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REVIEW

Research Progress on Neural Processing of Hand and Forearm Tactile Sensation: A Review Based on fMRI Research

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Abstract: Tactile perception is one of the important ways through which humans interact with the external environment. Similar to the neural processing in visual and auditory systems, the neural processing of tactile information is a complex procedure that transforms this information into sensory signals. Neuroimaging techniques, such as functional Magnetic Resonance Imaging (fMRI), provide compelling evidence indicating that different types of tactile signals undergo independent or collective processing within multiple brain regions. This review focuses on fMRI studies employing both task-based (block design or event-related design) and resting-state paradigms. These studies use general linear models (GLM) to identify brain regions activated during touch processing, or employ functional connectivity(FC) analysis to examine interactions between brain regions, thereby exploring the neural mechanisms underlying the central nervous system's processing of various aspects of tactile sensation, including discriminative touch and affective touch. The discussion extends to exploring changes in tactile processing patterns observed in certain disease states. Recognizing the analogy between pain and touch processing patterns, we conclude by summarizing the interaction between touch and pain. Currently, fMRI-based studies have made significant progress in the field of tactile neural processing. These studies not only deepen our understanding of tactile perception but also provide new perspectives for future neuroscience studies.

Keywords: neural processing mechanism, tactile perception, functional magnetic resonance imaging, review

Introduction

Tactile perception is one of the important ways through which humans perceive information about their external environment. It represents the earliest method by which individuals understand their bodies and connect with the world around them. The tactile sense enables humans to perceive important details about objects, including shape, texture, temperature, and other important information through touch, forming a fundamental basis for interaction with the surrounding environment. Concurrently, tactile perception plays a crucial role in motor performance and control. It can both facilitate and disrupt motor processes depending on various factors such as the nature of the tactile stimulus, the context of the motor task, and the individual's state of neural adaptation.[1,2] Furthermore, it is posited that social contact, which transcends verbal communication, serves as a potent vehicle for expressing emotions and conveying authentic intentions. Extensive animal studies underscore the profound effects of early physical contact on both neurological development and lifelong behavior.[3,4] Harlow's classic sheds light on the impact of a lack of comfortable and caring touch on young monkeys, revealing that it can lead to psychological stress, making them irritable and aggressive as they

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mature.[5,6] In humans, parental touch emerges as a critical factor in reducing an infant's physiological responses to stress and plays a crucial role in the normal development of the infant's nervous system.[7–10]

Touch, akin to other sensory modalities like vision and hearing, does not materialize spontaneously. Rather, it undergoes complex neural processing prior to converting external touch and pressure information into sensory signals.[11] The genesis of tactile sensation involves a complex interplay of neurophysiological processes. Low-threshold mechanoreceptors, located in the superficial layers of the skin, conduct non-noxious stimuli and constitute the foundation for afferent tactile information. These receptors respond to mechanical stimuli resulting from physical interactions such as pressure and vibration.

The Low-Threshold Mechanoreceptors (LTMRs) consist of the Merkel disc, Pacinian corpuscle, Meissner corpuscle, and Ruffini corpuscles. The Merkel disc, which is distributed in the epidermis, responds to sustained stimulation.[12,13] In contrast, the Pacinian corpuscle,[14] located in the subcutaneous tissue, and the Meissner corpuscle,[15] present in the dermis, are both responsive to transient stimulation. The Ruffini corpuscle, distributed in the dermis and subcutaneous tissue, shows a different response pattern, being sensitive to sustained changes in skin tension.[16] Merkel disc and Meissner corpuscles, characterized by smaller receptive fields, form the basis for perceiving skin light touch and roughness, with a higher density in areas requiring precise touch, such as fingertips.[17–19] In contrast, the Pacinian corpuscle, with its larger receptive field, excels in detecting high-frequency (20–1000Hz) vibrations. Ruffini corpuscles, on the fingers, demonstrate sensitivity to skin stretch, serving both as skin touch receptors and also responsible for proprioceptive function.[20–22] In hairless skin of healthy adults, Meissner corpuscles comprise approximately 43% of touch receptors, while Pacinian corpuscles make up about 13%. Merkel discs and Ruffini corpuscles represent approximately 25% and 19%, respectively, of the total touch receptors.[23] A previous study[24] demonstrated that receptor density increases significantly from proximal to distal regions, with a significant increase at the fingertips. The relative densities of receptors in the palm, fingers, and fingertips are approximately 1, 1.6, and 4.2, respectively. Merkel disc and Meissner corpuscles primarily contribute to these density variations, whereas the distribution of Pacinian corpuscle and Ruffini corpuscles shows little difference from proximal to distal regions.

