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"From Contact to Cortex: Exploring the Neural Dynamics of Sensorimotor Interactions"

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If the human brain were so simple
That we could understand it,
We would be so simple.
That we couldn't.

Pugh, G. E. (1977). *The Biological Origin of Human Values*. Basic Books.

Abstract

This thesis is a detailed study of the neural mechanisms of sensorimotor integration. It is mainly focused on the interaction between tactile information and action imagination and its regulation by neural circuits, including the primary motor cortex (M1), the primary somatosensory cortex (S1), and the dorsal premotor cortex (dPMC). Through a sequence of experiments, this research reveals how tactile feedback and the imagination of specific activities that require force and precision are handled and incorporated into the brain's motor system, showing the facilitatory role of touch on motor control and the selectivity of these effects in relation to the imagined action.

The initial study addresses the effects of tactile stimulation during action imagination on motor system activity, showing that tactile feedback increases motor evoked potentials (MEPs) in a force-dependent manner and that this effect is body-part specific. This improvement is associated with the vividness of motor imagery, suggesting a close link between sensory feedback and motor imagination.

Subsequent research extends these results to the social area by looking at the role of different types of touches (self-touch, touches of another individual, and a non-living surface) in the excitability of the motor cortex. Findings demonstrate the role of biological sources of touch, particularly in a social context, in the enhancement of motor system activation, thereby highlighting the social aspect of touch in action and its neural correlates.

Expanding the current knowledge, the final study focuses on the neural dynamics of motor imagery and uses continuous Theta Burst Stimulation (cTBS) to temporarily reduce the activity in S1 and dPMC. This approach allows for a nuanced understanding of these regions' roles in motor imagery, especially in tasks involving precision grip. The results indicate that the inhibition of S1 and dPMC activity influences task performance and motor system excitability. Thus, the role of these areas in the cognitive control of motor imagery is emphasized.

Altogether, these studies offer a comprehensive view whereby tactile feedback and motor imagery become integrated through the motor system, with specific neural

circuits playing a significant part in facilitating this process. The research contributes significantly to our understanding of sensorimotor integration, offering implications for enhancing motor control through tactile feedback and informing the development of interventions and technologies to improve motor function.

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Many individuals have played a significant role throughout this journey, and I am immensely grateful to each one. All interactions have a meaning we can never recognize, and their combined impact ripples into the future unabated. This is true even if I forget to acknowledge some of them, as I'm sure publicly will be the case.

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Glossary

ADM = Abductor digiti minimi

cTBS = Continuous theta burst stimulation

dPMC = Dorsal premotor cortex

ECR = Extensor carpi radialis longus

EMG = Electromyography

FDI = First dorsal interossei

FDS = Flexor digitorum superficialis

M1 = Motor cortex

MEP = Motor evoked potential

MEPs = Motor evoked potentials

MI = Motor imagery

NT = No-touch

s1 = Primary somatosensory cortex

spTMS = Single pulse transcranial magnetic stimulation

T = Touch

TMS = Transcranial magnetic stimulation

V = Vertex

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Chapter 1: Introduction

State of the Art

The main ideas presented, and the hypotheses tested in this dissertation lie within neurosciences, particularly the part of research that focuses on how the human brain behaves and processes information for adapting to different contexts, how our motor-cognitive capacities rely on the representations of information within our brains, from the simple operations of tying shoelaces to the complicated ones of solving equations or imagining far-off planets. These representations, which are dynamically reused to satisfy situational needs, help us interpret context, comprehend the words or actions of others, come up with new ideas, and plan and carry out activities. In order to support the breadth and variety of our motor-cognitive repertoire, we explore in this study the fundamental topic of how our brains encode and display information. In particular, we focused on the skin-mediated sensory modality of touch, which develops into the earliest and biggest perceptual system throughout fetal development and demonstrates astounding capability and endurance over protracted durations. Here with this dissertation, we hope to shed light on the complex mechanisms underpinning cognitive flexibility by investigating the distinctive properties of tactile perception and its function by focusing on "hand touch and manipulation". Touch often maintains its functionality and resilience over an extended period, even in the presence of age-related or other factors that may affect other sensory modalities. Despite its undeniable importance, the scientific exploration of touch has received comparatively less attention compared to extensive research conducted on other sensory domains. Consequently, there exists a significant research gap regarding the comprehensive understanding of the complex mechanisms underlying the sense of touch.

Here, my focus lies specifically on investigating the sense of touch in action. My aim is to address the following questions: How does touch information contribute to guiding our motor system? Does in turn the motor system influence the perception of touch, and if so, what are the mechanisms involved? Through a series of integrated studies, this research endeavor aims to unravel the complex interaction

between the sensory and motor systems from multiple perspectives. By comprehensively exploring the relationship between touch perception and motor function, we strive to enhance our understanding of this fundamental aspect of human sensory-motor integration. Let me tell you a story to better understand this latter point:

In the heart of Italy, on a sweltering summer day, the bustling city of Rome was teeming with life. The daily grind had you trapped, yearning for the freedom and relaxation the weekend would bring. Just as you readied yourself for another mundane workday, a thrilling spark of anticipation ignited within you. Imagination whisked you away to sun-kissed shores and the tranquil caress of the Mediterranean Sea. Glancing out into the mundane routine, you yearned for a small momentary escape and found inspiration in your garden. Lying innocently amidst the lush green grass was a volleyball—just there, waiting for you to pick it up and feel its weight in your hand. The corners of your lips curled into a playful smile as you realized the universe had handed you an invitation to indulge in the carefree joy of beach volleyball.

Replacing the bustling sounds of the city, waves crashed rhythmically, and beachgoers chattered cheerfully. Closing my eyes, I embraced my imagination, witnessing a flawless serve in my mind's eye. I pictured my fingers releasing the ball, visualizing the graceful arc it traced through the air and the satisfying thud it made upon meeting my opponent's hands. A surge of electrifying adrenaline propelled me into the air, commemorating an extraordinary point earned. A solid imagination, yet only an imagination, and for a fleeting moment, reality came crashing back. Your heart raced with the thrill of victory, and it felt all too real as you opened your eyes.

Its warmth and texture reminded you of the sensations your mind conjured...stimulated your motor cortex...igniting a connection...a momentary flight of fancy with a deeper impact...the ball still rested in your hand...pondered the newfound knowledge... the power of the imagination alone...little did you know...consciously realizing it...intrigued. Carried with wonder, you embraced volleyball as a reminder of our incredible ability to intertwine the physical and the

mental. The lines blur between the reality we perceive and the vibrant sectors we envision within our own minds. It becomes a testament to the boundless potential that lies within us, bridging the gap between what is and what can be.

I stopped the story here; now, in the context of the various sensory experiences within the human body, the question arises as to which sense holds the primary position in the aforementioned scenario. In the hierarchy of important factors, touch takes a significant spot because of its crucial role in an organism's well-being and its close tie to the physical representation that facilitates contact with the world around us. What sets touch apart from the other senses is that it bypasses the necessity of an intermediate sensory medium. Unlike vision, where we depend on the visual domain to make sense of our surroundings, touch grants us the ability to personally experience the tactile attributes of our own forms and subsequently comprehend them in others. Utilizing our own senses to investigate themselves, touch allows us to access and comprehend the spatial and solid attributes of external objects. This convergence of means and objects eliminates the need for sense mediation, thus highlighting the exceptional significance of touch. Unlike smelling, hearing, or seeing, touch involves the utilization of the spatial and solid characteristics of our bodies.

The sense of touch

Our perception of touch encompasses a range of experiences, from minor interactions to complex navigation. Factors such as time and space acquire specific relevance based on how we perceive them through touch. Unlike other senses, touch doesn't require an outside influence. Our bodies possess the ability to directly connect with and comprehend the physical properties of objects or bodies. Touch holds a prominent position due to the direct connection between our means of touch and the objects we perceive. This eliminates the need for sensory mediation. Touch perception can be categorized by its most basic form, where we briefly sense an object making contact with a specific point on our body, giving rise to various modes of tactile sensation. The foundation for more complex tactile experiences is built upon this basic unit. Feeling a bug crawl on one's leg is an example of a passive

sensation while exploring the surface of a textured object by moving one's hand over it, is an active action. Tactile perception relies on bodily sensation and can be used to navigate in challenging situations, such as finding one's way across a city when visually impaired or feeling one's way around a dark room. The basic unit of tactile experiences serves as a foundation for more complex interactions.

The idea of innate knowledge in the tactile sense and body sense suggests that animals are born with a certain level of understanding about their own bodies along with their interaction within a specific environment. Animal consciousness requires the capacity for a tactile experience, accompanied by innate knowledge about the physical world. This unique characteristic is not found in any other sense but applies to the senses as a whole (Mazur, 2014; Landau, 2017). Learning through tactile experiences is possible, either in a new environment or in the environment for which the species evolved. Animals possess the ability to learn from experiences in specific settings, demonstrating the existence of a suitable environment for displaying this learning capacity. This applies to sense perception overall, and to tactile perception in particular (O'Shaughnessy, 1989).

The remarkable relationship between tactile sense and body sense reveals their interconnected nature. Tactile sense leads us outward, while body sense directs us inward, reflecting each other like mirror images. The representative theory of tactile perception requires alignment between intermediate perceptions in touch and immediate perceptions in body sense (Ross and Jackson, 1978). Spatial properties perceived through touch must correspond to the spatial properties of body movements (Moscatelli et al., 2015; Dupin et al., 2017). Notably, merely perceiving the straightness of an edge is insufficient; an active perceptual goal extending beyond the body is necessary to focus on the object's spatial properties. However, despite this distinction, awareness of external spatial properties relies on corresponding body awareness. The combination of matching content and a causal link gives rise to a representational relation. The dependence of body sense on tactile sense underscores the vital role of perceiving our own bodies in understanding the physical world. It aims to establish a cognitive bridge to the expansive physical area, with touch playing a crucial role. As the primary sense, touch is intrinsically linked to the fundamental aspect of space in the physical

domain. The structure of sense perception fundamentally relies on the perception of our own bodies, highlighting the significance of body sense.
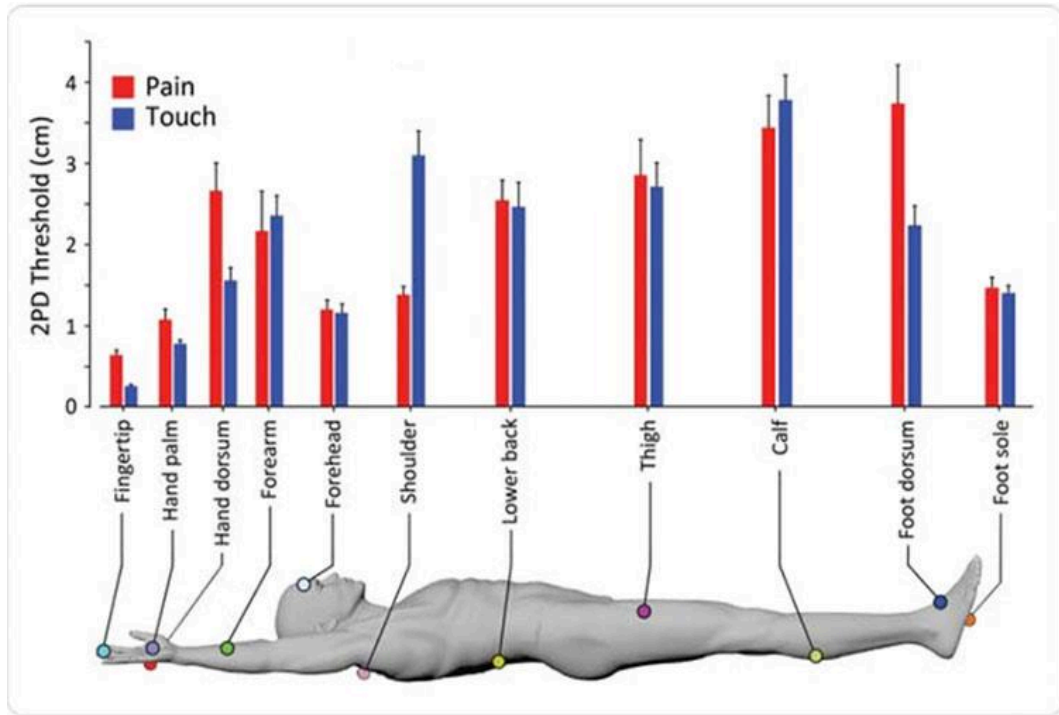
Figure (1): This figure shows the two-point discrimination test, where the distance between two pen-shaped objects is adjusted until the subject distinguishes them as separate points. Body parts with more touch receptors, like the face and hands, have lower discrimination thresholds, indicating higher sensitivity compared to areas like the back or calf. (Mancini et al., 2014) .

The above figure (see figure 01) illustrates the two-point discrimination test (Mancini et al., 2014). In this test, the subject is gently stimulated with two small pen-shaped objects, and the distance between these objects is gradually adjusted. The individual is then instructed to indicate when they can differentiate two distinct points instead of feeling them as a single point. This measure is referred to as the discrimination threshold, which is represented on the vertical (y-axis) of the graph. Body parts that play a significant role in exploring the surrounding environment, such as the face and hands, exhibit remarkably low discrimination thresholds. This implies that individuals can perceive two separate points even when they are positioned closely together. Conversely, regions with fewer touch receptors, such as the back or calf, require a more substantial spatial separation between the objects for the person to distinguish them as two distinct points. We see that the human body exhibits varying touch sensitivity across different regions due to the density

of touch receptors present. Areas with a higher concentration of touch receptors tend to have superior discriminatory abilities in perceiving tactile stimuli.

From contact to perception: The journey of touch signals and neural processing

The persuit through the integration of touch signals and brain processing within the human body is an engaging investigation into sensory experience. Our complex sensory system is built to process a wide range of inputs, with mechanical sensitivity reigning supreme. This sensory modality includes touch, pressure, vibration, tickle, and itch sensations (Kruger, 1988).

We investigated into the inner workings of our body to understand this process. Our skin, our biggest organ, acts as a barrier between the outside world and our internal sensory systems. The epidermis, dermis, and hypodermis are the three major layers. These layers are critical in the conversion of tactile information into brain impulses (Dehdashtian et al., 2018). The epidermis, being the outermost layer, is in charge of receiving tactile signals. A complex arrangement of mechanoreceptors and sensory neurons within the dermis assess mechanical inputs and convert them into nerve impulses. Finally, the lowest layer, the hypodermis, offers insulation and cushioning to preserve the underlying tissues. The skin's unique organizational structure within our body allows it to turn tactile input into neural impulses, which then go to the brain for additional processing and, ultimately, perception. Understanding these systems is critical for solving the riddles of human somatosensorial feeling (Abraira and Ginty, 2013; Handler and Ginty, 2021).

Neurons, the fundamental units of the nervous system, possess a distinct structural composition comprising a cell body, dendrites, and an axon. Dendrites, resembling antennas, extend from the cell body and serve as the primary recipients of incoming neural signals. Conversely, the axon, akin to an extended arm, carries information away from the cell body, transmitting it to other neurons or target tissues. The axon is responsible for transmitting action potentials and contains a transport mechanism called rapid axonal transport, which carries newly synthesized membranes to the

presynaptic ending. Dendrites, on the other hand, receive information and can also initiate and propagate action potentials. In some interneuron types, all functions are carried out by dendrites as these neurons lack a canonical axon (Waxman et al., 1995; Johnston et al., 1996).

Sensory axons can be classified into different types based on their size, myelination, and functional characteristics. One classification system identifies A-alpha, A-beta, A-delta, and C-fiber axons as distinct groups with varying properties (Nolano et al., 2003). A-alpha axons, the largest and fastest type, are primarily associated with proprioceptive neurons responsible for muscle stretch receptors (Field, 2001; Nolano et al., 2003). These axons play a crucial role in providing feedback about limb position and movement. A-alpha fibers, which are mediated by proprioceptive touch, carry important information regarding limb position and movement. Discriminative touch and emotional touch are two more categories of cutaneous touch. Discriminative touch is crucial for our perception in interaction with the surroundings. It can be described as the ability to localize touch stimuli with precision and gain access to textural, shape, and detailed information mediated by skin mechanoreceptors (McGlone et al., 2014). In contrast, emotional touch is related to affective experiences and is mediated by a separate set of nerve fibers termed C-touch afferents, which show optimal responses to gentle, caressing touches that can convey information about emotional states and social cues (Morrison et al., 2010). These two forms of touch contribute to our sensory experiences by providing detailed environmental information by including the emotional context of the tactile interaction.

A-beta axons, the second-largest and second-fastest group, include the discriminative touch receptors mentioned earlier, such as Meissner's corpuscles, JMerkel's disks, Ruffini endings, and Pacinian corpuscles (Vallbo and Johansson, 1984; Abraira and Ginty, 2013). These receptors are classified as low-threshold mechanoreceptors (LIMRs) and contribute to the perception of discriminative touch, such as detecting texture, shape, and vibration. A-delta fibers, the third type, are associated with nociceptors and cool receptors (Ringkamp et al., 2018). A-beta axons carry vibration and pressure sensations during discriminative touch, whereas A-delta and C-fibers carry painful and pleasurable stimuli during affective touch.

Nociceptors are responsible for the detection of potentially harmful or painful stimuli, while cool receptors contribute to temperature perception, particularly cool or cold sensations (Abraira and Ginty, 2013). Unmyelinated C-fiber axons encompass nociceptors, warm receptors, cool receptors, and most notably, C-tactile (CT) afferent receptors (Olausson et al., 2010). CT afferents are specifically involved in processing emotional or pleasant touch stimuli and have been linked to social bonding and affiliative behaviors (Löken et al., 2009; Morrison et al., 2011). While emotional touch involves the orbitofrontal cortex, cingulate cortex, insula cortex, and prefrontal cortex, discriminative touch predominantly engages the primary and secondary somatosensory cortex. Understanding the distinct characteristics and functions of these sensory axons contributes to our knowledge of touch perception and the detailed sensory processes underlying discriminative touch, pain, temperature sensations, and affective touch.

The relationship between touch and action control

The nuanced relationship between touch and action control is fundamental to our effective interaction with the physical world, enabling precise movements and adaptability to be changing circumstances. Our sense of touch serves as a vital source of feedback for our motor skills.

Johansson's series of experiments, focusing on the act of "grasping," sheds light on the significance of touch in various situations. Johansson highlights the critical role of our palm's glabrous (non-hairy) skin in regulating grip forces and manipulating small objects. He investigates how tactile feedback seamlessly combines with automatic control, facilitating adaptive actions during manipulation. While established neural programs primarily dictate control through muscle synergies, tactile signals play a pivotal role in promptly rectifying errors and adjusting parameters according to object properties, such as weight and friction. Additionally, somatosensory information can trigger sequential muscle commands in complex manipulation tasks (Johansson, 1991).

Within the domain of natural manipulative tasks that require the precision grip between the tips of the index finger and thumb (Johansson and Westling, 1984a, 1984b, 1987, 1988; Westling and Johansson, 1984) tactile afferent mechanisms play a central role. These tasks encompass both "parallel" and "sequential" coordination. In "parallel" coordination, the primary challenge lies in the fine-tuning of grip forces to harmonize with manipulative forces. This adjustment is vital for effectively countering opposing forces, such as gravity and kinetic forces when handling objects. Striking the right balance is of utmost importance, as the grip must be strong enough to prevent accidental slips while remaining gentle enough to handle delicate objects without causing damage or undue muscular fatigue. Furthermore, most of these manipulative tasks involve "sequential" coordination, entailing the linking of phases of coordinated actions and transitioning between them. For example, the transition from placing an object on a table to releasing it might require conditional adjustments to initiate new sets of muscle commands. The seamless integration of tactile feedback is indispensable for achieving success in both "parallel" and "sequential" coordination within these manipulative tasks (see Chapter 1 of Johansson, 1991).When we explore the role of touch in action control, it's essential to acknowledge the significant contributions of Jeka and his group's scientific research. In his numerous experiments, particularly concerning the influence of light touch on postural control, he unraveled a phenomenon. Jeka and Lackner probed whether the reduction of postural sway, achieved by lightly touching the index finger, could be attributed to the sensory information it imparts about body sway (Jeka and Lackner, 1994).

In one of their investigations, Jeka and Lackner examined the intricate relationship between postural sway and contact forces at the fingertip while subjects contacted a rigid metal bar. Strikingly, he found that light touch contact was as effective as forceful contact or visual input from the surroundings in diminishing postural sway when compared to conditions with no contact and closed eyes.

What's even more compelling is that body sway and fingertip forces were found to be synchronized when there was forceful contact, suggesting that fingertip contact forces were effectively counteracting body sway (see figure 2).

Figure 2 Subject depicted in tandem Romberg posture on the force platform in the touch (VT, DT) and force (VF, DF) contact conditions with the right index fingertip on the touch bar. In the no contact (V, D) conditions, the subject's arms hung passively by his or her side. The figure presented here is sourced from reference (Jeka and Lackner, 1994).

In contrast, when light touch contact was involved, there were substantial time delays between body sway and fingertip forces. This insightful finding indicates that the fingertip's light touch provides anticipatory information that influences the innervation of musculature to proactively reduce body sway (Jeka and Lackner, 1994). Jeka and Lackner's findings carry important implications for our understanding of the complex interplay of somatosensory, proprioceptive, and motor mechanisms involved in the reduction of body sway.

In another study, Jeka and colleagues examined the impact of haptic cues from a cane on postural control in sighted and congenitally blind individuals (Jeka et al., 1996). The findings revealed that light touch contact with a cane significantly reduced postural sway, and a slanted cane was more effective. This indicates a connection between head movement control and postural control, with implications for gaze stabilization reflexes. Jeka's research underscores the vital relationship between touch and action control, enhancing our ability to interact with the physical world and achieve precision in our movements.

In the area of tactile perception, the brain's electrical system dynamically reacts to variations in vibration, friction, and surface attributes as they interact with the human skin. For instance, Lederman and Klatzky (Lederman and Klatzky, 1987a) identified exploratory procedures, which represent characteristic hand
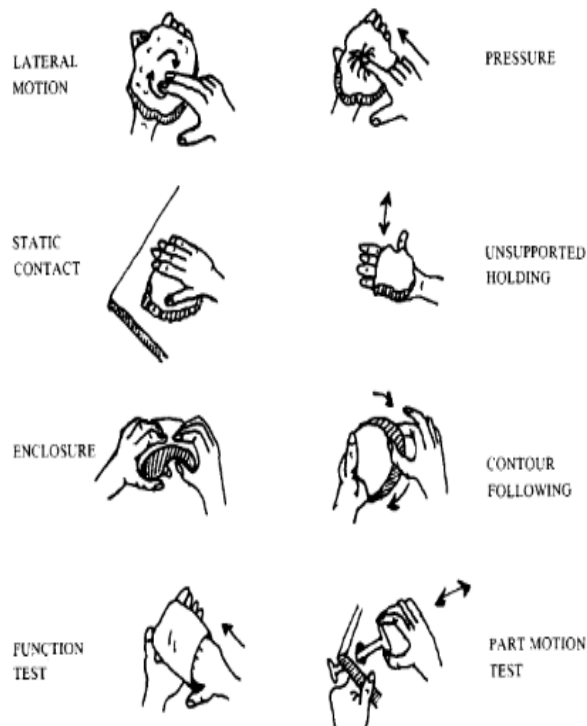
Figure 3 Typical movement pattern for each of the exploratory procedures (EPs) described in the accompanying text. The figure presented here is sourced from reference (Lederman and Klatzky, 1987a).

movements precisely designed to extract the most comprehensive data regarding object properties (see Fig. 3). Although the existing studies on this subject are limited, they underscore the subtle connection between an individual's specific hand movements and the sensory information accessible through the tactile channel. This relationship becomes especially evident when considering the physical attributes of the environment (see review by Ryan *et al.*, 2021).

Since tactile feedback plays a crucial role in providing information about limb position and displacement for motor control. In a separate investigation

(Moscatelli et al., 2019), participants engaged in a reaching task by sliding a finger across ridged surfaces. Manipulating ridge orientation disentangled tactile and proprioceptive cues, leading to consistent deviations in reaching movements. These findings support the concept that touch complements proprioception in active motor control. The behavioral outcomes were consistent with an ideal observer model, encompassing a range of somatosensory inputs, including skin deformation, a priori assumptions, and motor control.

Several studies in sensory-motor control have highlighted the close interconnection between tactile representation of surface texture and action. Delhaye and colleagues (Delhaye et al., 2019), explored the impact of texture on perception by changing the speed of motion. They found that certain textures consistently create the illusion of greater speed, while others offer more precise speed signals. The study also identified Pacinian corpuscle (PC) fibers as crucial in governing both aspects of texture-dependent speed perception. They measured the ability of humans to report the motion speed of a variety of natural textures, including thick corduroy, stretch denim, microsuede, wool blend, city lights, nylon, huck towel, metallic silk, vinyl, and chiffon. In the somatosensory cortex, two distinct neuron populations were observed: one displaying response linked to scanning speed, predominantly influenced by PC fibers, and another that remained insensitive to speed. The integration of both speed-dependent and speed-independent signals served to partially correct for the texture-dependent nature of speed perception.

Building blocks of tactile perception

In the previously mentioned story, tactile perception and action serve as a gateway to the vibrant territory of the mind. It demonstrates how the mind can shape and evoke physical sensations, igniting a sense of joy and freedom that transcends the boundaries of the present moment. Through the power of imagination and the integration of sensory information, the protagonist experiences a profound connection between their inner world and external reality, reminding us of the wonders of our cognitive abilities.

The simplest form of tactile perception is when we experience <u>momentary point of contact</u>, where we briefly sense something touching a specific point on our body. However, this contact provides minimal information, simply indicating that a solid object made contact at that point (Chen et al., 1995).

In the domain of bodily contact, we encounter the concept of "extensive contact" when a larger object makes contact with us (as described by Li et al., 2017). Momentary point contact refers to the brief interaction when something touches a specific point on our body. These simple tactile experiences serve as the building blocks for more complex structures of tactile perception. Our complete tactile perception is instead fully demonstrated by active exploratory movement(O'Shaughnessy, 1989). This movement requires deliberate and active exploration of an object using our hands, allowing us to feel its edges and shape.

