tactile perception in this population. However, the precision of blind participants is solely influenced by movement and not by non-informative auditory feedback.

III. High-pitched sounds have been consistently mapped to higher positions in space, while low-pitched tones to lower ones. The findings presented suggest that this frequency-elevation mapping, particularly with high pitch, can bias the localization of a transient tactile stimulus during explorations. This highlights the importance of considering cross-modal correspondence in cross-modal binding.

IV. Hemiparesis has been suggested to involve concurrent somatosensory and multisensory deficits, a phenomenon extensively studied in adults. Our study effectively assessed somatosensory deficits in children with hemiparesis, contributing to previous findings by leveraging innovative technology, thus offering new perspectives on addressing somatosensory deficits in this population. Results indicate the presence of visual-tactile interactions in both typically and atypically developing children, with vision modulating somatosensory perceptions, especially in the second group. Additionally, our findings underscore the significance of using the wrist as an "anchor point," highlighting it as a critical developmental milestone that may be adversely affected by hemiparesis.

The outcomes of this thesis extend beyond theoretical significance, potentially influencing assessment and rehabilitation methodologies following sensory or motor loss. In the rehabilitation field, this work emphasizes the need for interventions in the blind population, fostering the creation of contingencies between their sensory modalities, to tackle the reduced precision during active touch. In addition, I proposed the potential contribution of congruent visual-tactile information in the rehabilitation of children with hemiparesis, aiming to enhance their tactile, proprioceptive, and consequently, motor functions. In the technological domain, the aim of this thesis is to offer insights that can guide development of next generation haptic devices. In a world that fosters technological innovation and the introduction of haptic feedback in robotics (Pacchierotti and Prattichizzo, 2024), the introduction of new

products to the market is constant. However, their effectiveness is often compromised by a lack of understanding about human users. Research in assistive and rehabilitation robotics emphasizes the necessity for approaches centred around human interaction, ensuring they meet the nuanced needs of individuals they are designed to assist (For a review see Beckerle et al., 2017). This Ph.D. thesis suggest that (i) tactile devices utilized during active movement in blind individuals may result in impaired reliability of the tactile signal, particularly in the absence of training. This implies that technology designed for this population should either be adapted to the natural interactions with the environment or they should undergo proper training to effectively utilize them; (ii) the features of the auditory modality are specially relevant in haptic tasks; (iii) the incorporation of modulations in pitch can increase the perception of a stimulus as higher in a haptic display when paired with a high pitch tone, even when positioned parallel to a table; (iv) the integration of multimodal haptic technologies, particularly those capable of delivering visual-tactile congruent stimuli, can contribute to somatosensory clinical evaluation in the pediatric population. Furthermore, my work contributes to the theoretical foundation for the utilization of multimodal technology in sensory and motor rehabilitation protocols in children with hemiparesis.

Scientific production

Papers published:

- **Casado-Palacios, M.**, Tonelli, A., Campus, C., Gori, M. (2023). "Movement related tactile gating in blindness". *Scientific Reports*, 1–8.

- Bertonati, G.*, **Casado-Palacios, M***., Crepaldi, M., Parmiggiani, A., Maviglia, A., Torazza, D., Campus, C., Gori, M. (2023). "MultiTab: A Novel Portable Device to Evaluate Multisensory Skills". *Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE Engineering in Medicine and Biology Society. Annual International Conference, 2023,* 1–4.

  *Joint first authors

Papers accepted for publication:

- Terenti.M, **Casado-Palacios, M.**, Gori, M., Vatavu, R.D. "What Is the User Experience of Eyes-Free Touch Input with Vibrotactile Feedback Decoupled from the Touchscreen?". *International conference of Human-Computer Interaction.*

- **Casado-Palacios, M.**, Muller, K., Hömberg, V., Bertonati, G., Campus, C., Crepaldi, M., Maviglia, A., Gori, M. "Effective somatosensory and cross-modal evaluation in children with hemiparesis and neurotypically developing children using MSI Caterpillar". *Annual International Conference of the IEEE Medical Measurements & Applications.*.

Papers under review:

- **Casado-Palacios, M.**, Tonelli, A., Campus, C., Gori, M. Cross-modal interactions and movement-related tactile gating: the role of vision. *Scientific Reports*.

Papers in preparation:

- **Casado-Palacios, M.**, Esposito, G., Courtin, A., Tonelli, A., Gori, M., Collignon, O., Mouraux, A. "Auditory pitch modulates the localization of audio-tactile stimuli during active touch".

- Vitale, A., **Casado-Palacios, M.**, Balzarotti, N., Parmiggiani, A., Moscatelli., A. Gori, M. "Exploring how interindividual differences and stimulus reliability impacts on visuo-tactile integration in a motion direction task".

Conferences

Talks

- Workshop IEEE, World Haptics Conference (Online, 2/07/21) “Visual, audio and haptic integration and interaction for rehabilitation”.

- XXVII congresso nazionale della Sezione di Psicologia sperimentale dell’AIP (Lecce (IT), 8-10/09/21). “Multisensory spatial processing of dynamic stimuli in sighted and in blind individuals”.

- Workshop “Technology of multimodal interfaces” (Lille (FR), 30/05/2022 – 02/06/2022) “Cross-Sensory perception and deprivation”.

- Summer School Multitouch (Genova (IT), 20-21/10/22). “The influence of pitch over active explorations”.

- Conference of Experimental Psychologists (Regensburg (GE), 17-20/03/2024). “Tactile perception and multisensory processing in children and typical and blind adults”. Invited talk in symposium.

- IEEE Medical Measurements & Applications (Eindhoven (NE), 26-28/06/2024). “Effective somatosensory and cross-modal evaluation in children with hemiparesis and neurotypically developing children using MSI Caterpillar*”. Planned.

Posters

- 8th International Conference on Spatial Cognition (Online, 13-17/09/21). “Audio-Tactile dynamic multisensory integration in sighted and blind individuals”.

- Annual meeting Society for Neuroscience (SFN) (Online, 08-11/11/21). “Multisensory integration of dynamic stimuli and the role of active touch”.

- The Cognitive Neuroscience Society (CNS) 29th Annual Meeting (Online, 23-26/04/22). “The role of active touch: differential mechanism in blindness”. The 20th International Multisensory Research Forum (Ulm (GE), 04-07/07/22). “Effects of a non-informative auditory feedback over touch in the blindness”.
- 21st International Multisensory Research Forum (IMRF) (Brussels (BE), 27-30/06/23) “Auditory pitch modulates the localization of audiotactile stimuli during active touch”.
- 45th European Conference on Visual Perception (ECVP) (Paphos (CY), 27-31/08/23) “Electrophysiological responses of the movement-related tactile gating in blindness.

Organization scientific events

- Workshop “Fundamental of haptics and multisensory integration”, within Multitouch project (Online, 8/09/21- 21/09/21- 28/09/21- 7/10/21- 12/10/21- 21/10/21- 28/10/21.
- Workshop on assistive technologies, within Multitouch project (Dusseldorf (GE), 21/02/2022 – 22/02/22).
- Summer School Multitouch (Genova (IT), 20-21/10/22).

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