The classic touch signal transduction pathway posits that LTMRs receive diverse tactile signals and convert physical forces into neuronal signals.[25] Subsequently, these signals are conveyed from the periphery to the spinal cord via afferent fibers, such as the thick myelinated Aβ fibers or thin unmyelinated C-tactile afferent fibers (CT fibers).[26,27] Aβ afferent fibers serve as the main discriminative touch receptors distributed throughout the body. While CT afferent fibers are distributed on hairy skin, their presence on glabrous skin remains unclear, additionally, the function of CT afferent fibers is related to the transmission of social interaction, interpersonal relationships, and affective touch.[28–31] Following the transmission of tactile signals to the spinal cord, the pathway predominantly involves the posterior cord and the cuneate nucleus, crosses the medial lemniscus, and reaches the ventrolateral nucleus of the thalamus.[32] Finally, tactile information is projected to the cerebral cortex for representation and processing, particularly in the somatosensory cortex.[33–35]

Histological studies have provided the cutaneous physiological basis for touch production. Penfield et al[36] mapped the cortical sensory homunculus in the last century, determining the distribution of human sensory processing in the Primary Somatosensory Cortex (S1). However, as neurofunctional imaging technologies like functional Magnetic Resonance Imaging (fMRI) gained prominence researchers discovered representation of tactile stimulation signals is not confined to a specific functional area of the brain. It involves multiple neural functional networks such as cognition and emotion.[37–39] Consequently, the exploration of the central integrated and processing mechanism of tactile information remains a challenging issue.

fMRI is one of the most commonly used neurofunctional imaging techniques due to its non-invasiveness, non-radioactivity, and high spatial resolution. It reveals how the brain responds to and processes tactile information in different parts and forms. By observing activity changes in specific cortical areas of the brain under tactile stimulation through fMRI, the neural basis for tactile perception can be inferred. Therefore, fMRI emerges as an effective research tool for gaining a deeper understanding of how the brain perceives and processes tactile information.

Tactiles play an important role in object recognition, awareness of the current environmental state, and social and emotional communication. Therefore, studying how the healthy brain executes the processing of tactile perception forms the basis for understanding sensation and behavior. Moreover, investigating aberrant sensory processing in pathological conditions offers potential targets for clinical neuroregulation. Hence, the depiction of the somatosensory cortex is vital for comprehending the neural underpinnings of human somatic sensation. This article provides a brief overview of the basic principles of fMRI, summarizes the current findings of fMRI touch research, and elucidates the central nervous

system processing mechanisms of different aspects of touch. The possible pathological mechanisms of tactile impairment caused by some diseases are also summarized. Additionally, recognizing that pain induced by external nociceptive factors might share a processing pattern similar to touch in the human brain,[40] this article further explores the interaction between touch and pain based on a review of tactile neural processing.

The Principle of fMRI and Its Experimental Paradigm in Tactile Research

fMRI uses changes in blood oxygen concentration levels as an indicator of neural activity. When neural activity increases, the surrounding blood flow also increases to supply more oxygen, resulting in an increase in oxyhemoglobin levels in the local blood and a change in magnetism, producing a Blood Oxygenation Level-Dependent (BOLD) signal intensity across multiple functional areas of the entire brain.[41,42] By exploring the changes in BOLD signal intensity in multiple functional areas of the whole brain, we can infer the functional activity of the corresponding brain areas.[43]

Functional connectivity(FC) refers to the linking of spatially separated brain regions sharing similar functional attributes, commonly characterized by the temporal correlation of brain activity patterns during neurophysiological events.[44] Resting-state fMRI measures the spontaneous neural activities of the brain when there is no specific task requirement. Such signals mainly reflect the coordinated activity patterns among different brain regions in the resting state.[45,46] In tactile research, resting-state fMRI can help us understand the strength and patterns of FC among tactile-related brain regions (such as the S1, S2, insula) when there is no tactile stimulation. These patterns may provide a basic neural activity framework for tactile processing. If abnormal FC is observed in the resting state, it represents an inherent disorder of the brain's neural activities. For example, in stroke patients, it has been found that the FC between the ipsilateral S1 and the contralateral S1 is reduced in the resting state.[47] This may indicate a decline in the brain's ability to integrate sensory information during the process of tactile perception. Even when no tactile tasks are being performed, such potential neural abnormalities can still be detected. Resting-state fMRI serves as a tool to assess the strength of functional connectivity between and within the cerebral hemispheres.[48,49] However, this paradigm is currently less frequently applied compared to Task-based fMRI in this field.