Instead of focusing solely on our own body, we may extend our attention outwards to actively explore the surroundings such as objects. This differs from simpler tactile experiences which only contribute to our body awareness. Purposeful movement requires the recognition of certain spatial qualities like straightness, which can only be detected through active exploration. While vague descriptions like "large" or "moving" may suggest something about an object's space, terms like "rectangular," "parallelepiped," and "straight" demand a higher level of specificity. This recognition goes beyond detecting movement over time, as these properties remain present even when objects simply cross our body's boundaries.

Tactile perception and interaction

When we moved for instance our foot without actively touching anything, we discovered a different kind of spatial information. This finding suggests that our sense of touch isn't solely determined by the activity itself. Instead, how well we can feel things is influenced by the way we move our limbs, which affects our tactile experiences.

Our ability to sense touch depends on our brain's capacity to distinguish between different scenarios: when our body parts come into contact with objects and when

they are being touched by something else. This differentiation triggers various regions of the brain, leading to different perceptions of touch, as discussed by Bolanowski and colleagues in 2004 (Bolanowski et al., 2004).

Active versus passive touch

Active touch refers to a form of tactile exploration in which an individual voluntarily moves their fingers or hand across a surface to acquire sensory information. This process engages multiple sensory modalities, including cutaneous, kinesthetic, and proprioceptive senses. In contrast, passive touch involves the stimulation of an individual's skin by an external object, without any active movement on the part of the individual. In this type of touch, only the cutaneous receptors of the skin are activated.

Consider the following scenario: when you actively move and pick up a volleyball from the ground, this tactile interaction is referred to as "active touch." On the other hand, if the ball comes towards you from another player without your voluntary participation or any movement on your part, and you still experience the sensation of touch, this would be classified as "passive touch."

As consequently, active touch involves the activation of a wider variety of sensory systems than passive touch, including the cutaneous, kinesthetic, and proprioceptive senses (Chapman et al., 1987; Chapman and Ageranioti-Bélanger, 1991).

According to recent studies, active touch may be superior to passive touch in terms of the encoding of sensory characteristics. Due to the dynamic nature of the investigation, sensory data may be encoded more carefully, perhaps resulting in a better representation of the tactile experience. However, because there is no active movement or manipulation of the stimuli, passive touch may not necessarily promote the best encoding of information (Lederman and Klatzky, 1987a; Chapman, 1994).

Based on research, active touch and passive touch are controlled by different brain pathways and processes. Active touch involves the coordinated action of the cutaneous, kinesthetic, and proprioceptive senses as opposed to passive touch, which just stimulates the cutaneous receptors of the skin. Additionally, research has

shown that movement-related gating of sensory transmission, a process known as suppressing afferent input to the primary somatosensory cortex during active movement, occurs. This gating mechanism, which has been shown at the level of the lemniscal pathway, is essential for the effective encoding of stimulus features, particularly when there are many sensory inputs (Coulter, 1974).

Intra-active touch

Certainly! Intra-active touch is a thought-provoking idea that emphasizes the dual tactile experience. Both the body part that initiates the contact (active touch) and the body portion that receives the touch (passive touch) are involved in it (Bolanowski et al., 2004). When we use intra-active touch, such as when we touch ourselves "Self-Touch," we are cognizant of both the act of touching and the feelings it causes. For instance, when we stroke our own arms with our hands, we sense both the touch of our hands on our body's skin and the sensation of our hands moving. This simultaneous awareness of the toucher and the touched results in a singular and personal sensation of touch. On the other hand, passive touch describes the sensation of being touched by another person or an outside stimulus. In this instance, we are not actively managing the touch but only the contact's sensory information. For instance, we don't actively move our arm when someone touches it; instead, we focus on the feelings on our skin. The difference between passive and intra-active touch emphasizes how complicated our tactile perceptions are. Due to our cognitive awareness of our activities, self-touch during intra-active touch can be calming and reassuring. It also affects how we perceive ourselves and our bodies. Understanding the subtle characteristics of intra-active touch can help us better understand how people interact with one another and how deeply our minds and bodies are connected. Researchers are still drawn to this field of inquiry because it offers new perspectives on how touch affects our sense of self and social interactions.

Interpersonal touch

Interpersonal or affective touch is a key component of human interactions. It takes the form of diverse physical expressions, including reassuring pats on the back and soothing hugs. Affective touch acts as a non-verbal technique for expressing

feelings and support, creating bonds between people, and overcoming emotional divides beyond linguistic and cultural barriers.

It is important to recognize that the effects of affective touch are subjective and depend on an individual's degree of comfort and tolerance for physical contact. Respecting personal limits becomes essential to ensuring that emotive contact strengthens social bonds without creating discomfort.

Discriminative touch, which includes detecting the physical characteristics of touch such as pressure, texture, and warmth, is separate from affective touch, which is the bodily feeling that communicates emotional and social information (McGlone et al., 2014). Unmyelinated C-tactile fibers mediate affective touch, whereas myelinated A-beta and A-delta fibers mediate discriminative touch, both of which have distinct somatosensory purposes (Olausson et al., 2002, 2010; Löken et al., 2009).

Culture, interpersonal relationships, environment, and gender are major top-down influences on how affective contact is perceived. Distinct touch kinds have distinct meanings and levels of appropriateness that are shaped by cultural norms and values, while personal connections affect how different touch types are interpreted depending on the people involved (Morrison et al., 2010; Ellingsen et al., 2016). Depending on the location, contextual elements might also alter how affective contact is perceived. Additionally, gender might influence expectations and experiences with touching.

Depending on the nature, setting, and individual variations, the impact of emotional contact with another person can be either positive or unpleasant. Gains in comfort, trust, social connection, and stress and anxiety reduction are all positive outcomes (Croy et al., 2016b, 2016a; Ravaja et al., 2017). However, when affective touch is undesired, improper, or regarded as violent or abusive, negative repercussions can happen, leading to discomfort, anxiety, mistrust, and trauma. When analyzing the effects of emotive contact on people, it is essential to consider larger social and cultural norms and values.

Mapping motor control: Primary and secondary motor areas

Within the area of the human sensory-motor system, the multifaceted interplay between somatic sensors and movement plays a crucial role. Specifically, the sensorimotor system governing touch, orchestrates this dynamic interaction leading to enhanced connectivity between sensory inputs and motor responses (Fanselow and Connors, 2005). Exhibiting a parallel hierarchical structure, the sensorimotor system facilitates the transmission of signals across
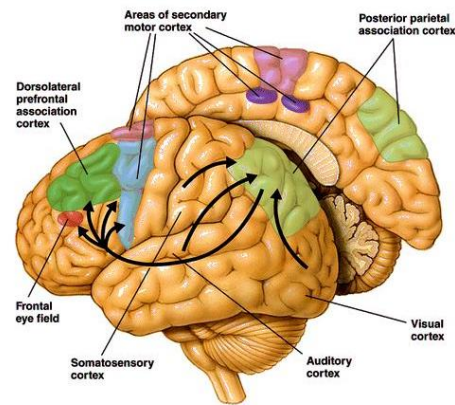
Figure 4 Sketch of cortical input and output pathways in the supplementary motor area (Paskari, 2023)

multiple pathways, allowing for the efficient flow of information between its various levels. Notably, functional segregation characterizes this system, with each level comprising distinct units that serve specific functions. Information primarily propagates in a downward direction within the sensorimotor system. The eyes, organs responsible for balance, skin receptors, muscles, and joints collectively function as vigilant monitors of the body's responses, providing valuable feedback to the sensorimotor circuits. Sensory feedback assumes a pivotal role in guiding and sustaining the continuation of the responses that prompted it. It is noteworthy that ballistic movements, characterized by their rapidity, such as swatting a wasp, are generally executed without substantial reliance on sensory feedback. During the initial stages of motor learning, conscious control governs each individual response. However, with extensive practice, these discrete responses seamlessly integrate into continuous sequences of action, flowing harmoniously and finely adjusted by sensory feedback without the need for conscious regulation (Verwey et al., 2010; Ruitenberg et al., 2014; Khattak et al., 2021; Mujahid et al., 2022).

The many anatomical areas involved in motor control make up the motor system. Primary and secondary motor areas can be distinguished among the motor regions of the cerebral cortex. These areas are made up of separate populations of neurons

that branch out from the cortex to the spinal cord and brain stem. Notably, the main motor cortex (M1) is a significant source of spinal cord output. M1 gets inputs from the thalamus, sensory regions, and other secondary motor areas in addition to premotor areas (PM1) and other secondary motor areas.

The significance of S1-M1 connections in tactile sensation and action

The interaction between the primary somatosensory cortex (S1) and the primary motor cortex (M1) in touch perception and behavior is a subject of profound significance. S1 is responsible for processing sensory inputs from the skin, muscles, and joints (Johansson and Westling, 1984a; Wheat et al., 2010), while M1 plays a key role in planning and executing motor actions (de Beukelaar et al., 2016). The reciprocal connections between S1 and M1 are crucial for integrating sensory and motor information during activities such as tactile exploration and object manipulation (Ghosh et al., 1987; Stepniewska et al., 1993). Sensory information from the skin is relayed to S1 when an individual touches an object (Rowe, 2001). S1 processes this information and transmits it to M1, which uses it to plan and execute the appropriate motor response, such as grasping or manipulating the object (Sobinov and Bensmaia, 2021). This interplay between S1 and M1 is essential for the successful execution of motor tasks (de Beukelaar et al., 2016).

In their 2015 study, Fortier-Poisson and Smith trained monkeys to explore small surface areas with their second and third digits to search for tactile targets without visual feedback. They recorded neuronal activity in the somatosensory cortex (S1) as the monkeys scanned various surfaces during 3–4-hour daily sessions, performing around 1000 trials. A digital video camera was used to monitor the two-finger exploration, and the instantaneous coefficient of friction, reflecting the ratio of tangential to normal force, was measured. The study found that S1 neuron activity was modulated by fingertip contact forces and correlated with the instantaneous coefficient of friction (Fortier-Poisson and Smith, 2015).

This experiment provides valuable insights into the cortical mechanisms involved in the optimized sensorimotor strategy of fingertips during tactile exploration. The findings suggest that the activity of S1 neurons is modulated by the contact forces applied by the fingertips and is correlated with the instantaneous coefficient of friction during tactile exploration of the surfaces.

The evolving role of the primary motor cortex in sensorimotor processing

The primary motor cortex is a part of the brain that is essential for regulating voluntary movements and integrating sensory data linked to motor activity. It takes in information from various cortical and subcortical regions and sends signals to alpha-motor neurons in the spinal cord, which regulate muscles (Sanes, 2010) (see Figure 5). Participating in the organization of motor behavior and processing motor-related information, recent evidence suggests that the primary motor cortex is involved in more complex functions (Pavlova, 2014).The spinal cord is thought to receive movement cues from different cortical regions and transfer them to the main motor cortex (Sanes, 2010). Recent research reveals that the primary motor cortex is engaged in more complicated processes in addition to organizing motor action and processing motor-related information(Pavlova, 2014). It displays sensory responses in modalities including vision and somatosensation, highlighting its variability in sensorimotor processing (Hatsopoulos and Suminski, 2011b). Studies have shown that the primary motor cortex may undergo plasticity and remodeling, making it a dynamic structure rather than a static one in response to pathological alterations, motor learning, and cognitive motor movements (Sanes and Donoghue, 2000). Additionally, it has been noted that the primary motor cortex reflects and predicts choice evidence during perceptual decision-making tasks (Bitzer et al., 2019). A recent study implemented advanced approaches to examine motor cortex interactions with the parietal cortex in primates, specifically macaques (Bresee et al., 2023). This study entailed a selective inactivation of parts of the primary motor cortex (M1) and an examination of the effects on movement generation within several parietal regions. Using this method, they demonstrated the interdependence

of the brain areas in the regulation of movement. The study revealed that areas 2, 5L, PF, and PFG in the parietal lobe are closely associated with M1 in the movement initiation process. On the contrary, area 1 seems to operate through an independent cortico-spinal system, enabling it to initiate movements without that much dependence on M1. These insights indicate the presence of two parallel networks managing motor control: - one that is posterior parietal and works with M1 and another that involves area 1, which functions almost independently of M1.
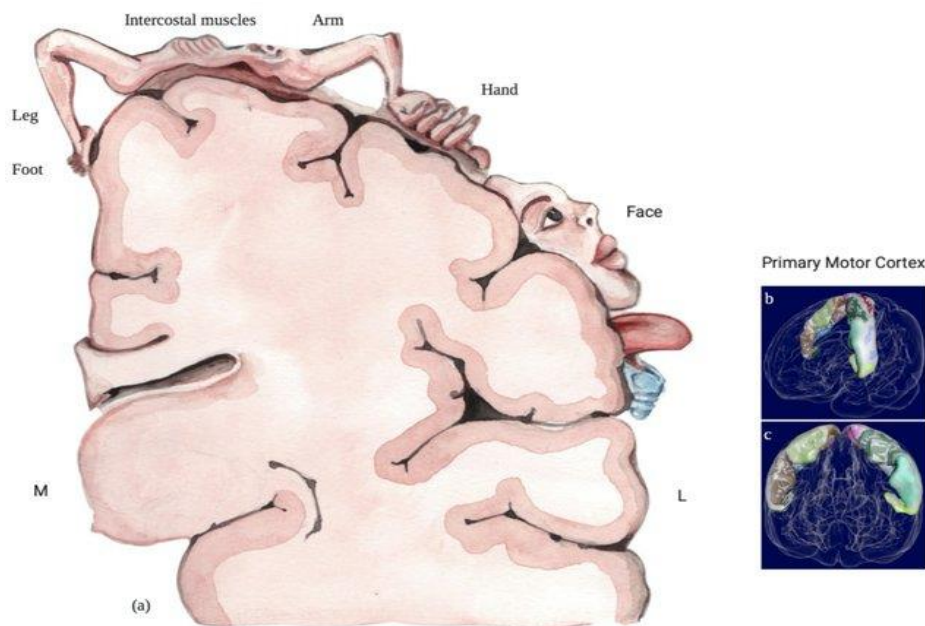
Figure 5: Proposed supplemental cortical motor homunculus including the cortical somatotopy of intercostal muscles: a cortical motor representation. b, c Primary motor cortex reconstructed with MeshLab opensource. The entire figure presented in this context is sourced from reference(Ghimire et al., 2021).

Observing others' actions and the complex dynamics of mimicry

Human behavior is a complex interplay of various cognitive processes, including mimicry, which involves the imitation of others' actions, expressions, and emotions. This nuanced phenomenon extends beyond mere actions and encompasses a wide range of behavioral and emotional expressions, such as facial expressions, postures, gestures, emotions, and even simple movements (Dimberg, 1982; Stel, 2005; Louwerse et al., 2012; Chartrand and Lakin, 2013; Genschow and Schindler, 2016). Within the context of "Action imagination, motor cortex activity, and social cues,"

I would like to discuss the underlying mechanisms that drive mimicry, connecting it to the intricacies of perception, action, and imagination.

Mimicry, as a behavioral phenomenon, finds its theoretical underpinning in perception-behavior theories (Greenwald, 1970; Prinz, 1997; Chartrand and Bargh, 1999; Hoegen et al., 2018). According to these theories, individuals imitate others because the mere perception of their actions triggers corresponding motor representations in the observer's motor cortex. This connection between perception and motor representation underscores the pivotal role played by motor cortex activity in the process of mimicry.

Empirical evidence supporting the involvement of the motor cortex in mimicry has been accumulating over the last few decades. Neuropsychological experiments, including functional magnetic resonance imaging (fMRI) studies (Calvo-Merino et al., 2005; Keysers and Gazzola, 2010; Campbell et al., 2021), motor transcranial magnetic stimulation (TMS) studies (van Ulzen et al., 2013; Borgomaneri et al., 2021; Syrov et al., 2021), and single-cell recordings in both monkeys and humans (Di Pellegrino et al., 1992; Mukamel et al., 2010), have consistently demonstrated the activation of the motor cortex in response to the observation of others' actions. This empirical support solidifies the connection between perception, motor cortex activity, and the phenomenon of mimicry.

A significant breakthrough in our understanding of the link between perception and action came with the discovery of mirror neurons. These mirror neurons are a population of neurons found in the brains of monkeys, and they exhibit activity not only when an individual performs a specific action but also when they observe someone else performing the same action (Hickok, 2010; Catmur, 2014). For instance, a mirror neuron may fire when a monkey picks up a peanut and when it observes another monkey doing the same. This remarkable discovery provides neuroscientific evidence that the motor cortex and perception are intricately linked, offering a neural basis for our innate capacity for mimicry.

Furthermore, research on anticipated action sheds light on the role of imagination and motor cortex activity in social interactions. This line of inquiry suggests that the act of imagining another person's actions, a form of action imagination, is

sufficient to trigger similar actions in the observer (Geake and Kringelbach, 2007; Haggard et al., 2008; Koziol, 2014; Genschow and Schindler, 2016; Genschow and Groß-Bölting, 2021). Even the anticipation of an action can activate the motor cortex and lead to behavioral responses. In essence, this research underscores the powerful role of imagination in bridging the gap between motor imagery and actual motor behavior, highlighting the capacity of mental simulation to produce real-world actions.

In another study, the researchers studied the phenomenon of motor resonance evoked by the observation of subtle nonverbal behaviors (van Ulzen et al., 2013). Their investigation likely employs experimental observations and neuroimaging techniques to uncover the neural mechanisms underlying this form of social interaction. The study discovered that excitability was significantly higher when participants observed face-touching gestures compared to conditions where no face-touching occurred, and there was consistently increased excitability in the left motor cortex compared to the right. These findings indicate that even subtle, unattended hand-to-face gestures during an ongoing action can induce rapid motor resonance in observers, highlighting the role of motor resonance in mimicry and demonstrating its study through a naturalistic mimicry paradigm. Within the framework of "Motor imagery, motor cortex activity, and social cues," we gain insight into the complex dynamics of mimicry. It reveals how individuals naturally replicate a broad spectrum of behaviors, emotions, and expressions, with the motor cortex playing a central role in this process. Additionally, it underscores the influence of perception, action, and imagination on our social interactions. The discovery of mirror neurons provides a compelling neural basis for the connection between perception and action, while research on anticipated action highlights the significance of imagination in driving mimicry. These collective findings enrich our comprehension of the advance interplay between perception, motor cortex activity, and the captivating phenomenon of mimicry in human behavior.

Advances in understanding M1's contribution to action observation

Action observation and performance are closely linked, with the primary motor cortex (M1) at the center of this neural interplay. M1, often recognized for its fundamental role in orchestrating voluntary movements, has garnered attention for its involvement in both executing and observing actions (Su et al., 2023).

Investigating into action observation, recent research has illuminated a fascinating connection between M1 and this cognitive process. It has been proposed that M1 plays a significant role not only in action execution but also in action observation, suggesting a neural overlap between these two seemingly distinct functions (Strafella and Paus, 2000; de Beukelaar et al., 2016). This persuasive concept traces its origins to the discovery of mirror neurons, initially identified in the premotor cortex of monkeys (Rizzolatti et al. 1996; Zarka et al., 2021).

The engagement of M1 in action observation goes beyond mere passive observation. It triggers a remarkable phenomenon where the observer's motor system becomes activated in a manner that mirrors the observed action. This suggests a simulation process at play, wherein M1 simulates the observed action within the observer's brain (Cretu et al., 2020; Bisio et al., 2021). This simulation is theorized to be instrumental in understanding and predicting the actions of others, thereby contributing to various cognitive functions, ranging from imitation to empathy (Dushanova and Donoghue, 2010; Betti, 2017; Pedullà et al., 2020). Advancements in neuroscience have allowed researchers to delve deeper into the role of the primary motor cortex in action observation. Non-invasive brain stimulation techniques, particularly Transcranial Magnetic Stimulation (TMS), have played a pivotal role in this exploration (Mulder, 2007; Aglioti et al., 2008). TMS enables scientists to transiently modulate neural activity within specific brain regions, shedding light on the causal role of these regions in various cognitive functions (Amoruso et al., 2018).

Vesia and colleagues conducted a study exploring the modulation of M1 plasticity in response to reversed visual input. Their research underscored the pivotal

influence of visual input on M1 plasticity, highlighting that our perception of actions can directly shape neural activity within the primary motor cortex (Vesia et al., 2013). In the study by Bisio et al. (2021), the researchers developed a novel approach combining two elements: action observation and proprioceptive stimulation. This blend was used to create an illusion of movement, which they termed AO-KI (Action Observation-Kinesthetic Illusion). Their findings revealed a marked increase in M1 excitability during AO-KI, with this heightened state persisting for up to an hour post-stimulation. Notably, participants with a more pronounced AO-KI response exhibited greater subsequent alterations in motor cortical activity, suggesting that the M1 response during AO-KI could potentially act as a neurophysiological indicator of individual sensitivity to the combined stimulation (Bisio et al., 2021). Building on this, another investigation by Bisio et al. (2019) delved deeper into the effects of kinesthetic illusions on M1 plasticity when coupled with action observation. Their results bolstered the notion that our sensory experiences during action observation can significantly mold the plastic alterations in our motor cortex (Bisio et al., 2019).

A study by Moriuchi and colleagues investigated how the video speed of observed action affects the excitability of the primary motor cortex (M1). The study found that M1 excitability was modulated by the speed of the video, especially during the observation of rapid movements (Moriuchi et al., 2017). Moreover, during action observation, Cretu and his group explored the modulation of early and late short-intracortical facilitation (SICF) peaks. The findings suggest that movement observation leads to widespread activation of different neural circuits within M1, including those mediating cortico-cortical communication (Cretu et al., 2020).

The studies by Donne et al. (2011) and Sartori et al. (2013) provide insightful contributions to our understanding of corticospinal excitability (CSE) in relation to action observation and social contexts. Donne et al. utilized transcranial magnetic stimulation (TMS) to assess how observing meaningless, goal-directed, and social behaviors affects CSE (Donne et al., 2011). Their findings challenged the notion that the human mirror system is more responsive to social contexts, as they discovered CSE was similarly enhanced by both goal-directed and social behaviors. This study also highlighted that the mirror system's response to observed motor

behaviors parallels actual action performance, indicating a strong attunement of the mirror system to social behaviors. Building on this, Sartori et al.'s 2013 study delved into how observing others' actions influences motor facilitation in an observer's muscles, specifically focusing on the modulation of CSE in social contexts (Sartori et al., 2013). They employed TMS/MEP and EMG recordings from the right ADM and FDI muscles, capturing the excitability changes at various points during action observation. The innovative aspect of their study was the use of video clips designed to elicit emulative and complementary responses. The key takeaway from their research was that humans are adept at distinguishing actions based on social or nonsocial conditions by observing minute kinematic cues. This ability enables observers to use these cues to predict future actions and activate appropriate motor responses in interactive situations. Both studies collectively enhance our understanding of the complex relationship between action observation, motor facilitation, and the role of social context in corticospinal excitability. Traditionally linked to voluntary movement control, the primary motor cortex also plays a role in action observation and understanding. Mirror neurons and techniques like TMS reveal their contribution to social interaction and empathy, showcasing intricate neural connections.

Motor excitability using motor imagery instead of action execution

Over the past decade, recent research has shown that certain cognitive states, like intended action, imagined action, observation of others' actions, and actions experienced during dreams, are associated with simulated actions (Jeannerod, 2001). These cognitive states can involve conscious awareness or not, but all of them have a consistent connection to action, both behaviorally and neurally. Interestingly, studies have found that imagined actions and their corresponding real actions exhibit similar temporal patterns during execution (Moore et al., 1989). The notion of mental simulation of movement triggers activation in the motor pathways. When individuals engage in motor imagery, there is often an increase in muscular activity compared to a state of rest. In such instances, electromyography (EMG)

activity is primarily confined to the muscles involved in the simulated action and tends to correlate with the level of imagined effort (Wehner et al., 1984).

In our scientific investigations, we have opted to use motor imagery, with a specific emphasis on motor imagery, rather than studying actual physical actions. The rationale behind this decision stems from the substantial body of prior research indicating that the neural pathways and motor cortex are activated similarly during motor imagery as they are during the execution of actual physical actions (Barhoun et al., 2022; Dekleva et al., 2023). By focusing on motor imagery, we seek to explore the extent of neural overlap between cognitive simulations of actions and the neural patterns observed during the concrete execution of actions. This method allows us to investigate the detailed mechanisms involved in mental representations of tasks, as well as their relationship to the underlying brain processes.
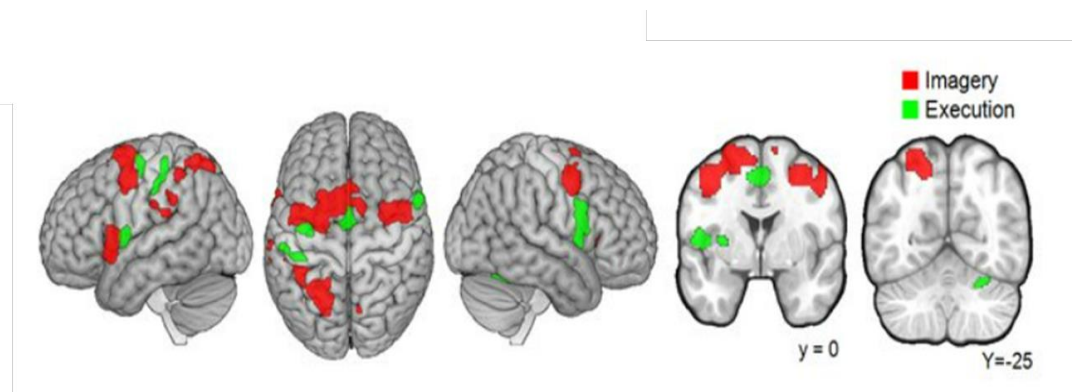
Figure 6: ALE contrast analyses identified regions more consistently implicated with one of the tasks when compared to another. The figure presented in this context is sourced from reference (Hardwick et al., 2017) .

The figure (see figure 6) presented in this context is derived from a meta-analysis study using ALE (Activation Likelihood Estimation) examined the brain correlates of motor imaging, action observation, and movement execution (Hardwick et al., 2017). The number of participants and activation coordinates in either MNI or Talairach space were obtained from many articles. For this study, tasks were divided into groups according to whether they required movement execution or motor imagery. The researchers examined the networks involved in action simulation by quantifying and comparing the degree of the activation of the various brain networks during different activities. They also sought to comprehend the connection

between these networks and individuals responsible for the implementation of real movements. The analysis's findings show that tasks requiring motor imagery and those requiring motor execution activate the same brain areas, notably in the premotor and parietal cortices. However, certain differences in the patterns of activation were seen, such as increased activity in the supplementary motor region during movement execution compared to tasks requiring motor imagery. The parallels and contrasts between the brain mechanisms involved in mental simulation and the actual execution of muscular activities are clarified by these studies.

Understanding Motor Cortex Function with Single-Pulse and Theta Burst Stimulation

Single-pulse transcranial magnetic stimulation (spTMS) and continuous theta burst stimulation (cTBS) are widely studied for their effects on the motor cortex. For example, spTMS, the application of a single magnetic pulse on a given region in the brain, is often used to test the excitability and functional connectivity of motor circuits. Previous studies have demonstrated that single pulses may elicit MEP in target muscles, thus directly measuring motor cortex output (Ruiz et al., 2018).

cTBS is characterized by the delivery of three high-frequency magnetic pulses occurring at 50 Hz, which are then delivered every 200 ms. This stimulation pattern has been demonstrated to have longer-lasting effects on neural excitability and plasticity. For instance, it has been proposed that cTBS to the primary motor cortex of people can induce effects in the motor cortex that are similar to long-term potentiation (LTP)-like and long-term depression (LTD), respectively, in the motor cortex, and thus change the excitability of the motor cortex from approximately one-hour poststimulation onwards (Arm, 2010).

In a similar study, the effects of cTBS on motor cortex excitability were tested through a combination of TMS and EEG. The results indicated that cTBS significantly increased power within the beta frequency band, indicating increased cortical synchronization and plasticity in participants (De Martino et al., 2024). A different study presented evidence that cTBS transiently degrades motor

performance, hinting at a possible role for the technique in terms of modulating motor learning and memory processes (Arm, 2010).

These results are important, as they give confidence in the potential of spTMS and cTBS for clinical and research applications. For example, in clinical applications for stroke rehabilitation, they could enhance motor recovery by modulating neural plasticity. Our research provides essential means in studying the functional organization and plasticity of motor circuits and helps to investigate brain-behavior relationships.

Action imagining and social signals.

The convoluted relationship between action imagining, motor cortex activity, and social signals is an exciting area in neuroscience that has received increased attention in recent years. The motor cortex, which is primarily responsible for planning, controlling, and executing voluntary movements within the cerebral cortex, exhibits provocative movement not only during physical actions but also during mental simulations of these actions, implying a shared neural substrate for both domains (Yoshie et al., 2016; Savaki and Raos, 2019).

This phenomenon indicates that when we anticipate executing an activity, we activate a sensory-motor network like when we perform that action. This empirical data supports the assumption that our conceptual representations are embedded in sensory-motor codes, meaning that motor cognition is embodied and modal (Savaki and Raos, 2019). Furthermore, the effect of social signals on motor brain activity is an intriguing aspect to explore. It is especially noticeable in scenarios involving imitation tasks, where social context modulates motor cortex activity, particularly in the dorsolateral prefrontal cortex, emphasizing the significant relevance of social signals in both motor control and social interactions (Marsh et al., 2016).

The ideomotor theory expands on this notion, claiming that seeing another person's activity might stimulate our own motor system, creating images of the predicted effects of that action (Paulus, 2012). This hypothesis proposes that mentally replicating or watching an action might elicit identical brain reactions as physically

performing it, giving insight on the fundamental mechanics of action perception and social cognition.

Similarly, the semantics of action words appear to correspond with somatotopic activity of the motor and premotor cortex, showing a linguistic aspect of the motor system's participation in action comprehension (Hauk et al., 2004).

When we take into account how social-evaluative situations can break the coherence between our intended actions and the perceived intentions of others, potentially affecting our motor output, the social dimension of motor cortex activity becomes even more evident (Yoshie et al., 2016). This highlights the complex brain processes underlying social interactions and the significant impact of social perception on motor execution. Overall, the motor cortex is involved in more than just carrying out physical actions; it is essential to action imagining, reacts to social signals, and is entwined with language and social cognition. The complex interrelationships among these components underscore the role of the motor cortex in comprehending human behavior and interactions, providing valuable insights into the intricacies of the human mind and its connection with the outside environment.

Thesis at a glance:

In my thesis, I will thoroughly investigate the neural mechanisms responsible for sensorimotor interactions, particularly emphasizing the primary motor cortex. This research endeavor comprehensively explores diverse scenarios related to tactile sensations and tasks that necessitate the mental simulation of movements. I have executed three distinct research studies to gain a comprehensive understanding of this compelling subject.

Study 1

The main aim here is to unveil the role that tactile information has in controlling action. We investigated how tactile stimulation (touching a surface) influences the

motor system during motor imagery (imagining exerting force with the index finger). Here, we used single-pulse transcranial magnetic stimulation over the primary motor cortex (M1) to measure the MEP in the target muscle during motor imagery with and without tactile stimulation. The research provides insights into how tactile information influences motor imagery and its impact on the motor system, highlighting the relationship between sensory feedback, motor control, and imagery processes.

Published: (Ali et al., 2023)

Study 2

The research aims to understand how touch and action interact in social contexts. The study investigates the neural connections between touch and action by having participants imagine exerting force with their index finger while experiencing different types of touch: their own touch, the touch of another person, the touch of a surface, or no touch. Using transcranial magnetic stimulation (TMS) on the motor cortex during motor imagery, we found that imagining touching another person while performing an action led to a significant increase in motor cortex activity, suggesting that the social component of touch influences the brain's motor responses specifically. The study provides valuable insights into the neural mechanisms underlying touch and action interplay in social contexts, contributing to our understanding of human social behavior and sensory-motor integration.

Published: (Ali et al., 2024)

Study 3

The goal of this study is to disclose the mechanisms behind the brain neuronal networks involved while imagining a simple action of precision grip. Using the analysis of two experiments that utilize continuous Theta Burst Stimulation cTBS to suppress activity in the primary somatosensory cortex (S1) and dorsal premotor cortex (dPMC), this investigation aims at identifying both how such inhibition affects task performances disclosing neural mechanisms through which commands are sent out from the primary motor Cortex (M1). This study suggests that inhibiting these areas would alter overall performance and illuminate the multisensory

system's relationship with the more central motor outflow. This discovery is critical for comprehending neural circuits involved in motor imagery and regulation. Thus, the results provide essential information regarding dPMC and S1 involvement in imagination-related actions, focusing on how these regions participate with or without touch feeling. The study provides knowledge of the neural processes for motor imagery by including cognitive control implications, making these findings useful for rehabilitation and brain-machine interface design.

Chapter 2: The touch in action: exploring sensorimotor interactions with motor imagery.

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Abstract

The current research investigates the role of tactile information and its associated neural substrates in controlling the action. We employ a combination of motor and sensory components by asking participants to imagine exerting force with the index finger while either touching or not touching a surface. Assuming action imagination and action performance present similar patterns of activation along the motor system, we applied single-pulse transcranial magnetic stimulation over the primary motor cortex (M1) during action imagination. We observed increased amplitude of motor evoked potentials (MEPs) of the relevant muscle when imagined actions were performed concurrently with tactile stimulation, suggesting a facilitatory effect of touch on the motor system. The motor system activity was scaled based on the different amounts of force required and crucially this effect was specific to the body part involved in the action imagined. An intriguing positive correlation was observed between participants' ratings of their imagery level of vividness and the activation of the motor system, indicating that those participants exhibiting MEPs scaled correctly also had strong visualization abilities, as reflected by their capacity to accurately distinguish between varying levels of force.

Introduction

The sense of touch is traditionally thought to be primarily associated with the perception of an object's fundamental characteristics, such as texture and hardness. Interestingly, however, movement is necessary to obtain this type of information. This is particularly true for hands in the act of manipulating objects (Ryan et al., 2021) where the movements of the hands are categorized according to the shape they form, considering factors such as object size, texture, or the type of action it affords (Gibson 1979; Lederman and Klatzky 1987; Cesari and Newell 1999, 2000a, 2000b, 2002; Newell and Cesari 1999; Todorov 2004). When the touch is considered in action, it is typically referred to as "active touch" or "haptic touch" (Klatzky and Lederman, 2011). Haptic touch information travels from the periphery, through afferent fibers, passing from the thalamus to the primary sensory cortex (S1) see review (Delhaye B.P et al., 2016), and like for S1, the primary motor cortex (M1) receives inputs from fingers mechanoreceptors, (Asanuma and Rosén 1972; Kwan et al., 1978; Lemon 1981). Both the primary sensory cortex (S1) and the primary motor cortex (M1) are densely connected to each other (Arce-McShane et al., 2016; Guo et al., 2018; Suresh et al., 2020; Umeda et al., 2019) and reciprocal neuronal interaction between S1 in M1 during haptic behaviors have been extensively documented across a wide range of non-human species (e.g., Hoffer et al., 2003; Ferezou et al., 2007; Zagha et al., 2013), and in humans (Hatsopoulos and Suminski, 2011a; Sobinov and Bensmaia, 2021). Examples in humans include S1 neurons interactions with the cutaneous receptive fields that are sensitive to movement direction during reaching (Baron-Cohen et al., 1994; Prud'homme and Kalaska 1994), along with specialized cells (corticomotor, CM) that present a firing rate associated with force production when a surface is touched (Maier et al., 1993). Moreover, neurons in the S1 cortex were classified to be motion-related, and to affect force direction (Warren et al., 1986; Fortier-Poisson et al., 2015), while texture scanning has been shown to be encoded by neurons in M1 (Jiang et al., 2018). Recently, Davis and colleagues (Davis et al., 2022) identified two distinct neuronal circuits for S1-M1 interactions one for precision and one for power grip. The functional connectivity between S1 and M1 appears to be organized in a somatotopic fashion, such that

S1 neurons with projected fields in one region, preferentially activate M1 neurons that are implicated in moving that hand region (Shelchkova et al., 2022).

Although some of the neural circuits that mediate sensorimotor interactions have been identified, there are still several aspects to be uncovered (Sobinov and Bensmaia, 2021). For example, for maintaining a stable grasp while manipulating objects, a correct fine-tuning of the grip forces is necessary. In turn, in order to grade the applied forces, access to tactile information about surface properties is necessary (Johansson and Flanagan, 2009). Indeed, patients which have lost the sense of touch, are unable to adequately control grip forces, let objects drop, or exert unnecessary high forces (Augurelle et al., 2003; Johansson and Flanagan 2009; Sobinov and Bensmaia 2021). However, how forces produced through hand actions are encoded in the sensory-motor system remains to be established.

One way to disentangle the role of perception from the action at the neuronal level is to ask individuals to imagine performing an action (without any apparent actual motion) while receiving perceptual information as for instance touching or not a surface. Indeed, despite the lack of understanding of the exact mechanisms, imagined movements appear to follow the same temporal features and physiological and pathophysiological constraints as executed movements (e.g. Angela et al., 1996; Ridderinkhof & Brass, 2015). Studies indicate similarity of the rules governing action, action observation, and imagination since the three processes share large neuronal substrates (Roland et al., 1980; Decety et al., 1991, 1994; Kiers et al., 1997; Lotze et al., 1999; Gerardin et al., 2000; Stippich et al., 2002; Calvo-Merino et al., 2005; Buccino et al., 2013). Moreover, movements imagined may share the same characteristics (e.g., kinematic properties) as the corresponding movements performed in daily life (Jeannerod, 1994).

Single-pulse transcranial magnetic stimulation investigations, assessing changes in cortico-spinal excitability, provide a valuable measure of motor activation during motor imagery. This experimental approach makes it possible to activate the primary motor cortex (M1) for then analyze the generated MEPs during motor imagery. MEPs amplitudes can then be used to fine-tune the excitatory/inhibitory influences on Cortical Spinal Excitability (CSE) during

motor imagery (Bruno et al., 2018; Luciano et al., 1999). According to studies using transcranial magnetic stimulation (TMS), the motor system is facilitated in a muscle-specific manner when we imagine doing specific motor tasks (Fadiga et al., 1995; Brighina et al., 2000; Strafella & Paus, 2000; Aziz-Zadeh et al., 2002; Maeda et al., 2002; Gangitano et al., 2004, 2006; Romani et al., 2005; Pizzolato et al. 2012), with the facilitation related to the amount of force imaged (Mizuguchi et al., 2013).

In a series of studies, Mizuguchi and colleagues (Mizuguchi et al., 2009, 2011) investigated whether corticospinal excitability during action imagination involving an external object was influenced by actually touching that object. The corticospinal excitability during action imagination is enhanced with the real touch of the object involved in the action. Because no modulation of touch was found to the responsiveness of the afferent pathway from the skin to the primary motor cortex, they concluded that the enhancement of MEPs was caused by a modulation along the corticospinal pathway including the primary motor cortex. In addition, they showed no tactile effect when the posture kept during imagination was not congruent with the posture imagined (e.g., keeping a flat palm while imagining squeezing a ball) suggesting that touching an object affects the corticospinal excitability as a final combination of tactile and proprioceptive information (Mizuguchi et al., 2011).

When the size of an object was manipulated, the excitability of the motor system during action imagination is influenced by the size of the object and resonates in a muscular-specific manner (Cesari et al., 2011). Specifically, Cesari and colleagues (2011) found that when imagining grasping small objects, the first dorsal interosseus (FDI) was more active than the abductor digiti minimi (ADM) and the flexor digitorum superficialis (FDS), indicating a specific pattern for a precision grip while the opposite happened for big objects. These findings support the somatotopic organization of S1 projections to M1, suggesting that the effect of touching could be better localized at a muscle-specific level (Bufalari et al., 2010; Cesari et al., 2012).

Within this framework, we will ask whether the individual's motor system during imagination resonates in a muscle-specific manner for task parameters like force production imagination when different tactile stimuli were administrated (Kilteni et al., 2018; Cesari et al., 2011). The main idea is to consider whether M1 is differently modulated when individuals imagine producing force with their index finger by having their hands passively in contact or not with a rigid surface. The posture kept during a force production imagination task consists in placing the digits on the surface in the same way in which one would hold a computer mouse for then press it to maintain a congruency between the actual posture and the one imagined. We applied single-pulse TMS while subjects imagined ~15N force production and ~1N of force production when a passive touch was provided beneath their digits and when it was not. Two hand muscles have been the main focus: First Dorsal Interosseous (FDI), the muscle related to the index finger the digit involved in the force imagination, and the Abductor Digiti Minimi (ADM) the muscle related to the little finger considered a control condition (Jong et al., 2009; Pizzolato et al., 2012). To avoid the postural effects on motor imagery reported in a previous study where they found greater MEPs in compatible hand position and the opposite impact in incompatible one, we maintain the same hand posture across the different experimental conditions (Vargas al., 2004; Mizuguchi et al., 2011).

This design allowed us to investigate different issues: (i) whether the sense of touch per se increases the motor system excitability during action imagination, by showing the increase in MEPs amplitudes when individuals touch a surface compared to when no surface is touched; (ii) whether the increment of the motor system excitability due to touch is particularly for the muscle involved in the force imagination compared to the muscle not involved in the force imagination; (iii) whether the motor system shows more activation when the task is to produce ~15N of force imagination as compared to the ~1N of force imagination and particularly when the touch is involved; (iv) and finally, to ascertain whether the same pattern of the motor system activation is present by comparing the action imagined with the same action but executed.

Material and Methods

Participants:

The study included twenty-three healthy volunteers, 11 men, and 12 women, ranging in age from 20 to 40 years (mean age = 24.5 years, SD= 5.26 years). All individuals had normal or corrected-to-normal eyesight and were right-handed. None of the volunteers were aware of the goal of the experiment, and none of them had any neurological, psychiatric, or other medical issues, nor did they experience any TMS adverse effects (Rossi et al., 2021). During TMS, there were no reports or observations of any discomfort or negative effects. Participants signed a written informed consent form before entering the lab. The procedures were in accordance with the ethical principles of the 1964 Declaration of Helsinki and approved by the local ethics committee (n.28.R1/2021).

Neurophysiological measurement with transcranial magnetic stimulation:

A figure-of-eight coil (outer diameter of each wing 110 mm) was used to apply a biphasic single TMS pulse (STM 9000 magnetic stimulator, Ates-EBNeuro, Italy). The coil was placed on an extended arm and located on the left side of the skull, at a 45° angle to the sagittal axis, tangentially to the skull (Brasil et al., 1992). Moving the coil in small steps laterally to the vertex in the left hemisphere and then administering TMS pulses at constant intensity until stable MEP amplitudes are evoked in the relaxed FDI (Jong et al., 2009). The resting motor threshold (rMT) was defined as the lowest stimulus intensity able to evoke MEPs with an amplitude of at least 50 μV in at least five out of ten trials in the muscles. This measure is used to determine the FDI optimum scalp location. During the experiment, the intensity of stimulation was set at 120% rMT (Hallett, 2000).To reassure the location of the same optimal scalp position during the entire experiment, a Neuronavigator (Softaxic Optic, Polaris Vicra Position sensor, Canada) was used.

Electromyographic (EMG) responses were recorded using a wireless system (Zerowire, Aurion, Italy) with two surface electrodes positioned on two muscles of the right hand: the first dorsal interosseous (FDI), and the abductor digiti minimi (ADM). EMG signals were online band-pass filtered (20 Hz- 2.5 kHz; plus 50 Hz notch, D360, Digitimer, UK), amplified at a gain of 1000 (Digitimer), digitized at 5 kHz with laboratory interface (Cambridge Electronic Design 1401, UK) recorded by Spike 2 (version 6, Cambridge Electronic Design), and then analyzed off-line. A customized Matlab script was used for this experiment, which programmed and executed the conditions of forces in a randomized block design for each participant. Both instructions and data processing were carried out using Matlab 2021b (MathWorks, MA, USA).

Procedure:

The task for the subjects was to imagine producing forces with the index digit of the right hand on a rigid surface. Subjects were invited to sit on a chair while keeping their right arm laying on the armrest. The hand was hanging from the wrist in the same position during the entire experiment, and in some conditions, the digits were touching a surface while in others there was no touch (figure 1a).

The ~15N force production imagination, and the ~1N force production imagination along with the touch (T) and no touch (NT) conditions were counterbalanced among subjects. The amount of forces selected referred to previous studies (Jeka, 1997; Papetti et al., 2017). Fifteen trials of TMS stimulation were delivered while touching a surface and 15 trials with no touch of the digits on a surface. By considering 30 trials for the ~1N force production imagination task (15 with touch and 15 without touch) and 30 trials for ~15N force imagination (15 with touch and 15 no touch), in total 60 trials were recorded from each participant (figure 1b).

Before the beginning of the imagination task, a training session was given. Participants were asked to practice producing a certain amount of force on a scale, by using the tip of their index finger. During the training, participants were asked

to retain the force production sensation as much as possible in order to be able to reproduce it in their imagination during the experimental trials. Then the subject was invited to be seated on the chair and asked to relax their arm at the side of the chair with their head facing forwards.
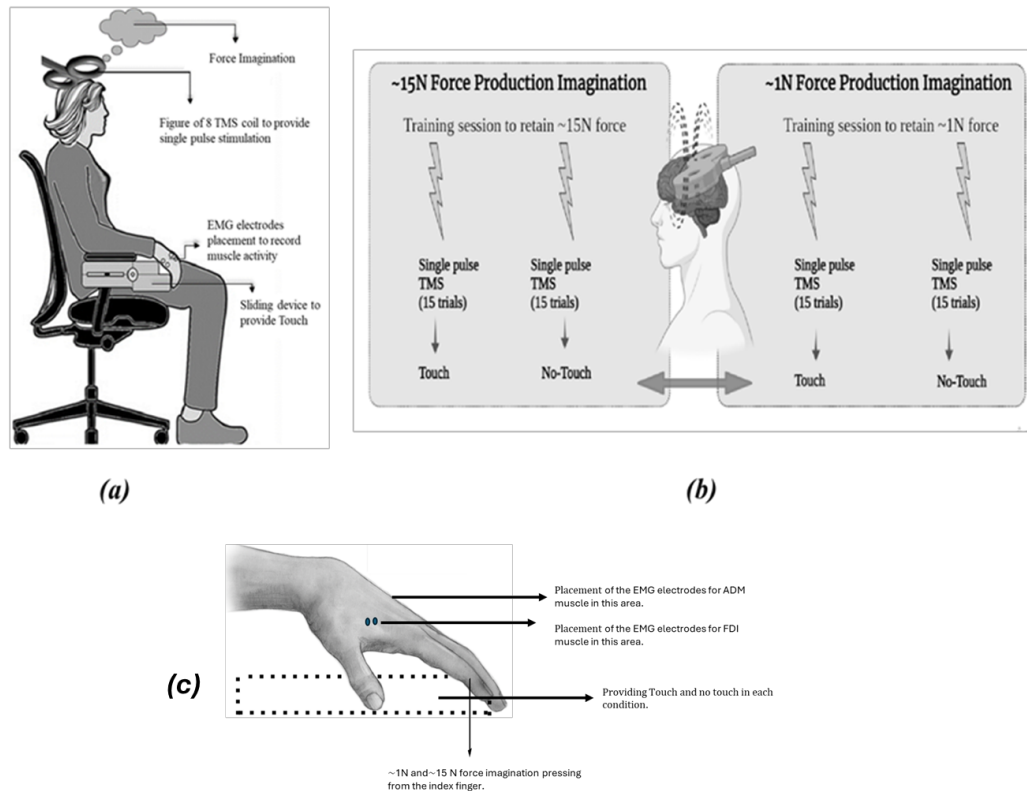
Figure 1a) Schematic illustration of the test situation and recording equipment; b) experimental design. MEPs were recorded while doing imagery tasks of ~1N and ~15 N force imagination by index finger while having touch and without any touch beneath (c) detailed illustration of the hand posture.

As mentioned before, the experimental task requires participants to imagine producing force with their index finger on a rigid surface. The amount of force produced to imagine with their eyes open was the same as the one they practiced during the training session. By keeping the same hand posture forces were imagined in two conditions: one digit was in touch with a surface, while in the other one, the digits had no touch. During the training session, subjects were guided to learn the timing of the task by following a registered voice that was

indicating three phases of the movement: the instant of action initiation, the time duration of force pressure, and the instant of force release. As soon as the participant became familiar with the timing of the task, the registered voice indicated for each trial just action initiation and action end.

During the whole experiment, subjects received no information concerning their performance. Fatigue was never an issue and rest was allowed every 30 trials. In each trial, a single TMS pulse was delivered. The TMS pulse could occur randomly, within the time window of 300, 450, 600, 750,1000 ms after the last vocal instruction, considering the instant of force initiation and the instant of force releases. The interval between two consecutive trials was approximately 5-10 s in order to avoid brain activity summation from one TMS pulse to the next (Wassermann et al., 2008). The entire experiment for each subject lasted for about 50 min. At the end of the experiment, participants were asked to use the questionnaire to test the effectiveness of their imagery after the experiment (Marks, 1973).

Control Experiment

An extra control experiment was conducted by testing 6 participants (2 men, and 4 women), ranging in age from 20 to 30 years (mean age = 25 years, SD= 4 years) from the imagination group, in order to measure the pattern of muscle activation (FDI and ADM) during the actual execution task. They were required to perform the same actions that they had previously imagined with their index finger in two conditions: ~1N Force Production Performance and ~15N Force Production Performance. EMG activity was recorded during action performance from the same muscles used in the imagination task i.e., FDI, and ADM. In this scenario, no TMS pulse was used, and 10 trials were collected in each one of the two conditions, for a total of 20 trials, from each subject.

Data analysis

EMG data were bandpass filtered (5Hz to 450Hz) and full wave rectified. The root means square (RMS) values of the background EMG in the [-105 -5] ms

window just before the TMS were calculated. Trials with background EMG activity greater than 15 µV were eliminated from the analysis (4.13% of the data). The peak-to-peak amplitude of MEPs (µV) was computed over the window [-10 100] ms and averaged for each experimental condition.

We analyzed the effect of touch, the amount of force, and the type of muscle on MEP amplitude using mixed-effect multiple regression modeling. Mixed-effect multiple regression models offer several advantages over conventional regression such as that they do not assume independence among observations, the ability to give unbiased results in the presence of missing data, the flexible specification of the covariance structure among repeated measures, the generalization for non-normal data, and finally, the greater power (Gelman and Hill 2006; Yu et al., 2022).

The model included three fixed effects and their interaction: touch (two levels: touch, no-touch), force (two levels: ~1 Newton, ~15 Newton), and muscle (two levels: FDI, ADM). In addition, because we were especially interested in considering the potential large interindividual variability in the motor imagery ability, the random structure of the model included by-subject random intercepts and by-subject random slopes for the factor force. Because data were not normally distributed but rather right-skewed, we applied a multiple regression model with Gaussian variance distribution and a logarithmic link function. To assess the significance of the main effects and interactions, we performed a Type III test, comparing a model in which only the corresponding effect is missing with the model containing the effect. The p-values were calculated via the likelihood ratio tests. P-values for multiple comparisons were corrected using the Benjamini-Hochberg procedure (Benjamini and Hochberg, 1995).
In addition, we assessed whether there was an association between the individual performance as predicted from the model and the vividness score obtained from the Vividness of Visual Imagery Questionnaire (Open and Close Eyes vividness score). As an operational measure of individual performance, we used the random effects of force, expecting that individuals with good visualization (imagery) ability would exhibit a larger effect of force, that is larger differences between the

~15N condition and the ~1N condition. From a technical point of view, random effects of force are the conditional modes of the distribution of the random effects (i.e., by-subject random intercepts and by-subject random slopes for the factor force) extracted from the model (Kliegl et al., 2011). More generally, conditional modes can be conceived as the difference between the population-level average predicted response for the given set of fixed-effect (i.e., touch, force, and muscle) values and the response predicted for a particular individual, in this case, for the effect of force.