The main paradigm for fMRI in tactile research is Task-based fMRI. The design paradigm encompasses active exploration[50,51] and passive touch,[52,53] and the task or stimulus presentation types include block design[54,55] or event-related design.[56] Task-based fMRI, on the other hand, measures the brain's activity when subjects are performing specific tactile tasks.[57,58] The general linear model(GLM) is used to analyze the task-related activation signals. The activation signals at this time reflect the reactive neural activities of the brain in response to specific tactile stimuli. Such activities are mainly related to the sensory, motor, and cognitive processes associated with the tasks. The activation analysis of task-based fMRI can identify which brain regions are recruited and to what extent they are activated during specific tactile tasks. By comparing the differences in brain region activation under different task conditions, the dynamic processing process of the brain for tactile information can be revealed. For example, when subjects touch surfaces with different roughness using their hands, S1 will encode the physical properties (such as texture) of the tactile stimuli, and the degree of its activation is related to the intensity and complexity of the tactile stimuli.[59,60] Meanwhile, depending on the nature of the task, the activation of other brain regions may also be involved. Mapping the brain based on the hands and forearms is particularly convenient and effective, as these body regions offer excellent representation within the brain and are easily accessible physically.[61] Subjects often use their fingers or palms as active touch areas to investigate the brain activation areas involved in discriminative touch. Stimulation methods that can be applied in passive touch include manually operated stroke tools, (eg watercolor brushes,[62] brushes,[54,63] real hand touch[64,65]), air puffs, pneumatically driven stimulators,[66,67] and piezo electric devices.[68–70] These methods are adaptable for tactile stimulation on various areas such as fingers, palms, or forearms, making them suitable for both discriminative and affective tactile investigations.

Neural Processing of Typical Tactile Perception in the S1 Area Represented by Fingers

Fingers constitute one of the most sensitive parts of the human body and are frequently used to interact with external objects. The tactile mapping of fingers occupies a significant area in the cerebral cortex, underscoring the high sensitivity

and complexity of finger touch.[71] Researchers have been exploring the intricacies of finger tactile mapping, examining the spatial location of different finger mappings and their interactions with other sensory systems.[72,73] Accurate mapping of cortical responses to finger stimuli at the individual level is crucial for comprehending and delineating abnormal sensorimotor cortical function or cortical reorganization. This aspect is also significant for the clinical application of fMRI.

The main brain response to hand touch is localized in the contralateral S1 and bilateral S2.[74] The main tactile processing function occurs in the S1, while the S2 is responsible for surface texture recognition.[60] When fingers are stimulated, fMRI typically enables the differentiation of finger responses across various subregions of S1.[61] The S1 is divided into four sub-areas, namely Brodmann Area 1 (BA 1), BA 2, BA 3a, and BA 3b, with BA 3 receiving the majority of thalamocortical projections from sensory input areas.[75] BA 3a is believed to receive proprioceptive information from muscles and joints,[76,77] while BA 3b, BA 1, and BA 2 process signals from the skin.[78]

The arrangement of human fingers in the postcentral gyrus is orderly,[61] with the primary sensory areas mapping from the thumb (D1) to the little finger (D5) in a continuous representation from lateral-anterior-inferior to medial-posterior-superior.[79,80] The BOLD signal strength of the thumb in S1 is the highest among all fingers, with higher stimulus selectivity,[72,81] followed by the ring finger (D4) and the index finger (D2).[71,82] This outcome is attributed to the thumb's greater functional demands for tactile exploration and fine movements, leading to more neurons responding in the S1 and a larger cortical volume. In other fingers, the cortical representation size correlated with finger length.[83] Although there are differences in the dominant hand, tactile perception sensitivity remains independent of hand dominance. Fingertip perception ability is similar between hands, and the finger representations' positions are generally comparable.[82] Furthermore, several investigations have been conducted to map the positions of tactile perception of various finger phalanges in BA3b. A previous study[68] indicated that the Euclidean distance between the area of the palm beneath finger and the activation peak of the distal phalanges is 5.0 ± 0.7mm in D5 and 6.7 ± 0.5mm in D2. These distance measurements provide a quantitative understanding of the spatial relationships between palm and finger activation areas. Schweisfurth et al[69] employed a Piezo-electric device to stimulate the phalanges of all fingers in the right hand and the corresponding areas of the palm beneath each finger. Their study revealed a continuous arrangement of homologous phalanges from medial to lateral, spanning from D5 to D1. This finding facilitates the establishment of a finger mapping atlas in BA3b. However, only an organized arrangement from the first to the third phalange was observed on D5. The BOLD response in BA3b exhibits strong finger-selective effective compared with other areas,[79] and the average cortical thickness in response to finger activation in this area is 1.75 ± 0.5 mm.[84] This suggests that this area is highly specialized for processing tactile information from the fingers. Martuzzi's study[83] investigated touch sensation on the distal two phalanges of the right-hand fingers in healthy individuals. It revealed that the brain representation of finger touch was most extensive in the BA3b region, spanning a distance of 15.5 ± 2.4 mm from Digit 1 to D5. This was followed by BA1 and BA2, with distances from D1 to D5 measuring 15.1 ± 4.3 mm and 8.6 ± 4.2 mm, respectively. Schweisfurth's study,[69] on the other hand, found that in BA 3b, the mapping distance between D1 and D5 was 16.7 ± 4.2 mm in the first phalanx, 14.7 ± 7.0 mm in the second phalanx, and 18.0 ± 3.2 mm in the third phalanx. The variation in mapping distances between different phalanx in BA3b may represent the complexity and specificity of neural processing in this region. Although the results of this study are not entirely consistent, they reflect a relatively stable range of finger mappings within the S1 subregion. The inconsistency in results can be attributed to several factors. Firstly, individual differences among subjects highlight the need for larger sample sizes in future studies to account for variability. Moreover, variations in detection and statistical methods can influence the identification of finger mapping overlap areas, potentially diminishing the detectability of overlapping activation.[85] Consequently, the measured distance of finger representation at BA3b may not align completely. Moreover, since the BOLD response serves as an indirect measure of neuronal activity, it can introduce spatial blur and broaden the spatial range of representation. Therefore, higher magnetic field strength is necessary to enhance BOLD contrast.[86] The above results highlight that the region of finger touch is mainly located in the BA 3b of the S1. The finger response area is larger, which implies greater sensitivity to finger touch. The brain's precise control of the fingers facilitates their engagement in more complex tasks. This underscores the close connection between fingers and brain areas, demonstrating that stimulation on the hands can regulate the activity of the corresponding brain areas. Sanchez-Panchuelo et al also found somatotopic maps in the BA3a