Statistical analysis was performed using the lme4 package (Bates et al., 2015), afex package (Singmann et al., 2022), and emmeans package (Lenth, 2022) in the R environment (Team., 2022)

Results

The entire dataset was considered for analysis. We investigated the effect of touch, force, and muscle type (FDI and ADM) on MEP amplitude. The model includes touch (two levels: touch, no-touch), force (two levels: ~1 Newton, ~15 Newton), and muscle as three fixed effects and their interaction (two levels: FDI, ADM).

The effect of the touch was significant χ^2 (1, N =22) =16.28, p<.001, indicating that, overall, the MEP amplitude was higher in the touch condition compared to the no-touch condition (M=1.41, SD=1.35, and M=1.19, SD=1.12, respectively). The effect of the force approached significance χ^2 (1, N =22) =4.01, p=.05, indicating that the MEP amplitude was somewhat higher in the ~15N condition compared to the ~1N condition (M=1.41, SD=1.32, and M=1.19, SD=1.15, respectively). The effect of the muscle was significant χ^2 (1, N =22) =1848.88, p<.001, indicating that the MEP amplitude was higher for FDI compared to ADM (M=1.82, SD=1.12, and M=0.78, SD=0.88, respectively). The two-way interaction touch by force was significant χ^2 (1, N =22) =4.96, p=.03, indicating that, independently from the effect of muscle, the effect of touch was significant for the ~1N condition only. The two-way interaction of touch by muscle was significant χ^2 (1, N =22) =9.16, p=.002, indicating that,

independently from the effect of force, the effect of touch was significant for FDI only. However, the three-way interaction of touch by force by muscle was significant χ^2 (1, N =22)=4.30,p=.04, indicating that the effect of touch (i.e., higher MEP amplitude in the touch condition compared to the no-touch condition) was significant for FDI, for both the ~15N condition (touch: M=2.17, SD=0.98, and no-touch: M=1.78, SD=0.79, p<.001), and the ~1N condition (touch: M=1.82, SD=0.82, and no-touch: M=1.51, SD=0.67, p<.001), while for ADM, it was not significant for the ~15N condition (touch: M=0.86, SD=0.73, and no-touch: M = 0.83, SD = 0.66, p = .19) but it approaches significance for the ~1N condition (touch: M=0.78, SD=0.65, and no-touch: M=0.63, SD=0.63, p=.05). (See figure 2)

Correlation

Results of the Pearson correlation indicated that there was a significant negative association between the predicted individual performance for the force effect and the Vividness score, r (20) = -.58, p=.005, indicating that higher individual effects of force on MEP amplitude (i.e., individuals with larger positive differences between ~15N and ~1N) were correlated with good visualization ability (i.e., individuals with low scores in the Vividness of Visual Imagery Questionnaire).
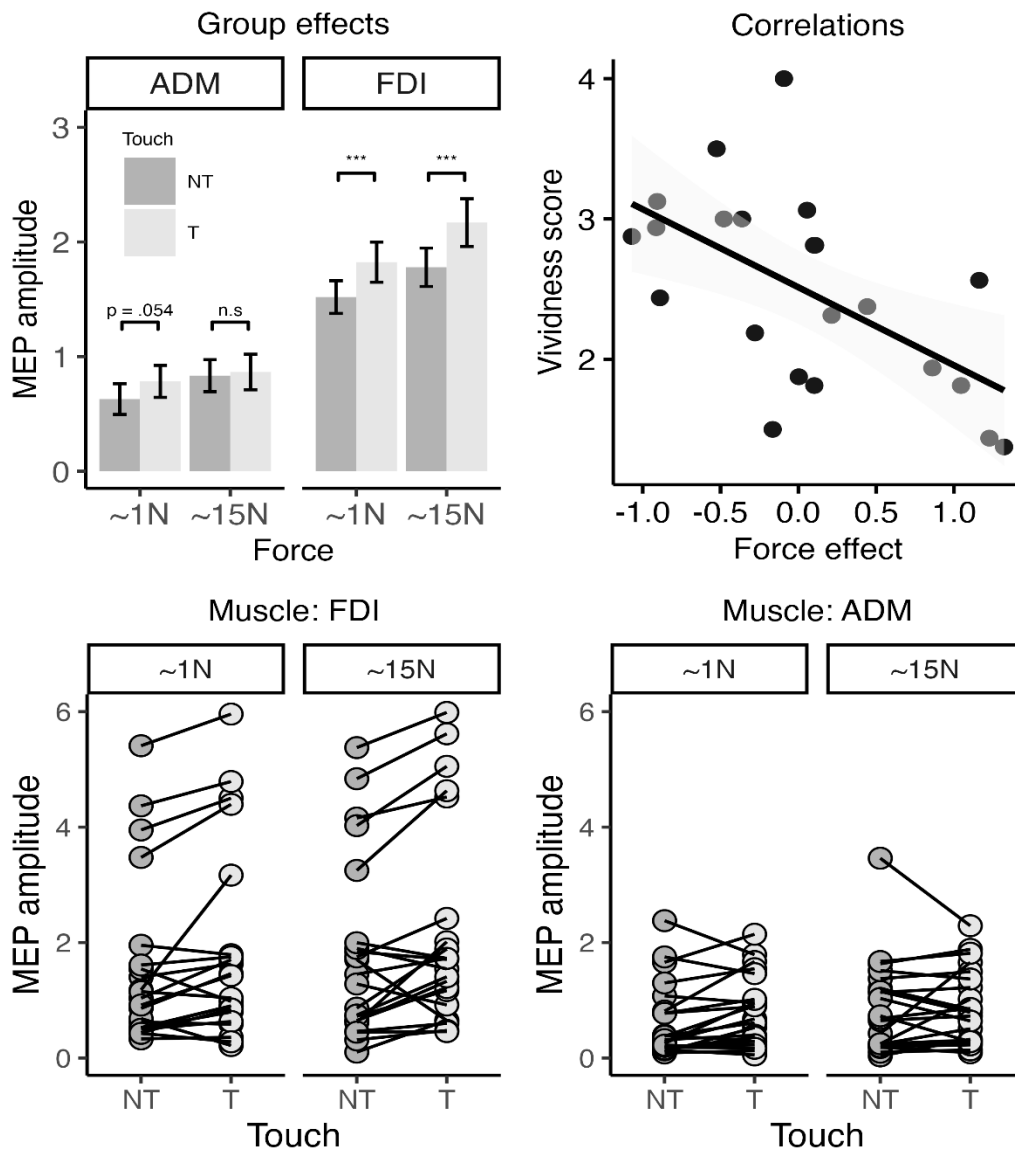
Figure 2 Upper left panel: Bar plot showing the group effects ∗∗∗P<0.001. Error bars represent the standard error of the means adjusted to correctly reflect the variance in the within-subject design (Morey, 2008). Upper right panel: Correlation between the Vividness questionnaire score and the model predictions for the force effect. Lower panel: Paired observations. The two muscles: FDI and ADM.

Control experiment

The effect of force was significant χ^2 (1, *N* =6) =16.16, p <.001, indicating that the EMG amplitude was larger for the ~15N condition compared to the ~1N condition (M=16.47, SD=20.14, and M=4.62, SD=8.93, respectively). The effect of muscle was significant χ^2 (1, *N* =6) =28.97, p<.001, indicating that the EMG amplitude was larger for FDI compared to ADM (M=14.48, SD=22.14,

and M=6.61, SD=8.99, respectively). The two-way interaction force by muscle was significant χ^2 (1, N =6) =17.76, p<.001, indicating that the effect of force was larger for FDI (~15N: M=23.45, SD=19.78, ~1N: M=5.51, SD=8.38) compared to ADM (~15N: M=9.49, SD=6.91, ~1N: M=3.73, SD=6.64).

Discussion

The aim of the study was to investigate the neuronal underpinnings underlying the influence of tactile information in the control of action that requires force scaling. Participants were imaged to produce with the index finger different amounts of force (~1N and ~15N) while touching or not a rigid surface. In order to measure the motor system excitability during action imagination we applied a single-pulse TMS paradigm and quantified the related MEPs amplitude (Farzan, 2014).

In accordance with our hypothesis, we found higher MEPs amplitudes during action imagination with surface contact compared to when it is not. The first dorsal interossei (FDI) muscle, which is involved in the action imagined, exhibited the highest MEPs, suggesting a muscle-specific effect of contact. We also confirmed the presence of greater MEPs when participants were asked to imagine producing ~15N of force as compared to ~1N of force, and again this effect was particularly pronounced while touching a surface. Finally, we confirmed a similar pattern of muscle activity by comparing the imagined action with the same execution. Following we discuss the results in detail.

We opted to employ action imagination, rather than action performance, to avoid the confounding factor that might affect our understanding about the specific role played by the sensory component (the actual touch of a surface) when combined with the motor component (the actual force) by assuming that an action imagined is considered as a reliable "mirroring schema" of the same action when it is performed. This idea is well supported by previous results indicating that action performance and action imagination share the same pattern of activation along the motor system (Kasai et al., 1997; Fadiga et al., 1999; Hashimoto & Rothwell, 1999; Li et al., 2004). In one study, Mizuguchi and

colleagues found that the scaling of applied forces was similar in both action and imagination (Mizuguchi et al., 2013). Additionally, another study showed that the absolute values of motor system activation differ when forces are imagined compared to when they are physically produced (Cesari et al., 2011).

The results of this study supported the hypothesis by demonstrating a larger MEP amplitude for higher force imagination as compared to the lower force imagination and the rate of increment was higher when the imagination was performed by having the digits in contact with the surface. The functional role of M1 neurons activated by cutaneous input has been already shown by Picard and Smith (Picard and Smith, 1992) when they observed changes in the motor neurons' activity as a function of force production in monkeys that grasped and lifted objects presenting different textures and weights. In particular, they observed that monkeys were properly scaling their forces based on the object's weight but more importantly, presented higher discharge of neurons activity for the objects with a rough surface. The lack of possibility to disentangle the neuronal activity between the force production and the type of texture touched during grasping maintained unsolved the problem of to what extent M1 neurons encoded just the details of tactile stimuli. Here by using action imagination we were able to eliminate this confounding factor and direct the attention toward the amount of the central motor commands sent in a feedforward manner from M1 to the periphery for producing different levels of force (Cesari et al., 2011). This was achieved by separating the two experimental conditions, with and without tactile input.

According to previous studies, tactile stimulation causes higher activation when using objects. Participants imagined squeezing a ball while passively holding or not the ball, resulting in increased MEP amplitude when the ball was passively held compared to the condition where no actual touch was allowed (Mizuguchi et al., 2009, 2011). Similarly, we observed higher MEPs for the combined action imagination and actual surface touch condition but without the involvement of an object. Instead, our task required the involvement of a single digit in producing different amounts of force. The results showed that M1

activation was related to the amount of force imagined, with larger MEP amplitude during the ~15N force production imagination compared to the ~1N force production imagination. This scaling effect is consistent with findings from earlier research, considering different imagery tasks, such as grasping different objects' sizes and shapes and performing different movement directions and amplitudes. (Bufalari et al., 2010; Cesari et al., 2011; Pizzolato et al., 2012, Mizuguchi et al, 2013).

Crucially, we observed that the magnitude of forces produced in the motor system was restricted to the body part (i.e., FDI muscle) which would be involved in the execution of the action. Indeed, M1 was selectively more active for the FDI muscle when the digits were in touch with a surface and significantly less active when the same force was imagined by having the digit, not in contact with the surface. On the contrary, for the digit not involved in the imagination of force production, i.e., the little finger (related to the muscle ADM), a barely significant difference in activation was present by having the digit in contact or not with the surface and just for the light force (~1N). Imagining a force of ~1N was more challenging than imagining a force of ~15N due to its smaller magnitude. As speculation, we may suggest that ADM could be inhibited to keep the light touch correctly, but further investigations are necessary. The novelty of our study lies in its task, which requires imagining the action with one digit. This allows us to compare the effect of the combination of tactile input and force production on both the muscle that is specifically involved in the action and the muscle that is not involved. To the best of our knowledge, our study presents the first experimental evidence that passive tactile stimulation selectively increases the excitability of the motor system for the muscle which would be involved in an action,

In the control experiment, we measured the muscle activation during the actual execution of the same task. After giving the training session, subjects were asked to produce force (~15N vs ~1N) while maintaining touch with their digits. The results showed the same pattern of activation that we found in the imagery task with a larger effect of force for FDI compared to ADM, this outcome

supports the idea that, despite being conducted mentally, the imagined action has been shown to activate brain areas that are involved in the actual movement. (Grèzes and Decety 2002; Hanakawa et al., 2003).

Remarkably, participants presenting tasks related to MEP's modulation presented better visualization skills. In particular, we found that individuals presenting proper motor system modulation with higher MEPs when imagining producing ~15N force and lower MEPs when imagining producing ~1N force were the best in imagery ability measured via the "Vividness of visual imagery questionnaire" (Marks, 1973). This result provides new evidence that the activation of the motor system is influenced by the ability to generate vivid images via motor imagery (Fourkas et al., 2006; Guillot et al., 2008; Williams et al., 2012).

In conclusion, we reported evidence of an increment of the motor system excitability in the presence of touch (Mizuguchi et al., 2009, 2011), and we added the notion that this excitability is muscle specific in the sensorimotor relationship between touch and action: the muscle involved in the imagined action i.e., FDI as the mobilizer of the index digit, presented a specific and related modulation in the motor system activity when compared with the other muscle i.e., ADM as a mobilizer of the little digit, even if the sensory component, tactile input, was present for both digits.

We think that the present topic is of great interest for what concerns new applications in user interface design, gaming and entertainment, education, and art but even more relevant for suggesting the possibility to develop a brain-machine interface to compensate for severely damaged sensory-motor functions (Hatsopoulos et al., 2005; Velliste et al., 2008; Ethier et al., 2012; Kumari et al., 2020). It would be possible to register signal from the motor cortex to control an external device or to stimulate the paralyzed muscles that can be reanimated after a spinal cord injury via electrical stimulation since M1 represents either intention to move via a feedforward mechanism as well as feedback mechanisms reflecting the sensory inputs (Ganzer et al., 2020). In this sense, the decoding from the cortical neurons of the details of the sensory inputs becomes relevant information.

Similarly, this result could have a positive impact in the field of virtual reality and increase the knowledge of the human-machine interface relevant to physiotherapy interventions as well as recreational and working situations.

Chapter 3: Neural underpinnings of the interplay between actual touch and action imagination in social contexts

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Abstract

While there is established evidence supporting the involvement of the sense of touch in various actions, the neural underpinnings of touch and action interplay in a social context remain poorly understood. To prospectively investigate this phenomenon and offer further insights, we employed a combination of motor and sensory components by asking participants to imagine exerting force with the index finger while experiencing their own touch, the touch of one another individual, the touch of a surface, and no touch. Based on the assumption that the patterns of activation in the motor system are similar when action is imagined or actually performed, we proceeded to apply a single-pulse transcranial magnetic stimulation over the primary motor cortex (M1) while participants engaged in the act of imagination. Touch experience was associated with higher M1 excitability in the presence and in the absence of force production imagination, but only during force production imagination M1 excitability differed among the types of touch: both biological sources, the self-touch and the touch of one other individual, elicited a significant increase in motor system activity when compared to touching a non-living surface or in the absence of touch. A strong correlation between individual touch avoidance questionnaire values and facilitation in the motor system was present while touching another person, indicating a social aspect for touch in action.

The present study unveils the motor system correlates when the sensory/motor components of touch are considered in social contexts.

Introduction

The influence of physical touch permeates our entire life by deeply influencing how we act. Through touch, we acquire information about the surface's physical components like hardness, roughness, softness, and temperature. By engaging in tactile experiences, we regulate the amount of pressure exerted while grasping objects. Self-touch and touching other individuals allow the processing of information about the self and the body (Martin, 1993). The experience of touch encompasses a complex interplay of cognitive and emotional factors, and pre-existing knowledge and expectations shape the individual's perception leading to the emergence of personal traits (Bensmaia and Hollins, 2003; Haans and IJsselsteijn, 2006; Jones, 2016).

Touch can be passively sensed or actively perceived through action. While passive touch relies on the activation of cutaneous receptors, active touch receives additional input from the kinesthetic and proprioceptive senses, resulting in a different pattern of brain activation (e.g., Simões-Franklin et al., 2011). Since the seminal work of Gibson (Gibson, 1962; West and Gibson, 1969) much effort has been put into distinguishing the effects that those different exploratory procedures exert on object perception (Sonneveld and Schifferstein, 2008; Smith and Collins, 2009; Simões-Franklin et al., 2011; Ackerley et al., 2012; Fernandes and Albuquerque, 2012). The basic ability to discriminate different textures appears substantially equivalent in passive and active touch (Lederman, 1981; Heller, 1989; Verrillo et al., 1999). However, during active touch, specialized exploratory movements, and adjustment of movement parameters such as force, displacement, and related derivatives, allow to optimize perceptual precision (Lederman and Klatzky, 1987a; Chapman, 1994; Srinivasan and LaMotte, 1995; Louw et al., 2000; Gamzu and Ahissar, 2001; Giachritsis et al., 2009; Kaim and Drewing, 2011; Drewing, 2012; Lezkan and Drewing, 2014; Metzger et al., 2018). In addition, more and more attention is devoted to the fact that to generate the appropriate percept, the afferent signal provided by the sensory receptors is integrated with the

predictions of the sensory consequences of one's own actions (generated as a consequence of the motor command, i.e., internal forward model or efference copy). In this way, not only the brain may extract the tactile signal more efficiently (Willemet et al., 2021), but the information about the perceptual context that is provided by the internal model can be critical to solving more complex tasks such as ambiguous shapes discrimination (Verrillo et al., 1999; Smith et al., 2009).

The tight functional coupling between touch and action is supported by strong neural interconnections between the somatic and the motor systems. After the initial processing within the primary somatosensory cortex (S1), tactile information travels through the secondary somatosensory cortex (S2), the posterior parietal cortex (PPC), and the primary motor (M1) cortex, (see review Delhaye et al., 2016). The primary motor cortex (M1) and primary somatosensory cortex (S1) are directly interconnected (Haegens et al., 2011; Ifft et al., 2013; Schwarz et al., 2014; Umeda et al., 2019). M1 and S1 work together to integrate tactile and proprioceptive feedback for skilled movements of the hand (Salimi et al., 1999; Gardner et al., 2007). Indeed, when the action of grasping is performed, a significant proportion of S1 neurons discharge in response (Sinclair and Burton, 1991), and some S1 neurons are sensitive to force direction (Fortier-Poisson and Smith, 2015; Fortier-Poisson et al., 2015). On the other hand, surface texture can be encoded by neurons in M1(Jiang et al., 2018).

An experimental approach aimed to differentiate the neural mechanisms underlying perception from those involved in the action is applying motor imagery. Participants imagine performing an action while receiving sensory input, without physically executing any movement. The prevailing theoretical framework assumes that imagined actions are an internal simulation of actual movements (Jeannerod, 1994; Jeannerod and Decety, 1995) and that the cognitive mechanisms involved in action generation, perception, and imagination share a common network (Prinz, 1997; Hommel, 2009; Cesari et al., 2011). Even though the mechanisms behind imagined movements are still not fully comprehended, empirical findings indicate that these mental representations exhibit physiological and temporal patterns that resemble those of actual movements (Bufalari et al., 2010). Moreover, pathophysiological

constraints seem to similarly affect both imagined and executed movements (Sirigu et al., 1996; Ridderinkhof and Brass, 2015).

Based on this method, few studies have examined the role of tactile information in controlling action (Mizuguchi et al., 2009, 2011; Ali et al., 2023), The corticospinal excitability of M1 during action imagination is enhanced by the real touch of the object involved in the action compared to the condition in which no touch is present (Mizuguchi et al., 2009, 2011), suggesting a facilitatory effect of touch on the motor system. Recently, we demonstrated that this excitability is muscle-specific (Ali et al., 2023). In our previous study, participants imagined producing different amounts of force with the index finger while touching or not a rigid surface. The facilitatory effect of touch scaled properly with the amount of force 'exerted', but crucially, the effect was restricted to the body part that would be involved in the execution of the action. (Ali et al., 2023)

The ability to discriminate physical properties through touch is accompanied by the integration and processing of affective and socially relevant information. Touch received from other individuals, i.e., social touch, is crucial for the development of the individual's social cognition, and then has a profound impact throughout the entire lifespan (Jönsson, 2017; Cascio et al., 2019). Affective touch is mediated by a specialized sub-modality of touch, the c-touch system (McGlone et al., 2014), and tactile stimulation from another person is associated with a distinct pattern of cortical activation compared to self-touch (Boehme et al., 2019; 2022). For example, Boehme and colleagues (Boehme et al., 2019) used fMRI, behavioral testing, and somatosensory-evoked potentials (SEPs) measured at the spinal and cortical levels, to examine the difference between the sensation of touching oneself and the sensation of being touched by another person. Stimulation from another person activated several areas including the somatosensory cortex, insula, superior temporal gyrus, supramarginal gyrus, striatum, amygdala, cerebellum, and prefrontal cortex. In contrast, self-touch was associated with deactivation in the insula, anterior cingulate cortex, superior temporal gyrus, amygdala, parahippocampal gyrus, prefrontal areas, and brain areas encoding low-level sensory representations. Somatosensory Evoked Potentials (SEP) analysis showed

reduced cortical amplitudes during self-touch, and in contrast, shorter latencies for other touch. Crucially, during self-touch, the functional connectivity between the sensorimotor cortex and the insula was accompanied by an elevated threshold for detecting additional tactile stimuli. The discrimination of self- or other-touch would be based on a mechanism of attenuation in which the internal forward model or efference copy allows the brain to predict the sensory consequences of one's own action (see e.g., Boehme et al., 2019; Boehme and Olausson, 2022). Subsequently, the brain can reduce or not these sensations depending on the task at hand (Juravle et al., 2017). However, the neural processes that mediate the attenuation or non-attenuation remain to be understood.

How exactly affective touch can influence action control is relatively unexplored. The amplitude of the readiness potential was modulated by the pleasantness of the stimuli to be grasped (compatible vs. incompatible, de Oliveira et al., 2012), or by the emotional context induced before performing a pleasant action (gently caressing a soft cloth, Campagnoli et al., 2015). The facilitatory effect on the motor cortex induced by the pleasant emotional context before the action, suggests that anticipating the outcomes of an action involves assessing the emotional value of a stimulus one is going to engage with and this is in line with the hypothesis of a general facilitatory effect of touch (Mizuguchi et al., 2009, 2011; Ali et al., 2023). However, because of the relevance of social interaction, and the role of affective touch in social contexts (Dunbar, 2010), it is plausible that the influence of affective touch on action control might be based on a different mechanism.

Based on this framework, the aim of the present study was to clarify the neural mechanisms of the difference between the self and other people's touch while the motor system is activated. Above we have briefly reviewed the thigh coupling between touch and action, and in particular how sensorimotor control and haptic exploration depend on the ability of the touch system to discriminate physical attributes. Much less is known about how affective touch can influence action control. We investigated whether the motor system resonates selectively for a task parameter such as force production imagination when different conditions of tactile stimuli are given (Cesari et al., 2011; Kilteni et al., 2018; Fukumoto et al.,

2021). Specifically, we examined whether the activity of the motor system is differently modulated when an individual imagines producing and not producing force with her/his index finger while having the hand touching different surfaces: Self-Touch (put in contact his/her right with the left hand's index fingertips), We-Touch (when subject receive the touch on his index finger from the index finger's tip of one other person), Surface-Touch (touch a hard surface with his/her index fingertip), and No-Touch (do not have the index fingertip or other parts of the hand in touch with anything). To measure motor cortex activity, a single pulse Transcranial Magnetic Stimulation (TMS) was delivered while participants imagined producing ~3N and not producing force (<~1N) with the index finger of their right hand. As the target muscle, we selected the First Dorsal Interosseous (FDI) which is involved in the flexion-abduction of the index finger, while as the control muscle, the Abductor Digiti Minimi (ADM) since it is involved in the flexion-abduction of the little finger.

Considering the touch condition, we hypothesized that the motor system will show higher cortico-spinal activation when biological sources are touched, i.e., when individuals are either touching themselves and when touching someone else, as compared to when they are touching non-living sources, or not touching at all. However, when social interaction is included, we might expect to find higher cortico-spinal activation when touching someone else compared to the self-touch condition since it has been shown that the processing of social information undergoes distinctive and privileged processing mechanisms (de Oliveira et al., 2012; Souza et al., 2012; Campagnoli et al., 2015; Boehme and Olausson, 2022; Grichtchouk et al., 2022). Alternatively, participants may perceive self-generated tactile stimulation as relatively weaker, when compared to external tactile stimulation (Kilteni et al., 2018). In this case, participants could enhance the level of applied force, resulting in higher Motor Evoked Potentials (MEPs) in the Self-Touch condition. When considering the MEPs modulation based on the level of force imagined, we expected to replicate the results obtained in previous works (Helm et al., 2015; Ali et al., 2023), i.e., higher activation when individuals imagine producing higher force as compared to lower force. Here we asked individuals to imagine producing on the provided surface ~3N of force (from now on referred as

~3N condition), and to imagine the digit lying on the provided surface without imagining force production (from now on referred as <~1N condition). For the interaction between the touch and the force conditions, we were expecting to find a generalized amplified effect of touch during the imagination of force production.

Material and Methods

Participants

The study included twenty healthy volunteers, 10 men, and 10 women, ranging in age from 18 to 26 years (mean age = 21.5 years, SD= 1.71 years). None of the participants were aware of the study's purpose, and none of them had any neurological, psychiatric, or other health conditions. They also didn't experience any negative effects from TMS (Rossi et al., 2021). There were no complaints of pain or adverse effects during TMS, and none were observed. Before entering the lab, each participant signed an informed consent form. The local ethics commission authorized the procedures, which adhered to the ethical standards set forth in the Declaration of Helsinki from 1964.

Equipment

A biphasic single TMS pulse was applied using a figure-of-eight coil; the outside diameter of each wing was 110 mm (STM 9000 magnetic stimulator, Ates-EBNeuro, Italy). The coil was positioned on an extended arm at a 45° angle to the sagittal axis on the left side of the head, tangential to the skull (Brasil-Neto et al., 1992). The coil was moved laterally in small steps to the vertex in the left hemisphere and TMS pulses were given once stable motor evoked potential (MEP) amplitudes were evoked in the relaxed FDI (Jong et al., 2009). The resting motor threshold is the lowest stimulus intensity that can elicit MEPs in the muscles with an amplitude of at least 50 V in at least five out of ten trials (rMT). This measurement was used to identify the best area of the scalp for FDI. Throughout the experiment, the amount of stimulation was set at 120% rMT (Hallett, 2000).

Procedure

The task required to imagine producing or not forces while lying the right hand's index finger on the various surfaces defining the different touch conditions. The subjects were asked to maintain their right arm relaxed on their lap, which was supported by a hard surface while sitting in a chair. Because the compatibility of the hand position could impact the MEP amplitude (Vargas et al., 2004; Casetta et al., 2020), the hand remained in the same position throughout the entire experiment, to ensure a posture compatible with the imaged action. The experiment was recorded in a block based on conditions where each block of four touch conditions contains two levels of force counterbalanced among subjects. The task was to imagine with closed eyes on two levels i.e., $<{\sim}1N$ and ${\sim}3N$ of forces. Fifteen trials of TMS stimulation were delivered for each combination of force condition and the types of touch condition i.e., Self-Touch when the subject receives the touch of one other person (We-Touch), Surface Touch, and without any touch (No-Touch). A total of 120 trials were recorded from each participant.

A training session was conducted prior to the start of the imagination task. Participants were instructed to practice, utilizing the tip of their index fingers, to produce a specific amount of force on the balance scale. During the training session, the experimenter provided guidance to the subjects regarding the timing of the task, including when to initiate the action, the duration of force application, and when to release the force. Once the participants became accustomed to the timing of the task, a recorded voice signaled the start and end of each trial. The participants were instructed to actively remember their experiences of producing force during the training session, with the goal of being able to mentally simulate the same experiences during the experimental trials. Following the training session, participants were instructed to maintain a seated position with their arms at rest and their heads facing forward for the entire duration of the data collection (see Figure 1).
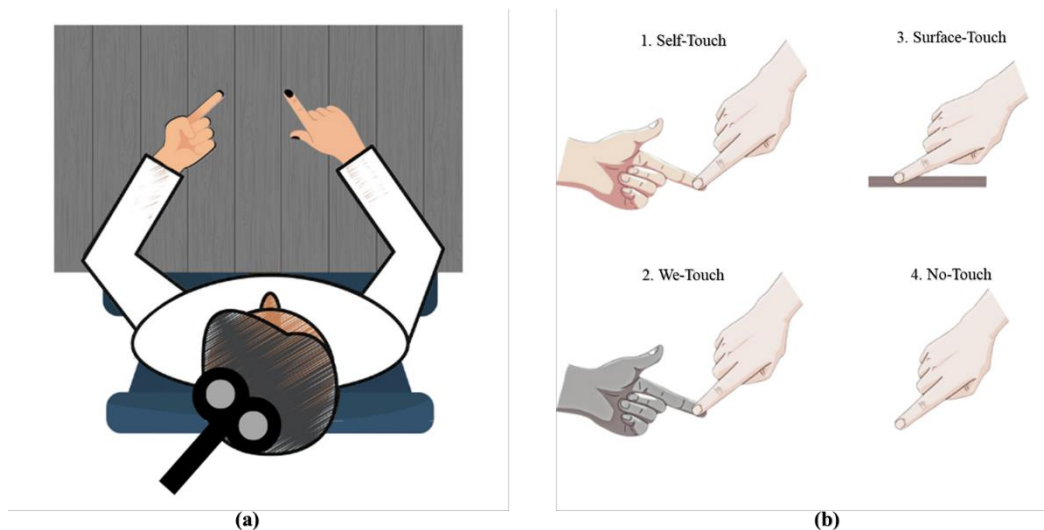
Figure 1 Schematic Illustration of Test Situations (a) Overview; (b) 1. Self-touch - Individual touching own index finger, 2. We touch - Another person touching the participant's index finger, 3. Surface touch - Surface provided beneath participant's index finger, 4. No touch - No touch provided.

As previously mentioned, the experimental task required participants to engage in mental imagery of force production (3N) and no force production (>~1N) using their index fingers. The magnitude of the imagined force was matched to the force levels practiced during the training session. Throughout the entire experiment, participants were not provided with any feedback regarding their performance. Fatigue was carefully monitored, and rest periods were incorporated every 30 trials to mitigate any potential fatigue effects. Each trial involved the delivery of a single transcranial magnetic stimulation (TMS) pulse. To avoid any potential effect associated with expectation, TMS was applied at random delays (selected among intervals of 300, 450, 600, 750, or 1000 ms, balanced across trials) after the vocal instruction. The inter-trial interval, approximately 5-10 seconds, was designed to prevent the accumulation of brain activity from one TMS pulse to the next, following the guidelines proposed by (Wassermann et al., 2008). The entire experimental session for each participant lasted approximately 80 minutes, encompassing multiple trials and TMS pulses. At the end of the experiment, participants were asked to fill out some questionnaires, the Vividness of Visual Imagery Questionnaire (VVIQ) to test the effectiveness of their imagery (Marks, 1973), and the Touch Avoidance measure, and touch Avoidance Questionnaire (Casetta et al., 2020) to assess the relevant personality dimensions.

Data analysis

We employed mixed-effect multiple regression modeling (Gelman and Hill, 2006; Yu et al., 2022) to examine the impact of touch, force, and muscle on MEPs amplitude. The model incorporated three fixed effects (touch, force, and muscle) and their interaction. Touch had four levels (you-touch, me-touch, surface-touch, no-touch), the force had two levels ($<\sim$1 Newton, $\sim$3 Newton), and muscle had two levels (FDI, ADM). The random structure of the model included by-subject random intercepts and by-subject random slopes for the force factor. To account for multiple comparisons, we applied the Bonferroni procedure for p-value correction (Simes, 1986). Observations with standardized residuals exceeding 2.5 standard deviations from zero were excluded (3.90% of the data), following guidelines by (Krajewski and Matthews, 2010).

In addition, we assessed whether there was an association between the individual differences between the Self-Touch and We-Touch conditions (that we refer to as the 'Self-We Touch effect'), and the touch avoidance measure obtained from the two questionnaires. As an operational measure of the 'Self-We Touch effect', we computed the ratio between Self-Touch and We-Touch, in the $\sim$3N force condition for FDI and ADM separately. Statistical analysis was conducted using the lme4 package (Bates et al., 2015), the afex package (Singmann et al., 2022), and the emmeans package (Lenth, 2022) in the R environment (Team., 2022)

Results

Based on the participants' overall VVIQ ratings, which were a 2.16 (SD = 0.7) average score for participants with open eyes and 2.26 (SD = 0.67) for closed eyes condition, all participants were referred to the group of "good visualizers" (Marks, 1973). All participants successfully performed force production imagination (3N) and no force production imagination ($<\sim 1N$) for the 4 levels of touch (Self-Touch, We-Touch, Surface-Touch, No-Touch) by using two muscles i.e., FDI and ADM. None of the participants reported discomfort during the stimulations.

Considering the motor-evoked potentials, the main effect of Force was significant ($F_{(1,18)}$ = 18.97, p < 0.001) indicating that, overall, MEPs were smaller for $<\sim 1N$ (M = 0.78, SD = 0.82) compared to $\sim 3N$ (M = 1.02, SD = 1.01). The main effect of Condition was significant ($F_{(3,4485)}$ = 26.58, p < 0.001), Post hoc comparisons

Figure 2 Bar plot showing the main effect of Touch ***P < 0.001, with n.s. indicating non-significance. Error bars represent the standard error of the means adjusted to correctly reflect the variance in the within-subject design (Morey, 2008).

using Bonferroni correction indicated that, overall, MEPs were larger for both Self-Touch (M = 1.00, SD = 0.83, p < 0.001), and We-Touch (M = 1.00, SD = 0.68, p < 0.001) compared to Surface-Touch (M = 0.83, SD = 0.64), and, for both Self-Touch (p < 0.001) and We-Touch (p < 0.001) compared to No-Touch (M = 0.77, SD = 0.61). MEPs for Self-Touch did not significantly differ from MEPs for We-Touch (p = 1.00), and MEPs for Surface-Touch did not significantly differ from MEPs for No-Touch (p= 0.72). The main effect of Muscle ($F_{(1,4488)}$ = 840.69, p < 0.001) was significant, indicating that,

overall, MEPs were larger for FDI (M = 1.22, SD = 0.80) compared to ADM (M = 0.57, SD = 0.60) (see Figure 2).

The two-way interaction force by muscles was significant ($F_{(1,4490)}$ = 19.18, $p < 0.001$), indicating that, MEPs were smaller for <~1N compared to ~3N for FDI (M=1.03, SD=0.38, M=1.36, SD=0.56, $p <0.001$) and ADM (M=0.5,

Force by muscle interaction
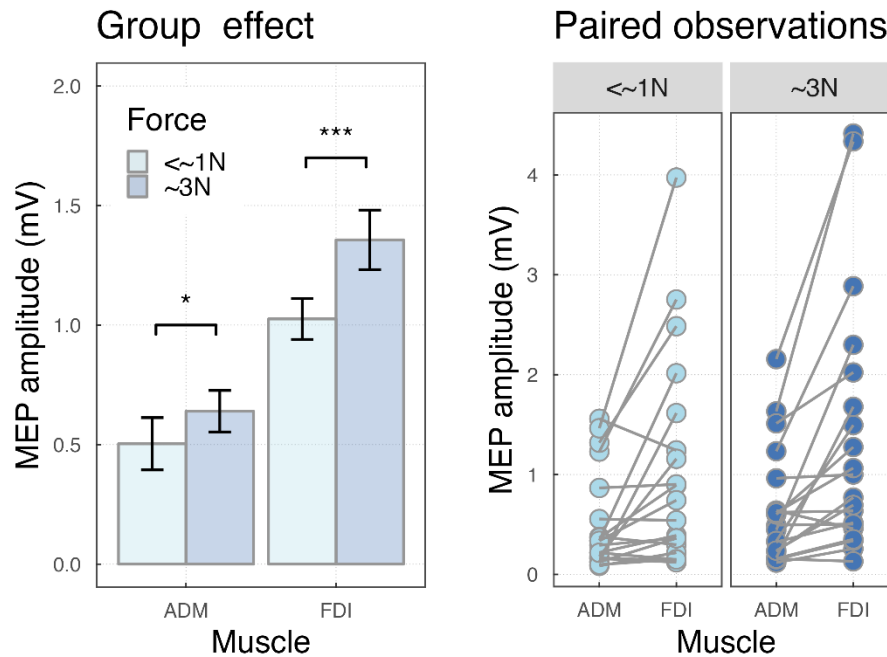
Figure 3 Left side: Bar plot showing the group effects of force by muscle interaction ***P < 0.001. Error bars represent the standard error of the means adjusted to correctly reflect the variance in the within-subject design (Morey, 2008). Right side: Paired observation of two muscles ADM and FDI in forces <~1N and ~3N.

SD=0.49, M=0.64, SD=0.39, $p = 0.03$), but the difference was larger for FDI (see Figure 3).

The two-way interaction of touch by force conditions was significant ($F_{(3,4486)}$ = 5.48, $p < 0.001$), indicating that, independently from the effect of muscle, in the <~1N force condition, MEPs were larger for Self-Touch (M=0.79, SD=0.31, $p = 0.01$), and We-Touch (M=0.78, SD=0.12, $p = 0.02$) compared to No-Touch (M=0.66, SD=0.22). In the ~3N force condition, MEPs were larger for Self-Touch compared to both Surface Touch(M=1.12, SD=0.48, and M=0.87, SD=0.35, p <.001) and No-Touch(M=1.12, SD=0.48, and M=0.84, SD=0.25, $p < .001$), and in the same vein, for We-Touch compared to both Surface Touch (M=1.12, SD=0.32,

and M=0.87, SD=0.35, p <.001) and No-Touch (M=1.12, SD=0.32, and M=0.84, SD=0.254, p < .001) (see Figure 4).

Touch by force interaction
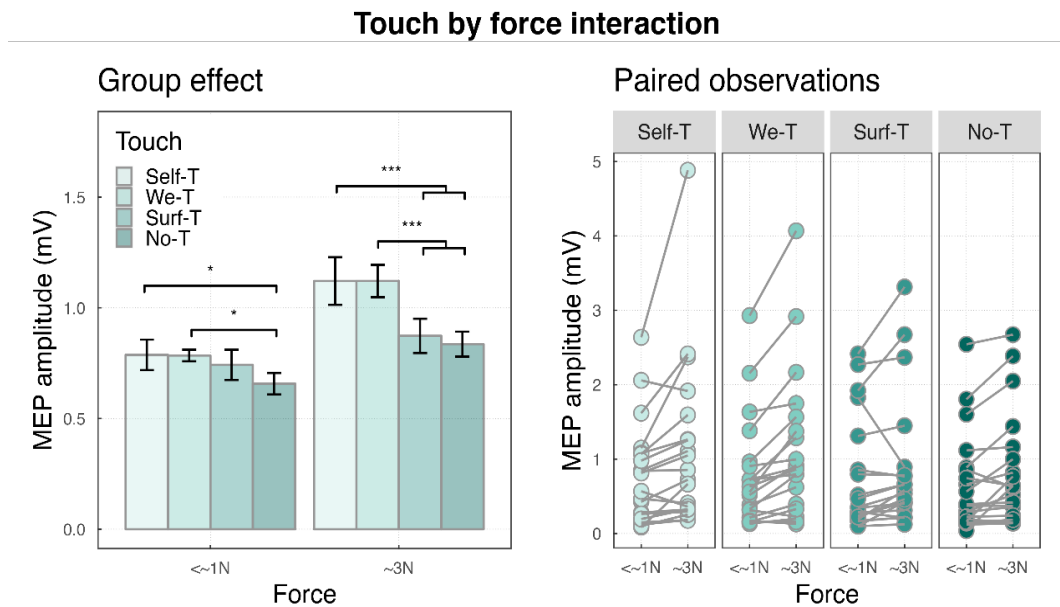
Figure 4 Left side: Bar plot showing the group effects of touch-by-force interaction ∗∗∗P < 0.001. Error bars represent the standard error of the means adjusted to correctly reflect the variance in the within-subject design (Morey, 2008). Right side: Paired observation of two forces, <~1N and ~3N with touch conditions.

The interaction touch by muscle was significant ($F(3,4485) = 21.11$, p <.001), for ADM muscle, MEPs were larger for the We-Touch condition compared to the Self-Touch condition (M=0.70, SD=0.46, and M=0.52, SD=0.47 p<.001), compared to the Surface-Touch condition (M=0.70, SD=0.46, and M=0.56, SD=0.45, p = 0.003), and compared to the No-Touch condition (M=0.70, SD=0.46, and M=0.48, SD=0.48, p<.001). For FDI muscle, MEPs were larger for the Self-Touch condition compared to the We-Touch condition (M=1.43, SD=0.28, M=1.29, SD=0.65, p <.001), compared to the Surface Touch condition (M=1.43, SD=0.28, M=1.08, SD=0.63, p<.001), and compared to the No-Touch condition (M=1.43, SD=0.28, M=1.04, SD=0.35, p<.001), MEPs were also larger for the WT condition compared to the Surface Touch condition (M=1.29, SD=0.65, M=1.08, SD=0.63, p=.002), and the No-Touch condition (M=1.29, SD=0.65, M=1.04, SD=0.35, p < .001) (see Figure 5).

Touch by muscle interaction
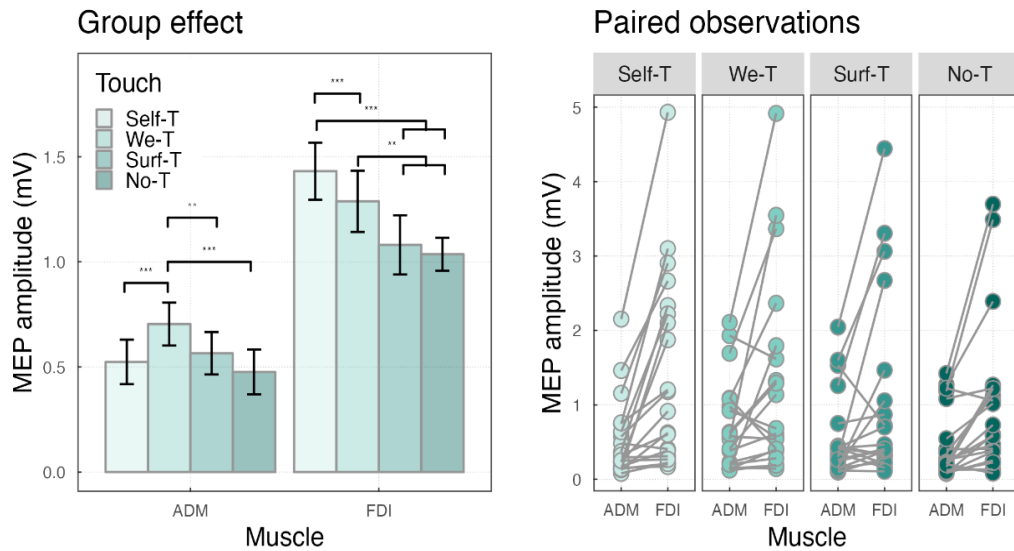
Figure 5Left side: Left side: Bar plot showing the group effects of touch by muscle interaction ∗∗∗P < 0.001. Error bars represent the standard error of the means adjusted to correctly reflect the variance in the within-subject design (Morey, 2008). Right side: Paired observation of two muscles ADM and FDI in all touch conditions.

The three-way interaction, touch by force by muscle, just approached significance (F (3,4485) = 2.48, p = 0.06).

Correlation

Results of the Pearson correlation indicated that there was a significant negative correlation between the 'Self-We Touch effect' -corresponding to the ratio between Self-Touch and We-Touch in the ~3N force condition, for the ADM muscle activity - and the touch avoidance measure score, r (18) = -0.56, p = 0.01. The finding indicates that individuals with a low index (therefore, individuals in which We-Touch was higher
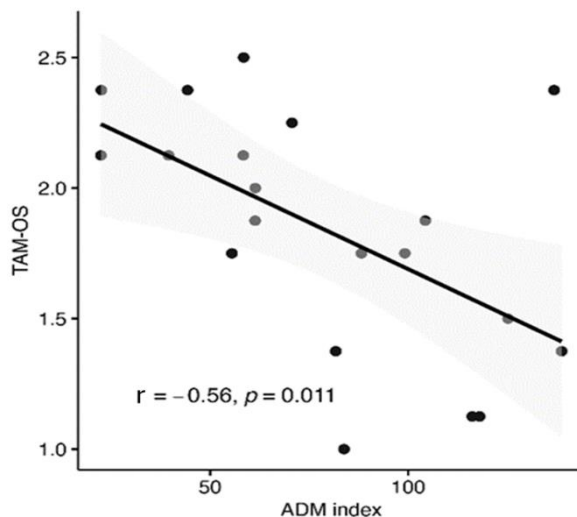
Figure 6: Correlation between the touch avoidance questionnaire in opposite sex TAM-OS score and the model predictions for the ~3N force effect of ADM muscle.

compared to Self-Touch) were associated with a higher level of touch avoidance (i.e., individuals with a high score in the touch avoidance measure) (see Figure 6).

Discussion

Our study aimed at investigating the neural cortico-spinal activity changes during action imagination when touch is involved. Specifically, we focused on examining the motor system activity during the mental simulation of force generation while individuals experienced various surfaces' touch The experimental conditions examined included Self-Touch (touching each other with the two index fingers of the two hands), We-Touch (being touched by another person), Surface Touch (touching a surface with the index finger), and a condition without any tactile involvement i.e., No-Touch. By employing single-pulse transcranial magnetic stimulation (TMS) on the primary motor cortex, we specifically targeted the First Dorsal Interosseous (FDI) as the muscle responsible for the force production through the index finger pressure imagination, and the Abductor Digiti Minimi (ADM) serving as control muscle. Our study sought to provide valuable insights into the modulation of the motor system associated with different contexts in which social and physiological components are intermingled. We utilized imagination instead of actual action to avoid potential confounding factors, and to ensure a more controlled and focused investigation into the distinct contributions of the sensory component (encompassing biological and non-biological touch) and the motor component (involving the application of physical force). This well-established approach is based on the substantial similarities between action and action imagination on psychophysical properties, and patterns of neural activations (Decety et al., 2001; Papaxanthis et al., 2002; Ehrsson et al., 2003; Lotze and Halsband, 2006; McAvinue and Robertson, 2008; Munzert et al., 2009; Hétu et al., 2013; Zabicki et al., 2017).

The results confirmed our main hypothesis that the motor system excitability is enhanced when biological sources are touched, i.e., when individuals are either touching themselves and when touching someone else, as compared to when they

are touching non-living sources, or not touching at all. We also replicated previous findings showing higher activation when individuals produce higher force as compared to lower force (Ali et al., 2023), and, as expected, the effect was stronger for the target muscle. The implications of these findings are considered in detail in the following discussion.

Overall, the amplitude of MEPs of the relevant muscle increased when imagined actions were performed concurrently with tactile stimulation, replicating the facilitatory effect of touch on the motor system (Mizuguchi et al., 2013; Ali et al., 2023). During the action, there is a complex interplay between the somatosensory system and the motor system to jointly control the movement and process tactile information (see review Delhaye et al., 2016). On one hand, action allows to optimize of tactile precision through various mechanisms, such as the adjustment of movement parameters and predictive processes (Lederman and Klatzky, 1987a; Chapman, 1994; Srinivasan and LaMotte, 1995; Louw et al., 2000; Gamzu and Ahissar, 2001; Giachritsis et al., 2009; Kaim and Drewing, 2011; Drewing, 2012; Lezkan and Drewing, 2014; Metzger et al., 2018). On the other hand, somatosensory information is integrated with other processes to control action. However, how exactly this interplay is implemented in the brain needs to be addressed. Here we showed that the processing of tactile information directly impacts M1 excitability during motor imagery.

We found increased activation of the motor system when participants imagined producing force (~3N) as compared to no-force production (<~1). Importantly, the scaling effect of force was larger for the target muscle, i.e., FDI, compared to the control muscle, i.e., ADM. That is the increased motor system activation when imaging to produce ~3N compared to <~1N was significantly more pronounced for FDI, the muscle that would be involved in the execution of the action (Bufalari et al., 2010; Pizzolato et al., 2012; Helm et al., 2015; Ali et al., 2023)(Figure 3). It is well established that M1 neurons encode grasp force (Cheney and Fetz, 1980; Wannier et al., 1991; Maier et al., 1993; Sergio and Kalaska, 1997, 1998; Shalit et al., 2012) and carry relevant information pertaining to grasp force (Intveld et al., 2018). In line with Ali et al., 2023, the present finding suggests that forces applied

during imagined actions are scaled similarly to physical actions and that the scaling is selective for the body part involved (Bufalari et al., 2010; Pizzolato et al., 2012; Helm et al., 2015; Grosprêtre et al., 2016), even when a modest magnitude of force is employed ($\sim$3N in the present investigation versus $\sim$15N in Ali et al., 2023). This scaling effect is consistent with earlier research that explored various imagery tasks, such as grasping objects of different sizes and shapes, performing movements in different directions, and varying the extent of movement (Bufalari et al., 2010; Cesari et al., 2011; Pizzolato et al., 2012).

The ability to discriminate physical properties through touch is accompanied by the integration of affective and socially relevant information. While studies over the past decades have provided important information about the reciprocal interplay between touch and action in general (Camerota and Celletti, 2014; Moscatelli et al., 2019), how social touch impacts movement control remains to be determined. Another important finding of the present study was the identification of how Self-Touch and We-Touch modulate the MEPs' amplitude during force imagination. In the condition ($<\sim$1), both Self-Touch and We-Touch showed higher activation compared to No-Touch, while there was no significant difference among the three touching conditions. In other words, the M1 excitabilities in the Self-Touch, the We-Touch, and the Surface Touch conditions were similar. On the other hand, when subjects were imaged to produce force ($\sim$3N force condition), the excitability of M1 in Self-Touch and We-Touch conditions was similar, both showing higher excitability than Surface Touch and No-Touch. Therefore, it appears that while the main facilitatory effect of touch was present even in the absence of action, the presence of action appeared critical to differentiate between touches when in contact with 'living' and 'not-living' materials. This finding strongly corroborates previous studies that have associated improved tactile perception with action, possibly attributed to the influence of predictive processes (Smith et al., 2009; Willemet et al., 2021).

Critically, the differences among the types of touch were manifest when comparing the patterns of activation of the two muscles. For the target muscle, i.e., FDI, both Self-Touch and We-Touch showed larger amplitude compared to Surface Touch and

No-Touch. However, in line with previous evidence indicating that self-touch and social touch are associated with different patterns of neural activation (Boehme et al., 2019), we found that MEPs' amplitude in the Self-Touch condition was significantly larger than the amplitude in the We-Touch condition. That is, the motor system activation was the highest when the right index finger of the subject was in contact with her own left index finger. This result sustains the hypothesis of the presence of sensory attenuation (SA) explaining why stimuli that are self-generated are associated with a reduction in the perceived intensity of the stimulus, explaining for instance why one cannot tickle oneself (Hughes et al., 2013). As a result, the discrimination between tactile signals produced by the action of the same person and signals that arise from non-self-causes is hypothesized to be based on this mechanism of SA (Blakemore S. J et al., 1998; Master and Tremblay, 2010). When a motor command is generated, an internal copy of this command, referred to as an "efference copy," is utilized to predict, and subsequently attenuate, the sensory outcome of the action (e.g., Kilteni et al., 2020). Consequently, self-generated tactile sensations are perceived as weaker compared to externally imposed stimuli (Bays and Wolpert, 2012). Therefore, it is tempting to explain the highest activation found in the Self-Touch condition for the target muscle as a neural signature of the consequences of sensory attenuation. Specifically, since the brain might have predicted the specific action (right index finger touching the left index finger) through an efferent copy, the sensory signal associated with the right hand could have been attenuated. Consequently, the amount of force 'exerted' by the right index finger to match the required force (~3N) might have been exaggerated. However, further research should be carried out to establish the validity of this hypothesis.

In stark contrast with FDI, the motor system excitability for the control muscle, i.e., ADM, was highest in the We-Touch condition, that is when the subject's right index finger was in contact with the index finger of another individual. The We-Touch condition showed a significantly larger amplitude compared to all the other conditions (Self-Touch, Surface Touch, and No-Touch), while among those, no significant difference was detected. Considering that ADM was not directly involved in the action (Ali et al., 2023), this finding confirms that affective touch may have a more pervasive influence compared to other types of touch, aligning

with the idea that the brain is hardwired around social dimensions (Dunbar, 2010), and that, social cues and contexts are processed as exceptionally influential information (Souza et al., 2012; Grichtchouk et al., 2022). Affective touch is mediated by a specialized sub-modality of touch, the c-touch system (McGlone et al., 2014), and fMRI evidence suggests that social touch is associated with widespread neural activity (Boehme et al., 2019). In line with that, the We-Touch condition may have engaged a specific and broader neural pathway encompassing ADM control.

Alternatively, some insight into the underlying mechanism of this effect may come from the correlation analysis that we carried out between the MEPs amplitude and the outcomes of the Touch Avoidance Measure (Casetta et al., 2020). We computed an index for each of the two muscles separately (ratio between Self-Touch and We-Touch in the ~3N force condition) to better identify the difference between the Self-Touch and the We-Touch condition, which we refer to as the 'Self-We touch effect'. Remarkably, we found a significant negative association between the ADM index and the scores on the Touch Avoidance Measure specifically concerning participants' comfort levels when touching someone of the opposite sex. Individuals who exhibited higher ADM activation in the other touch condition (lower Self-Touch and We-Touch ratio) were associated with a higher score in the Touch Avoidance Measure. In other words, participants who showed a tendency toward touch avoidance, as measured by the Touch Avoidance Measure, also showed higher MEPs in the We-Touch condition compared to the Self-Touch condition. The touch avoidance construct serves as an indicator of an individual's inclination towards initiating and receiving physical touch (Andersen and Leibowitz, 1978). Touch avoidance has been shown to diminish the perceived pleasantness of various forms of tactile stimulation (Hielscher and Mahar, 2017). The primary function of ADM is to move the fifth finger away from the fourth finger, and therefore, it is involved in each movement that requires the spreading or abduction of the little finger from the ring finger. Therefore, another possible explanation for the 'Self-We Touch effect' for ADM is that it reflects the intention to move the hand far away to avoid the somewhat unpleasant sensation associated with touching a stranger. Future work might focus on the Self-We Touch

differences, systematically varying parameter such as force magnitude and/or movement required and muscle involvement, to determine whether there is a causal link between the personality trait related to touch avoidance and specific muscle activation.

In conclusion, the purpose of the current investigation was to clarify the role of different types of touch during action imagination. In line with our previous study, touch was associated with higher M1 excitability, and as expected, the effect scaled with the force 'exerted' and was selective for the target muscle. Crucially, while in the absence of force production imagination, there was just a general effect of touch, when subjects imagined producing force, the effects of different types of touch become manifest. Touch conditions were arranged in a somewhat hierarchical order, with Self-Touch having the greatest impact, followed by We-Touch, Surface Touch, and finally, No-Touch, which exhibited the lowest amplitude of MEPs. Finally, the control muscle (ADM), showed increased activation during the We-Touch condition, which we attributed to the strong effect of the social context or as a possible inclination to avoid touching an unfamiliar person.

The present study contributes to our understanding of the integration between sensory and motor processes, and the reciprocal interplay between touch and action. Overall, the study strengthens the idea that action facilitates sensory discrimination, allowing better differentiation among different types of touch. We provide evidence in favor of the hypothesis that self-other discrimination is based on a mechanism of sensory attenuation. In addition, the study has been one of the first attempts to thoroughly examine how social touch impacts motor control at the level of motor system activation.

Chapter 4: Integrating Tactile Insights with dPMC and S1 Inhibition in Imagined Movements: A cTBS-TMS Study

Abstract

This study aimed to elucidate the neural mechanisms through which the S1-dPMC-M1 circuitry facilitates grasping movements, focusing on the role of tactile feedback in motor control. By employing Transcranial Magnetic Stimulation (TMS) and continuous theta burst stimulation (cTBS), we explored the modulation of motor cortex excitability and the effects of inhibiting specific brain areas on MEPs amplitudes during imagined grasping tasks. Our findings reveal that motor task complexity significantly influences MEP amplitudes, with more complex tasks like lifting a glass resulting in higher cortical excitability than less demanding tasks such as holding a glass or maintaining a static hand position. This supports the notion that the brain's motor circuits are highly adaptable, enhancing their activity to meet the demands of the task at hand. Providing tactile feedback significantly increased MEP amplitudes, indicating that sensory input from touch is integral to fine-tuning motor commands. This was particularly evident in the dorsal premotor cortex (dPMC) and the primary somatosensory cortex (S1), which showed increased activity in response to tactile feedback, highlighting their roles in sensory-motor integration. The dPMC showed enhanced activation with tactile feedback while imagining lifting the object; S1 maintained greater activation with tactile feedback along the entire action (lifting, holding and static). Interestingly, the study found muscle-specific effects in response to motor imagery and tactile feedback, with certain muscles showing higher MEPs across different motor conditions and brain area inhibitions. This suggests a nuanced interaction between motor imagery, tactile feedback, and neuromuscular activation, pointing to the brain's complexity of sensorimotor integration processes. Overall, our results highlight the importance of sensory input in

refining motor execution and the interplay between different brain regions in facilitating coordinated movement.

Introduction

The human motor system is unparalleled in its ability to process sensory signals, particularly for visual-tactile information when received from the hand, which expresses extraordinary dexterity and precision in grasping objects. Controlling the actions of reaching and grasping means involving cortical and subcortical structures in a highly complex sensorimotor system. This sophisticated network is essential for the precise configuration of the hand, which must adapt to the dynamics of the task and the object properties, as detailed in (Jeannerod et al., 1995; Grafton, 2010; Turella and Lingnau, 2014).

The neuronal circuits involving the dorsal premotor cortex (dPMC), the primary somatosensory cortex (S1), and the primary motor cortex (M1) play a critical role in organizing appendicular skilled movement. This dynamic entails an elaborate characterization of the integration involving action planning, sensory processing, action initiation, and control (Yeom et al., 2016; Johari and Behroozmand, 2018; Gardner et al., 2022). In particular, the dPMC plays a role in administering the timing traits of all types of actions with particular relevance for movement initiation and termination (Pollok et al., 2017; Ross et al., 2018; Yokoi et al., 2018). Moreover, the premotor cortex (PMC) plays a central role in conducting information to M1 for integrating motor programs merging from several sensorimotor networks (Rizzolatti and Luppino, 2001; Cisek and Kalaska, 2010). Importantly, dPMC has been shown to functionally represent actions in the absence of actual movements, as when actions are observed or imagined (Rizzolatti et al., 2014), when inhibited (Aron et al., 2014), or when a specific action needs to be selected (O'Shea et al., 2007b). In particular, the network connecting the prefrontal with the dorsal premotor cortex (dPMC) can select what type of action should be privileged and which should be considered not appropriate, guided by our subjective action experience, made possible by a continuous flow from perception to action.

The classical brain model that considers the sensory system sending information to some cognitive areas that, in turn, develop commands ready for the motor system to send out, has been challenged in the last 50 years (Rizzolatti et al., 2014). Sensory information is not unique, and there is no hierarchical modulation from the sensory to the motor. The same information might be developed in multiple afferent copies and directed to different sensorimotor systems at any level of computational complexity (Belger and Banich, 1992; O'Keeffe et al., 2022). Indeed, current models are developed incorporating different levels of complexity. A low level might represent a sensory-motor transformation for reaching a visual cue. A higher level of the sensory-motor transformation might be based on selecting actions for reaching a specific object (Legon and Staines, 2006; Li et al., 2020).

There are still several uncertainties about the sensory-motor network connections. We still lack knowledge about the mechanism that gives rise to the control of elementary action components such as movement velocity and force production. More importantly, we lack knowledge about how the brain solves the problem of redundancy of the degrees of freedom, such as how, among many different possible movements, the brain selects one, hopefully, as the most optimal one (Bernstein, 1967). This problem of redundancy is partially solved at the level of the spinal cord but defined in a goal-directed way at the level of the cortical motor system (Cusumano and Cesari, 2006; Latash, 2012) We do not know the neural pathway by which rule-based action selection is carried out through a sensory-motor network. Together, all these open questions require more detailed information about the effective coordination of appendicular skilled movements, particularly for action manipulations, in their specific synchronized interplay of motor planning, sensory processing, and initiation functions across the dPMC, S1, and M1 regions.

Neurophysiological studies have contributed to the knowledge of neural systems underlying hand movements in grasping activities and the important functions played by motor and somatosensory cortices. Studies show significant activation of motor cortical neurons during grasping, underscoring the involvement of the motor cortex in the initiation and execution of these movements (Bodda and Diwakar, 2022; Rens et al., 2023). At the same time, neuroimaging studies in

different species have shown consistent grasp-related neuronal modulations within both the primary motor cortex (M1) and primary somatosensory cortex (S1), indicating an organized interplay of these regions during grasping (Nelissen and Vanduffel, 2011; Fabbri et al., 2016). Electrophysiological studies also show a dynamic interplay between M1 and S1, as the activity of M1 is decoded from the movement-related activities in S1, which means that there is direct neural information going to motor control (Umeda et al., 2019). Additionally, direct mapping of S1 connectivity to M1 responses has recently been demonstrated, which underscores their close functional connection (Osborn et al., 2021; Glanz et al., 2023).

The importance of collaborative functioning by the primary motor cortex M1 and the primary somatosensory cortex S1 during grasping movements (Tia et al., 2017; Parikh et al., 2020; Gardner et al., 2022) plays a significant role in the processing of tactile and proprioceptive feedback which is essential for performing complex movements. This connectivity with S1, which is critical for obtaining excitatory inputs from M1, results in refining motor actions according to sensory input, thus enabling proper incorporation of somatosensory feedback into motor plans that are required for accurate and flexible control of movement (Salimi et al., 1999; Umeda et al., 2019). Key to this network is the dorsal premotor cortex (dPMC), which has been known to be vital in motor behavior actuation and execution. The network formed by the interaction of the dPMC with M1 integrates functions for producing motor commands (Roth et al., 1996; Mochizuki et al., 2004; Vesia et al., 2018). The importance of this interaction for the accurate transmission of information required for movement implementation highlights the comprehensive and dynamic nature characterizing these cortical areas in motor control.

The interaction between the dPMC, M1, and S1 is particularly relevant. The dPMC's function in movement planning and initiation, along with its S1 projection, forms a feedback loop, which handles sensory information from the body and is necessary for precision adjustments of movements. This enables the motor actions to be corrected and refined in real time, which is vital for proper initiation and conduct of movements, along with their adequate tuning based on

ongoing sensory information. This mechanism is essential for skilled motor performance, especially in the functional architecture of the parietal-frontal network, as stressed by Rizzolatti & Luppino (2001) to unveil the precise network by directing attention to its function in sensorimotor transformation (Rizzolatti and Luppino, 2001).

New studies have provided insight into the neural bases of grasping, specifically somatosensory feedback and activation in dPMC. Research such as Suresh et al., 2020 reveals that the dynamics between the primary somatosensory cortex (S1) and primary motor cortex (M1) during grasping are mainly guided by somatosensory feedback (Suresh et al., 2020). The dPMC has an essential function in the control of goal-directed reach-to-grasp movements, especially integrating motor representations with visual information for error correction, mainly under conditions limiting the ability to grasp where its activity rises to match changing requirements of grasping (Begliomini et al., 2007).

The need to investigate the complex network connection between the main brain areas, such as the primary motor cortex (M1), the primary somatosensory cortex (S1), and the dorsal premotor cortex (dPMC), has become vindicated in contemporary neuroscience, especially concerning grasping tasks. For example, the research conducted by Vesia et al. in 2018 studies functional connectivity between DPMC and M1 during grasp planning, which indicates that these regions have an interdependent function (Vesia et al., 2018). Nevertheless, as Murata et al. (2016) observe, there is a significant dearth of research that systemically studies their functional connections (Murata et al., 2016).

The use of inhibitory protocols in these brain regions, especially in networked processes, provides clues as to the functions they collaborate on for motor actions. For instance, Decramer et al. (2021) studied the neural encoding of objects during grasping in the frontal cortex (Decramer et al., 2021), while Cavina-Pratesi et al. (2018) explored how grasping, reaching and pointing movements engage critical nodes within visuomotor networks (Cavina-Pratesi et al., 2018). Moreover, Allart et al., 2019 studied the parietofrontal connectivity using transcranial magnetic stimulation and provided additional insight into these complicated relationships

(Allart et al., 2019). Given these insights, the necessity for an inhibitory protocol in our study becomes vital since it serves as a primary means to unlock the complex and hidden mechanisms of interaction and functioning within these brain regions which will lead to further comprehension of motor control processes.

In our present study, we have focused on action imagination instead of action performance, following the notion that " motor imagery (MI) designates cognitive processes as mental simulation or imitation based principally on internal mode manipulations of these representations" originating from motor activity, a concept first postulated by Jeannerod (2001), who proposes that MI is a mental rehearsal of the movement activating neural circuits similar to those active when the same action is performed (Jeannerod, 2001). Support of Jeannerod's theory comes from a large number of neuroimaging studies that have provided strong evidence for some overlapping in brain regions during MI and ME (motor execution). This has been evidenced by the findings of a number of important studies (Decety et al., 1994; Porro et al., 1996; Lotze et al., 1999; Munzert et al., 2009). These studies have consistently shown that the neural substrates of interest during actual task performance are also interested in considering or planning human activities. Thus, this overlap highlights the functional similarity between MI and ME – which further supports our rationale for concentrating on action imagination in our research.

The main goal of our study, which builds on this theoretical foundation, has been to determine the mechanisms underpinning how S1-dPMC-M1 neural circuits promote the output of grasping actions. To achieve this, we designed a series of action imagination tasks, involving three distinct movements: imagining lifting a glass with the index finger and thumb, holding a glass in the same manner, and maintaining a static hand position. In all scenarios, the participants' hands remained at rest. We focused our measurements on the First Dorsal Interosseous (FDI) muscle, with the Abductor Digiti Minimi (ADM) and Extensor Carpi Radialis (ECR) muscles serving as controls.

One of the chief steps in our methodology envisaged analysis of primary somatosensory cortex (S1) activation. This was achieved in half of the trials

provided with touch and no touch in the remaining halves; respectively, a hard surface touch was provided beneath the index finger. Such an approach was based on the fact that single-pulse Transcranial Magnetic Stimulation (TMS) results in activation of interneurons and their subsequent corticospinal neuron discharge. This leads to a discharge that creates motor-evoked potentials (MEPs) in the target muscle, which is indeed regarded as an index of corticospinal excitability (Hallett, 2007). In addition, we applied Continuous Theta Burst Stimulation (cTBS) as well. This technique apparently decreases the functional connection within several parts of the brain with compensation between the stimulated part of S1, including dPMC dorsal premotor cortex cerebellum, basal ganglia, as well as anterior cingulate part (Valchev et al., 2015). Our purpose was to transiently attenuate the activity of two targeted regions, S1 and dPMC, and one control region, Vertex, so that we can have a better view of possible functions played by these regions in action imagination along with neural circuits underlying such phenomena.

To examine the neural bases of action imagination, we performed two independent experiments. In the first experiment, our main concern was to observe only how motor cortex (M1) excitability occurs when no external modulation is done during its natural state. We used single-pulse Transcranial Magnetic Stimulation (TMS) to quantify M1 excitability while participants performed action imagination tasks. Such an approach was, therefore, helpful in providing us with a reference point of what the brain would have done without interference from any other neuromodulation techniques as we undertook these tasks.

The second study was aimed at understanding the neural dynamics underlying it further and used Continuous Theta Burst Stimulation (cTBS) instead. Volunteers were asked to come for three different sessions in a row, with each of the sessions being targeted at suppressing one precise area from their brain using cTBS. Each day, cTBS was applied to a different area—S1, dorsal premotor cortex (dPMC), and the control Vertex in the interhemispheric fissure—to temporarily suppress its functional activity. We stimulated the M1 immediately after the cTBS application and determined MEPs. This method enabled us to monitor the M1 excitability changes and subsequent action imagining effects while suppressing randomly different areas of the brain.

The purpose of our study is to get a clear picture and understanding of which brain regions are directly related or engaged during the cognitive process called motor imagery, especially with simple precision grip tasks. The main aim is to establish if these regions play a role in domain-specific cognitive control or, instead, if the effect is more general. Thus, we predict that a description and comparison of the results obtained in two different experiments could allow for uncovering intrinsic facets associated with effects on the primary somatosensory cortex (S1) and the dorsal premotor cortex (dPMC), which transpire as a consequence of continuous Theta Burst Stimulation inhibition(cTBS). We foresee that suppressing these regions would not only impact the general level of performance in tasks but will also shed light on how neural signals guiding motor commands reach M1.

In addition, we suggest that even after the S1 was inhibited by applying cTBS it can show enhanced activation and high amplitudes of Motor Evoked Potentials (MEPs). These differences are postulated to account for the increase in MEP amplitudes by several factors; these include dissimilarities of the task, involving tactile interactions and muscle involvement (largely functioning due to sensory feedback given out into the target muscle i.e. First Dorsal Interosseous – FDI). The focus of this aspect of the study is to untangle the complicated relationship between sensory feedback and motor output, thus increasing knowledge on how neural circuits that are associated with it govern motor imagery and control.

Material and Methods

Experiment 1

This first study included 13 healthy volunteers, 6 men, and 7 women (mean age = 23 years, SD = 1.98 years). All individuals had normal or corrected-to-normal eyesight and were right-handed. None of the volunteers were aware of the goal of the experiment, and none of them had any neurological, psychiatric, or other medical issues; nor did they experience any TMS adverse effects (Rossi et al., 2021). During TMS, there were no reports or observations of any discomfort or negative effects. Participants signed a written informed consent form before entering the lab. The procedures were in accordance with the ethical principles of

the 1964 Declaration of Helsinki and were approved by the local ethics committee (n.28.R1/2021).

Subjects were asked to sit in an armchair with their right arm resting on an armrest. The hand remained hanging from the wrist in a constant posture throughout the experiment. In some cases, the fingers made actual contact with the surface, whereas in others, there was no physical contact. The participants' distribution of task and touch conditions was balanced.

The tasks for subjects were to imagine kinesthetically three different actions:

1. Lifting (L): Participants were asked to imagine lifting a glass from the table using their index finger and thumb. This includes the effort given by the glass weight.
2. Holding (H): Participants were instructed to imagine holding a glass with their index finger and thumb without lifting it. This does not include any effort given by the glass weight.
3. Static (S): Participants were instructed to imagine their hands at rest, without any movement.

For each action imagined, two touch conditions were introduced:

1. No-touch: Participants had no surface beneath their index finger during the imagination task; in other words, the index finger was not touching a surface.
2. Touch: The participant's index finger was in contact with a surface while performing the motor imagery task, in other words, the index finger was touching a surface

Data were collected from two muscles during the experiment:

1. First Dorsal Interosseous (FDI)
2. Abductor Digiti Minimi (ADM)

Each task condition included 20 trials of transcranial magnetic stimulation (TMS) over M1, both with and without touch, along with a baseline made of 20 trials. In total, 140 trials were carried out during the experiment.

Participants went through a training session before beginning the imaging tasks. They were practicing while keeping their muscles relaxed. During the training, participants were encouraged to deeply immerse themselves in the sensations and imagine the actions kinesthetically. During the training, participants were directed to internalize the time of the activity by a prerecorded voice that highlighted three phases of the movement: the preparation of the action (READY), the start of the action (START), and the finish of the action (END) and come back to the original place from where the movement starts. Following this, participants were seated in the chair and asked to relax their arms on the chair's side while facing forward.
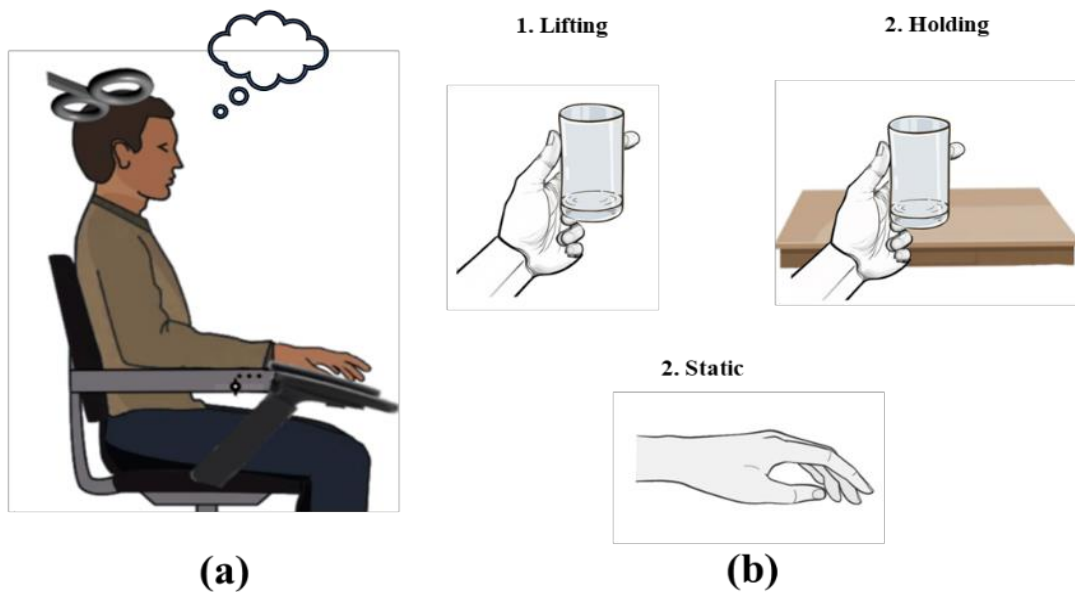
Figure 7 Schematic illustration of test situations. (a) Overview; (b) Kinestetic Imagery Tasks

The 3 motor tasks were imagined by keeping the same hand posture but in two different touch conditions: one with the index finger in touch with a surface and the other with no actual touch.

Participants were not given performance feedback at any point during the trial. To avoid tiredness, breaks were taken after 30 repeated attempts. Each trial involved a single TMS pulse given at random 300, 450, 600, 750, or 1,000 milliseconds after the last voice instruction during the period when participants were actively

engaged in mental imagery of the action, corresponding to the start and ending of the action. To avoid excessive brain activity, the gap between subsequent trials was established at approximately 5-10 seconds. Each participant's whole experimental process lasted around 50 minutes. Participants were asked to complete a questionnaire at the end of the experiment to rate the efficiency of their mental images (Marks, 1973).

A figure-of-8 coil (outer diameter of each wing 110 mm) was used to apply a biphasic single TMS pulse (STM 9000 magnetic stimulator, Ates-EBNeuro, Italy). The coil was placed on an extended arm and located on the left side of the skull, at a 45° angle to the sagittal axis, tangentially to the skull (Brasil-Neto et al., 1992). Moving the coil on the scalp in small steps laterally to the vertex in the left hemisphere and then administering TMS pulses at constant intensity until stable MEP amplitudes are evoked in the relaxed FDI (Jong et al., 2009). The resting motor threshold (rMT) was defined as the lowest stimulus intensity able to evoke MEPs with an amplitude of at least 50 μV in at least 5 out of 10 trials. This measure is used to determine the FDI optimum scalp location. During the experiment, the intensity of stimulation was set at 120% rMT (Hallett, 2000). To reassure the location of the same optimal scalp position during the entire experiment, a Neuronavigator (Softaxic Optic, Polaris Vicra Position sensor, Canada) was used.

Electromyographic (EMG) responses were recorded using a wireless system (Zerowire, Aurion, Italy) with 2 surface electrodes positioned on 2 muscles of the right hand: the FDI and the ADM. EMG signals were online band-pass filtered (20–2.5 kHz; plus 50 Hz notch, D360, Digitimer, UK), amplified at a gain of 1,000 (Digitimer), digitized at 5 kHz with laboratory interface (Cambridge Electronic Design 1401, UK) recorded by Spike 2 (version 6, Cambridge Electronic Design), and then analyzed offline. A customized Matlab script was used for this experiment, which programmed and executed the conditions of forces in a randomized block design for each participant. Both instructions and data processing were carried out using Matlab 2022b (MathWorks, MA, United States).

Experiment 2

The second experiment included inhibitory procedure and considered 13 healthy volunteers, 11 men and 12 women ranging in age from 20 to 40 years (mean age = 24.5 years, SD = 5.26 years).

For this experiment, we replicated the exact conditions and protocol utilized in the first experiment. However, we added one more muscle ECR to the existing muscles FDI and ADM. Before collecting data using the single pulse TMS, participants underwent an inhibition protocol, which is described below.

During the experiment, we implemented a continuous theta burst stimulation technique for a duration of 40 seconds involving a total of 900 pulses to inhibit three specific brain areas, namely the dorsal pre-motor cortex(dPMC), the primary somatosensory cortex (S1), and the vertex (V). The resulting inhibitory effect lasted for a period of 40 minutes (Huang et al., 2005). For Continuous Theta Burst Stimulation, we utilized the Magstim D70 Air Film Coil (AFC) along with the Magstim Rapid² Stimulating Unit (Magstim Co., Ltd., Whitland, UK). Subsequently, the experiment was followed by reapplying the same task procedures, including the administration of single-pulse stimulation to the motor cortex. The participants came for three days, and every day a different area was inhibited randomly. We employed the E-Prime V2 software from Psychology Software Tools, Inc. to deliver sound cues for preparation, initiation, and termination. Additionally, we administered TMS stimuli at random time intervals, consistent with the methodology used in Experiment 1.

Single pulse TMS was performed using Magstim 200 stimulator (Magstim Co., Ltd., Whitland, UK) connected to a 70 mm butterfly coil. At the beginning of the experimental session, spTMS was administered with the coil positioned tangentially to the scalp and over the left primary motor cortex (M1) to determine the individual resting motor threshold (rMT). The optimal scalp position (OSP) was set where larger and more stable MEPs were obtained (hotspots) from all muscles.

Electromyography (EMG) signals were captured from the first dorsal interosseous (FDI) muscle, as well as the abductor digiti minimi (ADM) and extensor carpi radialis longus (ECR) muscles of the right hand. The active electrode was placed over the muscle belly and the reference electrode over the nearest joint of the same muscle. The ground electrode was placed over the left wrist. The signal was amplified, bandpass-filtered online (20 Hz–3 kHz) and digitalized (sampling rate: 20 kHz). To make sure that there was no unwanted background EMG activity before the magnetic pulse, we had the signal of each muscle displayed additionally in separate channels set at high sensitivity (50 µV), which was continuously monitored by the experimenter during the experimental session. To gather data, we used 9-mm-diameter surface cup electrodes along with the BIOPAC MP160 system, which includes the AMI100D Amplifier Input Module and the Acqknowledge 5 software. The criteria to define the RMT were the same as in experiment 1. The MEP peak-to-peak amplitude (in microvolts) was collected and stored on a computer for offline analysis using Biopac AcqKnowledge 5 software.

The participants wore a tightly fitting bathing cap on which the scalp position for stimulation was marked. The coil was held by hand, and its position with respect to the mark was checked continuously to easily compensate for small movements of the participant's head during data collection.

After finding the optimal scalp position, the specific brain regions targeted for inhibition were the dorsal premotor cortex (dPMC), sensory-motor cortex (S1), and Vertex (V). The M1 site corresponded to the OSP. The dPMC site was localized 2 cm anteriorly and 1 cm medially to the OSP, following a previously applied procedure (O'Shea et al., 2007a). The S1 site was identified by moving the coil 1 cm posteriorly to the OSP on a line parallel to the interhemispheric scissure, in keeping with previous TMS studies that successfully targeted S1 with reference to the motor hotspot (Sugishita and Takayama, 1993; Tegenthoff et al., 2005). While the vertex was measured manually. All the areas were mapped and marked with the help of Neuronavigator (Softaxic Optic, Polaris Vicra Position sensor, Canada).

Data analysis

Data Analysis of Experiment 1

The MEPs recorded were examined offline (Spike 2, version 6, Cambridge Electronic Design). A visual assessment of the data was undertaken to confirm that there was no background EMG activity distorting the MEP analysis. During the experiment, if there was a change in activity 100 milliseconds before the MEP, if the MEP amplitude could not be differentiated from background activity, or if overt movements were seen during recording, trials were discarded. Trials with MEP amplitudes that were 2.5 standard deviations or higher and lower above the mean were also excluded from further analysis. 8% of the trials were removed. EMG signals were processed using the filter Butterworth, bandpass 5Hz cut-off frequency using MATLAB (2022b).

Data have been analyzed with a mixed analysis of variance (ANOVA). The mean MEP amplitude recorded in each condition was entered into the statistical analysis. Within-subjects factors were Muscle (two levels: FDI, ADM), Touch (two levels: touch, no touch), and Action (three levels: Lifting, Holding, and static position). Post-hoc comparisons were performed by means of F-tests applying Bonferroni correction for multiple comparisons when required. The p-value was set for all comparisons at $p < 0.05$; the effect size is partial eta squared. In all the analyses, the significance level was set at $p < .05$, and the data are reported as mean± standard error; the analysis was performed using IBM SPSS Version 22 (IBM, Armonk, NY, USA).

Apart from analyzing raw MEP amplitude(mV), we employed a normalization method to standardize our data for each stimulation session and muscle. The baseline measurements were used as reference points. Motor facilitation under different experimental conditions was calculated using the formula (Condition - Baseline) / Baseline. This approach allowed us to detect deviations from a baseline index of 0. In addition to the aforementioned methodology, the 'intercept effect' was integrated into our analysis as an auxiliary parameter. This component was incorporated to assess the presence of a general facilitation trend across the experimental conditions.

Data Analysis of Experiment 2

The EMG signal was digitized at 6250Hz and band-pass filtered (5Hz to 2000Hz) using the acqknowledge software 5.0. Individual mean MEP amplitudes were measured peak-to-peak (in uV) for each experimental condition. Since background EMG activity affects motor excitability (Devanne et al. 1997), MEPs with preceding background EMG activity in the 60 ms window before the TMS pulse deviating from the mean by more than 2 SD were removed from further analysis. Further, we excluded trials where MEP amplitudes were lower and higher than 2 SD from the participant's mean in each experimental condition.

Data have been analyzed with repeated measure (ANOVA). The mean MEP amplitude recorded in each condition was entered into the statistical analysis. Within-subjects factors were Brain Area (three levels: dPMC, S1, and Vertex), Muscle (three levels: FDI, ADM, and ECR), Touch (two levels: touch, no touch), and Action (three levels: Lifting, Holding, and static position). Post-hoc comparisons were performed by means of F-tests applying Bonferroni correction for multiple comparisons when required. For all comparisons, the p-value was set at $p < 0.05$, the effect size is partial eta squared. In all the analyses, the significance level was set at $p < .05$, and the data are reported as mean± standard error; the study was performed using IBM SPSS Version 22 (IBM, Armonk, NY, USA).

Apart from the analysis of raw MEPs amplitude, we have done another analysis using normalized data, as mentioned in the control study.

Results

Results of Experiment 1:

The statistical analysis of the experimental data yielded significant results for the variables of Conditions and Touch. The ANOVA for the Conditions factor showed a significant main effect, $F_{(2, 11)} = 9.538$, $p = 0.001$, with a partial eta squared ($\eta^2 p$) of 0.443, indicating a substantial proportion of variance attributable to this factor. Notably, the Lifting condition demonstrated a significantly higher mean (0.560 ± 0.285) compared to the Static condition (-0.294 ± 0.208), with a p-value of 0.012. Additionally, the Holding condition also showed a significantly higher Motor Evoked Potential (MEP) amplitude (0.216 ± 0.182) in comparison to the Static condition, as indicated by a p-value of 0.006(see fig 2a).
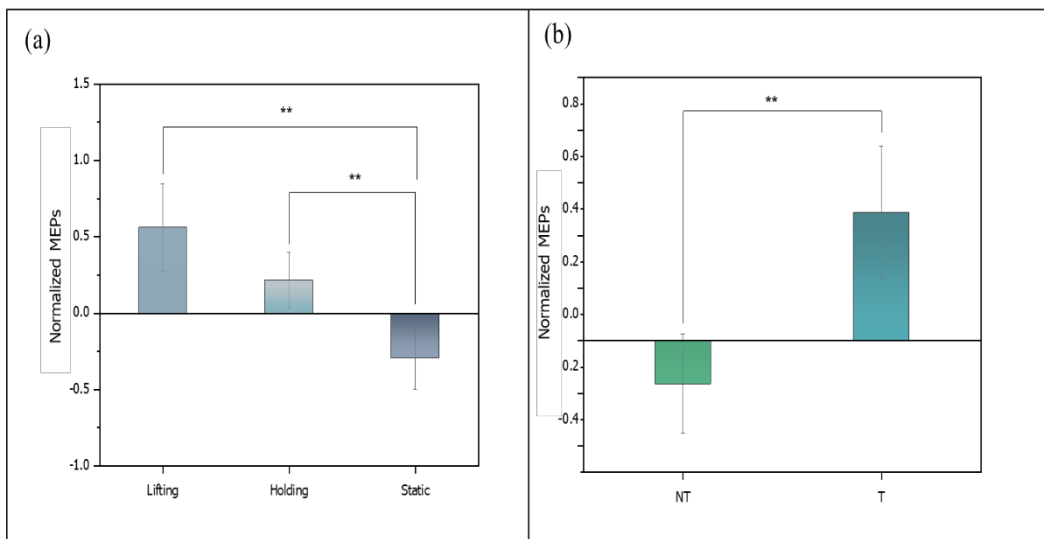
Figure 2: 2a presenting Task conditions and 2b for Touch condition.

Regarding the Touch factor, ANOVA results also revealed a significant main effect, $F_{(1, 12)} = 10.689$, $p = 0.007$, with a partial eta squared of 0.471. This result emphasizes the impact of the Touch condition in the experiment. The mean MEP amplitude for the Touch condition was significantly greater (0.486 ± 0.252) than that for the No-Touch condition (-0.165 ± 0.189), as denoted by a p-value of 0.007. This finding highlights the significant influence of tactile stimulation on MEP amplitude within the tested conditions (see Fig 2b).

Results of Experiment 2:

In our analysis, we investigated the effects of motor conditions and touch effects on neural activity. The ANOVA results for motor conditions indicated a significant main effect ($F_{(2,11)} = 5.333$, $p = 0.012$, $\eta^2 p = 0.308$). Specifically, the Lifting condition (0.415 ± 0.098) showed a significant difference from the Static condition (0.138 ± 0.062, $p = 0.022$), but not from the Holding condition (0.311 ± 0.086) (see Fig 3a).

Regarding touch, the ANOVA revealed a significant main effect ($F_{(1,12)} = 26.256$, $p < 0.000$, $\eta^2 p = 0.686$). The No-Touch condition (0.152 ± 0.062) significantly differed from the Touch condition (0.425 ± 0.082, $p < 0.001$), indicating a substantial impact of tactile feedback on neural responses (see Fig 3b).

Furthermore, a post-hoc comparison of the interaction between brain area and touch showed significant results ($F_{(1,12)} = 4.666$, $p = 0.019$). In the dPMC area, the Touch condition (0.519 ± 0.166) demonstrated significantly larger amplitudes compared to the No-Touch condition (0.226 ± 0.124, $p < 0.001$). A similar effect was observed in the S1 area ($p = 0.002$), where the Touch condition (0.607 ± 0.145) showed more activation than the No-Touch condition (0.154 ± 0.103). These findings underscore the influential role of tactile feedback in modulating neural activity across different brain areas (see Fig 3c). Whereas in Vertex, the Touch condition (0.150 ± 0.101) showed higher activation than the No-Touch condition (0.075 ± 0.066), but without any significant difference.

Post-hoc analysis revealed a significant interaction among these factors, with $F_{(1,12)} = 2.889$, $p = 0.032$, indicating that tactile feedback distinctly affects motor output depending on the brain area and condition.

In the dPMC area, during the lifting condition, the touch condition exhibited a notably higher activity level (0.891 ± 0.291) compared to the no-touch condition (0.259 ± 0.122, $p = 0.016$). This signifies a significant impact of tactile feedback on motor output in this specific brain region and condition.

Moving to the S1 area, a distinct pattern emerged where all conditions showed significant differences between touch and no-touch conditions. Specifically, during the lifting condition, activity was higher in the touch condition ($0.730 \pm$

0.188) than in the no-touch condition (0.287 ± 0.122, p = 0.043). In the holding condition, the touch condition again demonstrated higher activity (0.628 ± 0.185) compared to the no-touch condition (0.230 ± 0.142, p = 0.015). Finally, in the static condition, the touch condition showed greater activity (0.462 ± 0.170) than the no-touch condition (-0.057 ± 0.113, p = 0.025) (see Fig 3d). These findings in the S1 area underscore the consistent and significant influence of tactile feedback across different motor conditions.
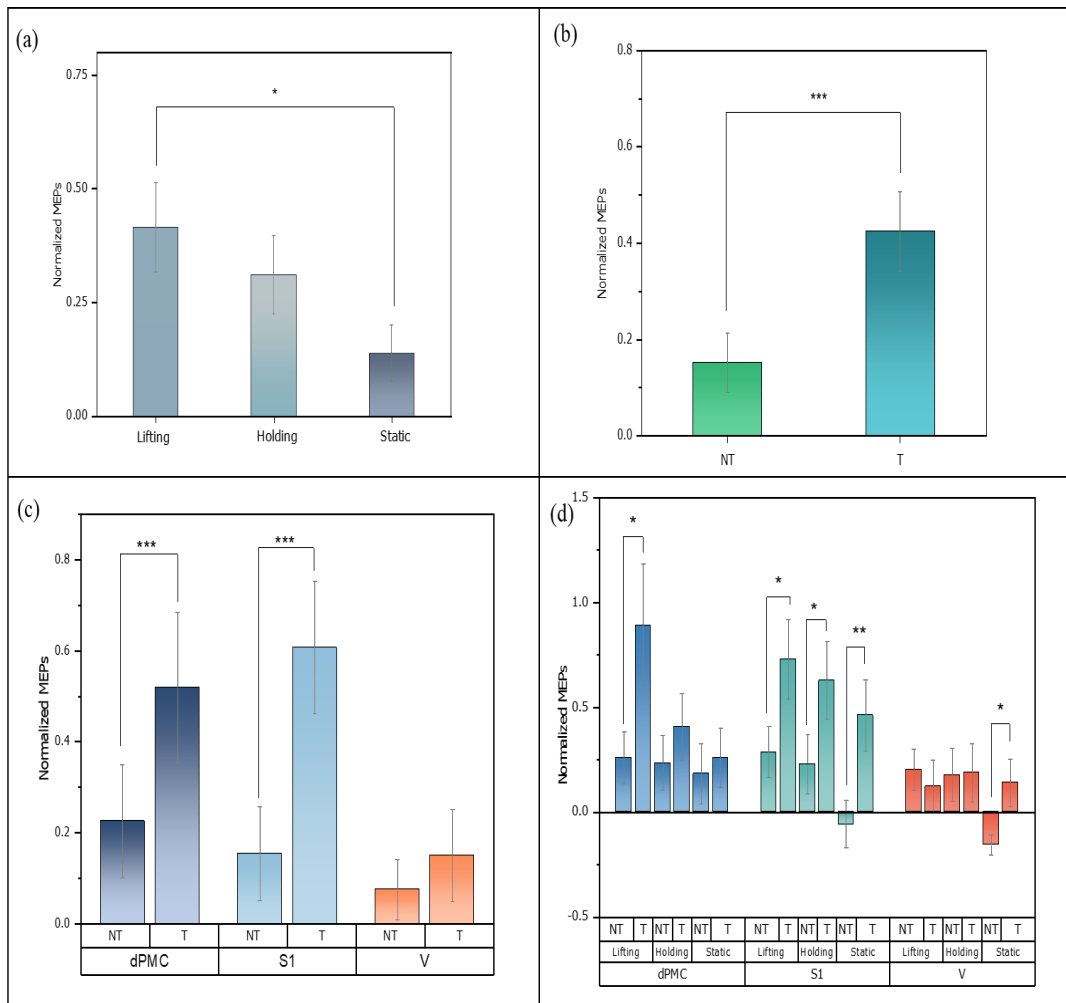
Figure 3: Upper Row: 3a shows Task conditions and 3b depicts Touch conditions. Lower Row: 3c represents interaction between Area and Touch conditions, and 3d for interaction between Area, Touch, and conditions.

In the Vertex area, our analysis revealed that during the static condition, the touch condition (0.140 ± 0.112) was significantly more active than the no-touch condition (-0.155 ± 0.048, p = 0.025). This result further supports the notion that

tactile feedback plays a crucial role in modulating neural activity in response to motor tasks.

The overall analysis yielded a significant interaction across these factors, as evidenced by $F_{(1,12)} = 2.159$, $p = 0.037$. This suggests that muscle responses are influenced by the specific brain area engaged, the condition, and the presence or absence of tactile feedback.

Figure 4: Four-way interaction between Area, Muscles, Condition, and Touch in dPMC area

In the dPMC area, during lifting conditions, the FDI muscle demonstrated a significant increase in activity in the touch condition (0.978 ± 0.391) compared to the no-touch condition (0.264 ± 0.137, $p = 0.049$). The ADM muscle also showed a notable increase under the touch condition (0.993 ± 0.311) compared to the no-touch condition (0.307 ± 0.190, $p = 0.012$). Furthermore, the ECR muscle's activity was significantly elevated in the touch condition (0.702 ± 0.246) as opposed to the no-touch condition (0.206 ± 0.105, $p = 0.036$) during lifting. A similar pattern was observed in static conditions,

Figure 5: Four-way interaction between Area, Muscles, Condition, and Touch in S1 area specifically

where the ECR muscle activity was higher in the touch condition (0.257 ± 0.119) compared to the no-touch condition (0.044 ± 0.110, $p = 0.050$) (see Fig 4).

In the S1 area, the FDI muscle's activity was significantly greater in the touch condition (0.822 ± 0.308) than in the no-touch condition (0.165 ± 0.116, p = 0.048) during lifting. During holding conditions, this muscle again exhibited higher activity in the touch condition (0.584 ± 0.281) compared to the no-touch condition (0.038 ± 0.104, p = 0.041). The ADM muscle, under static conditions, displayed a significant increase in activity in the touch condition (0.749 ± 0.280) as opposed to the no-touch condition (-0.073 ± 0.137, p = 0.007). The ECR muscle in the S1 area also showed higher activity in the touch condition (0.613 ± 0.125) compared to the no-touch condition (0.351 ± 0.122, p = 0.028) during lifting. This trend continued in holding (0.673 ± 0.180 in touch vs. 0.344 ± 0.156 in no-touch, p = 0.005) and static conditions (0.400 ± 0.192 in touch vs. 0.020 ± 0.118 in no-touch, p = 0.015) (see Fig 5).

Figure 6: Four-way interaction between Area, Muscles, Condition, and Touch in Vertex area specifically

In the Vertex area, particularly during static conditions, the ECR muscle exhibited significantly higher activity in the touch condition (0.162 ± 0.103) compared to the no-touch condition (-0.173 ± 0.070, p = 0.031) (see Fig 6).

Discussion:

The study's main goal was to clarify the pathway through which S1-dPMC-M1 neural circuits mediate the execution of grasping movements. Central to our approach was the analysis of primary somatosensory cortex (S1) activation, modulated by tactile feedback. Thus, our study included two main experiments. In the first experiment, a baseline was established for the excitability of the motor cortex (M1); it was carried out using single-pulse Transcranial Magnetic

Stimulation (TMS) during the participants' action imagination tasks of grasping actions. The second study further investigated neural dynamics by utilizing continuous theta burst stimulation (cTBS) to temporarily inhibit selected brain areas – S1, dPMC, and vertex as a control – in three separate sessions. This made it possible to measure the effects of focal area inhibition connected with M1, considering the MEPs amplitude during motor imagery of grasping action. The findings from the experimental analysis provide a deep understanding of the role of motor and tactile feedback on neural activities by reinforcing the knowledge of sensory-motor integration.

Indeed, comparing Motor Evoked Potentials (MEPs) across different movement phases – lifting a glass, holding a glass, and static hand position – reveals robust findings that fall in line with the wider view of task complexity given the control of action at the higher levels of physical manipulation and coordination of muscle activities. The lifting condition manifested a significant increase in the amplitude of MEP, which indicates the heightened activation of the brain's motor circuits. Such an observation fits well with those of Devanne et al. (1997) when they pointed out that the excitability of the motor cortex grows with the complexity of the motor task as it underscores the adaptive structures of the brain to facilitate the implementation of such a task (Devanne et al., 1997).

Despite requiring active engagement, the holding condition showed less enhancement in MEP amplitude than lifting but remained significantly higher than the static condition. This differential firing rate among conditions further highlights the capability of the brain to adjust its response depending on the intricacy of the motor task. Ziemann et al., 1996 substantiate this claim, demonstrating that there is a certain proportionality between the level of excitability of the motor cortex and the force production via muscle contraction for modulating relative changes at the level of the task (Ziemann et al., 1998).

The lowest MEP amplitude was found for the static condition, which reflects minimal muscle engagement, showing that minimal cortical activity is required to maintain a position without active manipulation. As suggested by various studies, static or less challenging activities lead to a decrease in the activity of the motor

cortex, thus promoting the validity of the disparities (Post et al., 2009; Sander et al., 2010; Taube et al., 2015; Ali et al., 2023, 2024). In addition, studies on the plasticity of the motor cortex following various motor tasks have provided further evidence supporting the observed differential modulation of cortical excitability across conditions as in our experiment (Li et al., 2001; Ziemann and Siebner, 2008; Peters et al., 2014). Therefore, these results, taken as a whole, demonstrate that the brain can dynamically modulate the activity in response to the task requirements. The change in neural activity from static to holding to lifting situations is yet additional proof of the flexibility of the motor system in adapting its output to fulfill task standards. This adaptive modulation principle is very well supported in the literature (Cesari and Newell, 2000a; Cesari et al., 2011; Ali et al., 2023) to provide solid ground for the understanding of the dynamic nature of M1 excitability for task complexity.

The significant effect of tactile feedback on motor evoked potentials (MEPs) observed emphasizes the importance of afferent input in regulating neural activity in the motor system. The facilitation of MEP amplitudes in the Touch condition relative to the No-Touch condition provides further evidence of the critical role of tactile information in the control of action. Evidence obtained by Rosenkranz and Rothwell in 2004 emphasizes the significance of sensory feedback in the control of movements, showing that sensory inputs from the skin modulate motor cortex excitability and motor output (Rosenkranz and Rothwell, 2004). This agrees with the results of our study, wherein the MEP amplitudes following the provision of tactile feedback indicated increased neural activity, which can be attributed to the incorporation of information from the sensory system with the motor commands. In addition, the study by Johansson and Flanagan (2009) reveals the mechanism of the central nervous system's (CNS) use of tactile feedback in predicting and calibrating motor commands for object manipulation, thus underlining the particular importance of touch in the performance of accurate and coordinated movements (Johansson and Flanagan, 2009). These findings resonate with the increased MEP amplitudes under the Touch condition observed in our study and, once again, emphasize the augmented neural activity made possible by tactile feedback integration. Furthermore, the works of Zatsiorsky and Latash considered

the coordination of each individual digit in force production and the role of grip force in preventing the slippage of an object, thus demonstrating the multistage interaction of sensory information and motor performance (Zatsiorsky et al., 1998, 2000; Latash et al., 2004; Zatsiorsky and Latash, 2004). Collectively, they strengthen our results and prove that tactile feedback is not only ancillary but also an essential entry into the motor control system, greatly stimulating the input of nerves and drives. Overall, the robust influence of haptic feedback on MEP amplitudes we observed in the current study is supported by literature, highlighting the pivotal contribution of the afferent signals for refining motor control and execution. One can leverage the integration of tactile signals and motor commands to accurately deliver coordinated movement, a critical process in active physical environment engagement.

Moreover, the differential effects of the tactile feedback on regions of the brain, such as the dorsal premotor cortex (dPMC) and the primary somatosensory cortex (S1), served as an indication of the functions these involved brain regions performed in the process of sensory-motor integration. The dPMC, critical in movement preparation and initiation, shows increased activation due to somatosensory feedback, especially on tasks that call for active manipulation, like lifting. This pattern of response implicated the dPMC in the use of external cues during motor planning and is therefore in line with earlier findings by Davare et al. (2006), which underscored the role of the dPMC in the incorporation of sensory information for the guidance of movement execution (Davare et al., 2006).

Likewise, the S1 region, involved with processing sensory feedback, registers remarkable increases in neural activity following tactile feedback in different motor states. This is a very important aspect that thus highlights the necessity of S1 as the integrator of sensory information and motor commands – required during the fine-tuning of motor behaviors due to sensory information. The studies conducted by Iwamura, 1988 have shown that S1 is implicated in the analysis of tactile information and its role in sensorimotor integration, which is congruous with the observed enhancement of the neuronal activity (Iwamura, 1998).

Additionally, the continued research on the human dPMC, concerning the functional anatomy during motor and sensory processing, further explains the involvement of the dPMC in motor sensory integration, thus emphasizing the prime position of the tactile feedback in the planning and execution processes (Hoshi and Tanji, 2007; Hardwick et al., 2015; Omrani et al., 2016; Cléry et al., 2018). Furthermore, in their study, Burton et al., 2008 showed how the role of S1 in sensual processing and motor planning provides an understanding of how useful information enhances motor output in the brain by integrating with sensory information, thereby highlighting S1's importance in this process (Burton et al., 2004). All these results underscore the elaborate roles that the dPMC and S1 play in sensory-motor integration, with tactile feedback essential in boosting neural activity in these two regions. This heightened response helps fine-tune motor functions in response to sensory stimuli, showing the complexity of sensory feedback and motor command mixing.

The interaction between the Area, task condition and touch highlights that for the dPMC, sensory input positively increased the neural activation during action imagination, requiring precision to utilize force and motor coordination to lift a glass. This improvement highlights the important role of sensory feedback during complex motor control. The results align with the study by Kazennikov et al., 1999 which showed an active sensory feedback integration of dPMC during the precise motor movement coordination, especially during fine motor skill learning paradigms (Kazennikov et al., 1999). Meanwhile, maintaining a static position and holding a glass did not exhibit significant effects, likely attributable to diminished motor activity reducing the distinction between touch and no touch influence.

This is in sharp contrast to the primary somatosensory cortex (S1), which showed a uniform enhancement in neural activity with the delivery of tactile feedback regardless of the motor condition, thus highlighting the invasive contribution of sensory feedback to motor output. Thus, this statement is proved by Overduin and Servos' work 2004 since they proved that the S1 is a basic element of processing investigational information in motor control, despite the character of the motor task itself (Overduin and Servos, 2004). Adapting to rather tactile feedback under various states could indicate a general processing system at work in which sensory

signals are assimilated to control motor functions or actions by the S1. These interaction effects, thus, capture the complexity of the relationship between tactile feedback, motor conditions, and brain region specificity. The enhanced response of the dPMC to the tactile feedback in maintaining accurate motor tasks emphasizes that this is a site for sensory-motor integration for complex actions. At the same time, the uniform impact of the tactile feedback on the S1 activity, regardless of motor conditions, underpins the basic aspect of the feedback role in motor control. These results demonstrate the dynamic nature of interactions between sensory stimulation and motor performance under the control of specialized brain regions adapted for role-task-related activity. Conversely, our findings reveal a notable distinction in the Vertex under static conditions, a phenomenon further elucidated through our detailed analysis of quadruple interactions.

Further results showed the complex interplay of how the performance of muscle tasks is influenced by tactile feedback, thereby showing that the nature of the activated brain regions, the nature of the muscle task itself, and the presence or absence of tactile feedback all have significant effects. This complexity highlights a more advanced sensorimotor integration process, in which the brain adjusts its response to sensory input precisely depending on the type of motor task and the muscles used. Some specific motor patterns, sensory signals, and muscle activation produce several increases in the activity of neurons, indicating the detailed interaction necessary for accurate motor control.

Our finding demonstrates that after inhibiting the dPMC, muscle activation significantly influences the action imagination of lifting while having touch or no touch. We observed activation across all three muscles studied: the primary muscle (First Dorsal Interosseous, FDI) and two control muscles (Abductor Digiti Minimi, ADM, and Extensor Carpi Radialis, ECR). As mentioned before, the lifting task demands increased force and muscle activation. Consequently, the significant rise in the amplitude of MEPs indicates enhanced motor circuit activation within the brain. This aligns with the findings of Devanne et al. (1997), who demonstrated that motor cortex excitability escalates with the complexity of a

motor task, reflecting the brain's adaptive mechanisms to facilitate task execution (Devanne, Lavoie, & Capaday, 1997).

Conversely, in the holding condition, no significant differences were observed in muscle activation among the FDI, ADM, and ECR muscles in both touch and no-touch scenarios. Interestingly, in the static condition, the ECR muscle—serving as a control—showed significant differences between touch and no-touch conditions. Although this finding may seem peripheral due to the muscle's role as a control, it subtly underscores the differential neural mechanisms engaged during static versus dynamic motor tasks.

Continued the same interaction, inhibiting the primary somatosensory cortex (S1) significantly alters the activation of the First Dorsal Interosseous (FDI) muscle while having no-touch and touch conditions during the imagined lifting and holding tasks. This effect highlights a pronounced muscle-specific response, with the FDI muscle being more involved in the imagined motor activities when compared to the Abductor Digiti Minimi (ADM) and Extensor Carpi Radialis (ECR) muscles. The FDI muscle, more involved in the action imagined than ADM and ECR muscles, produced higher MEPs, indicating a consistent muscle-specificity effect. Such phenomenon demonstrates a subtle interaction between motor imagery and neuromuscular activation so that the imagined motor tasks can increase corticospinal excitability in task-related and task-unrelated muscles to various degrees (Bakker et al., 2008). Higher MEPs amplitude has been shown in target muscle (FDI) during imagery finger abduction tasks (Hovington and Brouwer, 2010), which indicates influences of the task nature on the specificity of motor imagery effects on corticospinal excitability. In addition, prolonged training on a particular skill has been found to set a tone for variable motor cortex plasticity and increased corticospinal excitability in the appropriate muscles, emphasizing the specific neuronal process during motor imagery for motor synergies (Kumpulainen et al., 2015). This result is in keeping with the idea of muscle specificity in motor imagery and control, implying that the neural representation of different muscles varies depending on their role in the current task.

Moreover, the ECR muscle, serving as a control, showed significant variation in activation across all motor conditions, notably in relation to the ADM muscle during static conditions. This observation suggests an enhanced role of sensory processing in static conditions, potentially due to the lack of dynamic motor execution, which might amplify the sensory feedback mechanisms.

When we applied inhibition to the Vertex as a control area, our observations did not reveal any notable differences overall. However, a slight variation was noted in the Extensor Carpi Radialis (ECR) muscle during the Static condition. This outcome did not provide substantial insights into the neural mechanisms under investigation, primarily due to the ECR muscle's minimal relevance within our control design. Supporting this, research on cortical stimulation and muscle activation patterns underscores the specificity of motor cortex contributions to different muscle groups and tasks. For instance, studies by Coxon et al. (2006) and others have shown that the primary motor cortex and connected areas have distinct roles in motor control, with variations in response depending on the targeted muscle and the nature of the task (Coxon et al., 2006). This specificity might explain why inhibiting a control area like the Vertex does not yield significant changes across muscles or provide clear insights into the neural mechanisms, especially when considering muscles not directly involved in the primary tasks being studied. Moreover, the selective impact on the ECR muscle, while minimal, aligns with findings from Matsumura, Sawaguchi, and Kubota (1992), who discussed the nuanced effects of cortical stimulation on motor activity, suggesting that even subtle changes could be part of a complex neural interaction network (Matsumura et al., 1992). However, the relevance of these subtleties in understanding broader neural mechanisms remains limited, particularly when the changes occur in muscles that do not play a central role in the designed control conditions.

Furthermore, additional perspective about touch is in line with current studies, which have invariably established that tactile feedback is critical to establishing motor control through the facilitation of neuroplasticity and informing special regions of the brain on executing motor commands under different stimulation demands. For example, research has shown that tactile feedback is very capable of

modulating motor performance and that the primary motor cortex (M1), the primary somatosensory cortex (S1), and the dorsal premotor cortex (dPMC) are key areas for processing information from feedback, and integrate this with commands for voluntary movement (Jones and Lederman, 2006; Proske and Gandevia, 2012). These regions interact to guarantee rapid modification of motor action plans according to environmental feedback, ensuring optimal interaction between the body and the surrounding world (Wolpert et al., 1995). In addition, the importance of the tactile effects response of the brain, found in our results, is consistent with the compliant neural models of sensorimotor integration, suggesting that the brain uses predictive coding for anticipating the sensory consequences of motor actions to improve the economies, and the accuracy of motor output (Wolpert et al., 1995). This adaptative power is important for performing convoluted motor duties, thereby permitting motor desires to be tweaked in reply to the stream of sensory information.

However, there are also a few methodological weaknesses in the study. The principal limitation is the small sample size, which may hamper the ability to generalize the results that may be biased and lack generalizability. Even though the task selected is quite specific, the application of alternative tasks might better include the complexity of the phenomena examined. Besides, there are inherent limitations when using Transcranial Magnetic Stimulation (TMS) and continuous Theta Burst Stimulation (cTBS) techniques. These consist of spatial resolution for the stimulation, as it is currently not accurate to the desired sites in the brain, and the inconsistency among individual responses again leads to inconsistencies in the data. These methodological constraints underscore the essential need for a cautious interpretation of the findings of the study and the necessity for conducting further research with larger sample sizes with a greater variety of tasks to confirm and build on the results.

To conclude, our study offers highly insightful information into the detailed workings of sensory-motor integration, where the S1-dPMC-M1 neural circuits play pivotal roles in executing grasping actions. In a series of experiments, we have shown that the presence or absence of tactile feedback profoundly affected neural activity under different motor conditions and within different brain regions.

Our results thus highlight the subtle interactions between the type of motor task, sensory feedback, and the muscles' identity, indicating the brain's advanced ability to orchestrate neural activity based on these parameters. This study showed us that motor control can be improved by using tactile feedback and demonstrates how the brain can adapt to different motor executions and functions of different brain areas in unifying sensory information with motor commands. Ultimately, these findings improve our understanding of the complex mechanistic operations that drive motor implementation and control and underscore the complexity of the sensorimotor interaction within the human brain.

Chapter 5:

Epilogue

The objectives of the present Ph.D. thesis were to reveal the neural foundations governing tactile feedback's role in motor control, specifically how tactile sensations affect force scaling, cortico-spinal activity during imagined force generation, and the subtle mechanisms of grasping. This comprehensive investigation focuses on the integration of somatosensory feedback within critical motor regions: the first motor area of the cortex (M1), primary somatic sensory cortex (S1), and dorsal premotor cortex (dPMC), thus improving our knowledge of sensory-motor interplay. For this purpose, three different studies were conducted.

The Impact of Tactile Feedback on Motor System Excitability and Force Scaling in Action Imagination:

In the initial experiment, we investigate the neural mechanism responsible for how tactile feedback influences forceful action control. This study was more specifically aimed at elaborating on the role of tactile information during the scaling of force in action imagination. In these studies, the participants were required to mentally simulate exerting varying force levels with their index fingers (at approximately ~1N and ~15N), with and without the touch of a hard surface. The study was focused on evaluating the excitability of the motor system during these imagined movements using a single-pulse TMS technique and measuring the amplitude of the evoked MEPs in accordance with a paradigm described by Farzan 2014 (Farzan, 2014).

Accordingly, the results were all consistent with our original hypothesis, and the MEP amplitudes were significantly larger in the condition of action imagery with tactile contact compared to those without tactile contact. Such influence was especially strong in the muscle First Dorsal Interosseous (FDI), which is focal to mentally performed action, which indicates the muscle-specific character of the

action of cutaneous contact. In addition, the study revealed that the imagination of a greater force applied (~15N) produced larger MEP amplitudes compared to the imagination of a lesser force (~1N), and this effect was even magnified by tactile contact. This similarity of muscle activity pattern was also observed between mental images of actions and real execution of the same actions. This clearly indicated that the same neural mechanisms were involved in both mental images and their actual execution.

Notably, the decision to concentrate on action imagery rather than real performance had a strategic underpinning since potential confounding factors could impede the highlight of the specific impacts of tactile feedback on motor control. The feasibility of this approach stems from a line of research evidence that points to an overlap in the neuromotor pathways and patterns of motor system activity between action performance and 'imagining' them, albeit with rich differences in the extent of activation that occurs with actual force application and its imagining side (Kasai et al., 1997; Fadiga et al., 1999; Hashimoto & Rothwell, 1999; Li et al., 2004). The present similarity further underpins the idea that an imagined action is a sound' mirroring schema' of the performed action and is thus a valid platform for probing the sensory-motor integration without the physical implementation of the action.

The significance of this research is its refined analysis of how tactile information uniquely modulates the excitability of the motor system and force scaling during action mental simulation. The study provides original conclusions to the functional significance of M1 neurons activated by cutaneous inputs when dissociating the effects of assistance for touch from those of force production, as previously proposed by Picard and Smith (1992) (Picard and Smith, 1992). Thus, their work revealed adjustments in the functioning of motor neurons, which were associated with the generation of force as monkeys manipulated objects characterized by different textures and weights; this study accentuated the relevance of the discussed tactile feedback in force production. This study generalizes this knowledge to human subjects and the domain of mental actions, showing that tactile stimulation, irrespective of the absence of direct manipulation of objects, increases excitability of the motor system at the level of muscles. This

result highlights the complex link between touch sensitivity and littoral control and can be virtually used in several areas, such as rehabilitation, and feasible brain-control motivation outline.

Deciphering Touch Types: How Biological Interactions Elevate Motor System Responsiveness:

Our second experiment broke new ground on the analysis of separate aspects within which different haptic inputs modulate neural cortico-spinal activity during motor imagery of force production. The nature of this study is crucial because it structures the explanations of the subtle relationships between sensory experiences and motor system responses, paying considerable attention to the impact of touch types while imagining actions. The research accurately distinguished the conditions of Self-Touch, We-Touch, Surface Touch, and No-Touch, utilizing transcranial magnetic stimulation TMS to stimulate activity in the First Dorsal Interosseous FDI and the Abductor Digiti Minimi ADM muscle. This strategy played a key role in separating the roles of sensory and motor elements in cortical activity, particularly in the primary motor cortex (M1).

The study aimed to separate the effects of the sensory component on motor system activity, thus eliminating the potential for avoiding the confounding factors that are present when performing physical action. This was done by coupling action imagination with changing tactile stimuli. This methodological decision is critical to shed light on the process of sensory-motor integration, as this way, it is possible to investigate more reliably the separate roles of touch and force production.

The findings of the study supported the hypothesis of the enhancement of the motor system excitability in conditions of tactile stimulation, with a specific focus on the biological forms of the stimulation source (Self-Touch and We-Touch) as compared to the non-biological source or the effective absence of the sense of touch. This result is consistent with the other previous studies, for example, the work by Mizuguchi et al., 2013 and Ali et al., 2023 (Mizuguchi et al., 2013; Ali et al., 2023) in which they showed a facilitatory effect of touch on motor system

activation. With regard to higher force imagination tasks, such specificity of this effect is emphasized through the increased MEPs witnessed at the FDI muscle, further asserting the fact that the response of the motor system to tactile stimuli is not only global and selective depending on the muscle being stimulated and the nature of the action being imagined.

Therefore, the differentiation between various kinds of touch and their effects on the level of motor system excitability can be regarded as the first and most obvious contribution made by this study. Increased excitability, specific to ST and WT conditions, may indicate a more complicated role of somatosensory-and-motor initiating network interaction, which is influenced by the social and physiological background of touch. This is consistent with the larger body of literature on sensory-motor integration, which argues that tangibility matters for movement control, and its processing in the brain varies from one source of tangibility to another and in different contexts. For example, Delhaye et al. (2016) have considered the optimization of tactile acuity via action, and they emphasized the predictive mechanism that adapts movement variables through tactile feedback (see review Delhaye et al., 2016).

A review of contemporary literature will help to better define the logical grounds of the research's approach as well as the vision that was used for making the findings. Studies on the neural mechanisms of touch and action, through works such as Lederman and Klatzky 1987 and Chapman 1994, have demonstrated that tactile sensations can have manifest motor organization and implementation (Lederman and Klatzky, 1987a; Chapman, 1994). These results also clearly indicate that any touch stimuli, the self-produced ones or delivered by the experimenter, are utilized by the motor controller to make the action more beneficial. The present study improves this comprehension by revealing that the thought of movement in combination with tactile stimulation preserves the ability to regulate motor system activation. It reflects the highly context dependent nature of the brain to integrate sensory information with motor plans through specific local changes.

Also, the fact that different effects are seen between Self-Touch and We-Touch conditions vs Surface Touch and No-Touch conditions highlights the biological context of touch. This is evidenced by the studies that have been conducted in relation to affective touch and indicated that the processing of social touches as well as self-touches are also different at brain level thus having some implications on emotional and social communication (Boehme et al., 2019). The findings of this study fill a gap of this knowledge since they indicate that these differences also apply to the modulation of excitability in motor system and thus provide a neural component of approach that combines affective and sensory information both for controlling movements.

This study provides an interesting view of the sensory-motor integration process and, specifically, shows the role of touch in regulating motor system performance. By employing a rigorous methodological approach and grounding its findings in the context of existing literature, the study contributes further to our understanding of how the brain manages to combine sensory information with motor signals, thus facilitating the further exploration of the neural effects behind the process of sensory-motor unification and the emotional connotation of touch.

Selective Inhibition of S1 and dPMC Sheds Light on Pathways Orchestrating information to M1.

The third experiment that we conducted addresses the complex interplay among the primary motor cortex (M1), the primary somatosensory cortex (S1), and the dorsal premotor cortex (dPMC)– brain areas that are associated with the development of grasping actions. This study seeks to advance this since lots of foundational studies have offered knowledge regarding the dynamic relationships amid these regions in acts involving motors, focusing on the integration of sensory inputs used to regulate the execution of movements. This study does not replicate previous research but provides a novel contribution to the field; it closely examines how these brain areas cooperate to achieve the complex process of precision grasping, moving beyond previous studies by applying inhibitory techniques to tease apart the specific contributions of each area.

Our research aimed to uncover how neural circuits involving M1, S1, and dPMC support the execution of grasping actions through imaginative tasks. Respondents are tasked to describe that they do something, for example, lifting, holding a glass, or something similar, that requires the work of muscles, some of which were control muscles. This permitted us to study the functional connectivity of these areas in a non-moving state through non-invasive methods like Transcranial Magnetic Stimulation and Continuous Theta Burst Stimulation, whereby their significant occurrence in Motor Imagery would be investigated.

By conducting two distinct experiments – one assessing the baseline excitability of M1 during imaginative tasks and the other examining the impact of targeted cTBS on brain regions, we reveal insights into cognitive activities in motor imagery, particularly precision grip. We learned that selective inhibition of areas such as S1 and dPMC will not only affect the performance of the task but also show us the patterns through which motor commands are relayed to M1. The findings of this research demonstrated a marked increase in neural activity levels between motor conditions in terms of lifting, holding, and static. The lifting condition that required the most muscle engagement had high MEP amplitude, indicating vigorous neural engagement. The holding condition was less demanding than the lifting, as witnessed by the higher amplitude of MEPs elicited under static conditions but lower than in lifting. This pattern of results highlights the vibrancy of the brain's response given the complex nature of the motor tasks, with the static condition and minimal muscle effort reflecting the lowest level of neural activation.

The research also accentuated the significance of tactile input in controlling neural activity. Tactile feedback significantly increased MEP amplitudes pointing out the role of sensory information to perfect motor regulation. This improvement indicates that the brain combines with the motor gesture from the touch cues to help in optimizing the movement, a process that is essential for accurately and consciously performing an organized action. Additionally, our data indicated brain area–dependent responses to somatosensory feedback by dPMC and S1, respectively. For active manipulation tasks, such as lifting, the dPMC – an essential void that is responsible for the initiation of movement and movement

itself – showed a strong response to tactile feedback. This answer emphasizes the function of the dPMC in the processing of external cues to guide the motor plan. The S1 region, which is involved in the processing of sensory feedback from the body, demonstrated greater positive activation with tactile feedback regardless of motor condition, highlighting its importance in sensory motor integration.

The study revealed significant interaction effects; this means that the contribution of the afferent stimuli to neural activity was different in the different motor conditions and brain regions. For instance, after implementing tactile feedback, a significant increase in neural activity within dPMC was observed during lifting as an indicator of the importance of sensory stimulation in accurate motor output. In all motor states studied cutaneous tactile feedback effectively increased neuronal activities in the S1, underscoring the general role of sensory feedback during the adjustment of motor output. Lastly, the study revealed that muscle responses to tactile feedback are profoundly influenced by the engaged brain area, the motor condition, and the tactile feedback presence. This complexity illustrates the sophisticated nature of sensory-motor integration, where the brain's response to sensory input is finely calibrated based on the motor task context and the specific muscles involved.

Concluding remarks

In this Ph.D. thesis, we pushed the boundaries to comprehend the complex modulation of motor control by tactile feedback, untangling the web of sensorimotor integration and unmasking neural mechanisms. Therefore, our study was not limited only by the determination of the effects of somatosensory stimulation on the motor excitability and force scaling of the downstream effects as it synthesized these peculiarities into the comprehensive narrative structure of the relationships between the M1, S1, and dPMC.

The originality of our finding is that we understand that tactile feedback, particularly of a biological nature, enhances motor system excitability. This enhancement, however, is not uniform across all touch modalities. Notably, increases in motor excitability were significantly more pronounced during self-touch and interpersonal touch compared to non-biological or absent touch

conditions. This distinction underscores a critical insight: the brain has developed a rather complex mechanism for processing tactile inputs and coaching motor responses to synaptic input patterns.

Additionally, our study fills the space between tactile feedback and motor imagery, explaining that kinesthetic touch specific to motor imagery could facilitate MEPs in target muscles and highlight the possibility of the perfect force scaling by the motor system even without movement. This implies the possible use of tactile feedback to improve motor control. This is a good indication and an interesting area of research for focusing on the developments of rehabilitation technologies as well as the designs of prosthetics that are more responsive and even those of the brain-machine interface.

Further, our investigation of the functional connectivity of M1, S1, and dPMC during grasping tasks enhances our knowledge, demonstrating the way the regions contribute to support the complicated process of forming the grasping. This understanding of the neural circuitry that sustains the grasping execution emphasizes that the sensory response is a critical constituent of motor control, suggesting that habitual motor function engrosses a vibrant conversation between sensory input and motor output within these primary motor areas.

Overall, the outcomes of our research contribute a novel and significant body of knowledge to the field of sensory-motor integration, offering a fresh perspective on the principles of tactile feedback in motor control. In emphasizing the contrasting impact of tactile feedback, the value of sensorimotor integration, and the practical implications offered by our discoveries in rehabilitation and technology, we provide a unique and valuable synthesis to sensory-motor neuroscience. This research not only contributes to knowledge about the neural processes involved in controlling movement but also paves the way for strategies to improve human engagement in the physical and social environment.

Future research direction

Although this intense focus on motor imagery is critical to the isolation of the neural mechanisms of touch and action, it also raises issues with the ecological

aspect of such findings. The question of how imagined actions translate into real actions is critical.

In this technique, motor imagery is the mental simulation of movements in the absence of their actual execution. Researchers can study neural processes unconfounded by muscle activity through this.

However, accurate motor control of the outside world is a complex and dynamic interaction between the senses and acts, not perfected in motor imagery studies. Indeed, proprioceptive feedback, environmental variability, and physical constraints play significant roles in actual movements and are largely negated or minimized in motor imagery. This discrepancy might significantly reduce the possibility of generalization from the findings to the control of real-world movements.

For instance, motor imagery will only provide insight into how the brain plans and sequences a movement. Still, it will not capture the actual adaptive mechanisms the brain uses to react to unexpected changes or errors introduced during the actual movement. The neural activation patterns observed during motor imagery may differ in magnitude and spatial distribution from those seen during accurate motor execution, further affecting the interpretation of sensorimotor integration processes. Future research should combine motor imagery with tasks that involve movement so that the findings can be validated and extended. Tasks of real-world motor planning alongside imagined action can then serve to evaluate precisely how well the findings for motor imagery transfer to real-world tasks. In addition, VR environments can replicate real-world conditions in which researchers can maintain experimental control.

It enables immersive and interactive experiences that closely mimic real-world motor tasks, providing a halfway house between pure motor imagery and physical execution. In this way, researchers will be able to investigate similar and different aspects of imagined and actual moves in natural contexts. The neural mechanisms for touch and action, as found through motor imagery research, could represent a valuable step in better understanding the ecological validity of the findings. Combining motor imagination paradigms with everyday real-world tasks and

state-of-the-art technologies, the application to the ecologically valid scenarios of everyday motor control will improve, thus gaining a fuller understanding of sensorimotor integration.

Future research must understand how attention on different tasks, for example, the tactile sensation or imagined movement of one's hands, affects the neural response and sensorimotor integration. What is truly needed is an insight into such interactions, providing critical information on how the attention shifts interact with the temporal evolution of touch-induced effects and, specifically, the inhibition of brain areas. For example, increased attention to tactile sensation may induce higher precision on neural responses and higher sensitivity in somatosensory regions. Inversely, imagined movement may result in more excellent motor planning and execution strength.

Of no less importance is the investigation of the specificity of touch modalities to these domains, including texture, temperature perception, and vibration, which are likely to affect motor imagery and sensorimotor integration differentially. Texture perception might be underlain by fine-grained sensory processing in the somatosensory cortex, while temperature changes are bound to activate different thermal receptors and pathways. In contrast, vibrations may affect proprioceptive feedback mechanisms and motor control. In this way, their diversity in characteristics might reveal various facets of neural plasticity and integration.

In addition, research should tap beyond the current focus on the primary motor cortex (M1), the primary somatosensory cortex (S1), and dorsal premotor cortex (PMC) for the involvement of other brain regions. For example, the parietal cortex could play an essential role in integrating sensory information and in the planning of the motor system. In contrast, the insular cortex could be crucially implicated in interoceptive awareness, for instance. Combining such areas would allow a comprehensive understanding of the neural circuitry underlying touch and motor imagery.

It is also essential to consider that individual differences might interfere with the outlined roles. Touch and action imagination might block operational variables, such as age, expertise, and personality traits. Older adults can show different

patterns of neural plasticity compared to young people, which could affect their sensorimotor integration capabilities.

Similarly, people with specific skills in any of the tasks that are tactile or motor may present with better neural responses and more effective integration. Even the personality type, sensory processing sensitivity, could lead to different perceptions and reactions to touch and imagery of movements. A comprehensive approach that integrates these diverse factors will further deepen our understanding of the neural mechanisms underlying sensorimotor integration and could provide personalized therapeutic strategies. Tailored interventions, for example, for enhancing motor recovery in stroke patients or improving motor skills in athletes, could consider specific attentional focus, touch modality preferences, and individual characteristics.

As I neared the end of my thesis, my mind wandered back to the recollection I had recounted in its introduction - the tale of Volleyball. This narrative ignited my entire scholarly journey. In the opening paragraphs of my thesis, I depicted the profound impact that the touch of volleyball had on my mind and heart. It was as though that single touch whisked me away to a faraway beach, where I could envision myself sprinting along the coastline, relishing the sensation of sand beneath my soles, and basking in the tranquil symphony of crashing waves upon the shore.

As I conclude my thesis, I want to emphasize that everything unfolded as a result of my detailed explanation of the brain circuits' complex mechanisms. Specifically, by bringing the sensory and motor areas into play, a touch could trigger a vibrant imagination and a stirring of interconnected pathways within your mind. This experience kindled an intense yearning to relive the beach once again and establish a profound connection with nature in its purest state.

Finally, this thesis became a testimony to the power of knowledge about incredible mechanisms in minds. It pointed out the great power a single tap and an active imagination, if interconnected with an understanding of brain wiring, could have on one's mind and emotions. It reminded us that, on occasions, it is enough for

inspiration to create a spark and awaken the hidden potential of our mind to set our soul on fire, allowing us to discover ourselves again in pursuit of passion and satisfaction.

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