area of fingers in their study,[87,88] and speculated that the reason why other studies rarely found similar results may be related to statistical methods and stimulation patterns. Group-level analysis may be affected by statistical methods, which makes it difficult to reveal this fine-scale organization. In addition, BA3a does not respond as strongly to weak skin stimulation as area 3b and 1, and requires stronger skin stimulation to activate.

Neural Processing of Discriminative Touch

Touch, encompassing mechanical stimulation such as touch, sliding, and pressure, serves as a vital means for humans to perceive information about the external environment. Its uniqueness lies in its discriminative properties, enabling the identification of different objects and the perception of their properties through touch. This involves multiple aspects, including texture, shape, softness, stickiness.[89] The processing and integration of tactile discrimination of different object features primarily occur in the somatosensory cortex of the cerebral cortex. This cortex plays a pivotal role in the careful processing of tactile information, enabling the brain to generate more complex cognitions and experiences based on touch.[90]

Neural Processing of Tactile Surface Texture

One of the touch's primary functions is to identify objects, including size, material, hardness, smoothness.[89] The finger pads are particularly sensitive to discriminative touch.[17–19] Current research on discriminative touch commonly employs methods such as true hand touch, Braille, textured plastic samples, etc. The research typically involves two stages: the encoding stage, where different tactile stimuli are presented, and the recognition stage, where the test stimulus is assessed for its similarity to the encoding stimulus.[91,92] The complexity of the texture correlates with higher brain activation intensity, proportion, and percentage signal change.[75]

Research indicates[59,60] the involvement of the Primary Motor Cortex (M1), inferior parietal lobule, and supramarginal gyrus in tactile perception. However, the main information processing occurs in the S1. It was previously reported that tactile information is first received by BA 3b in the S1 sub-region, and then object size and shape information are projected to BA 2.[75] Another study on Braille recognition observed significant activation of contralateral BA 2 during tactile perception.[67] Further discrimination of texture information is completed by S2, mainly for parietal operculum (OP)1 and OP4,[60,93] and the somatosensory association cortex. While it is generally accepted that both contralateral S1 and bilateral S2 are activated in discriminative touch,[39,74,94] and the activation intensity of S1 on the opposite side during active exploration is higher compared with that of passive touch.[95] Unilateral touch stimulation induces a higher BOLD response in contralateral S2 during the encoding stage, with no difference observed in the recognition stage.[92] Ipsilateral S2 exhibits consistent activation level in both stages, and presents with psychophysiological interaction effects, representing an interaction between the time series of brain regions and task design variable,[96] observed with the contralateral Posterior Parietal Cortex (PPC) during the recognition stage. Previous studies suggest PPC's involvement in functions such as sensorimotor conversion of human movement planning[97] and decision-making.[51,98] Therefore, the functional network formed by ipsilateral S2 and contralateral PPC may play a key role in texture recognition. The activation pattern of finger tactile stimulation may also change with age. Brodoehl et al[99] found that the pattern of decreased S2 activation and increase S1 activation in the elderly aged 62–71 years was similar to that in young adults aged 21–28 years. Another study[53] speculated that this phenomenon may be related to the aging trajectory.

Furthermore, the prefrontal cortex, particularly the dorsolateral prefrontal cortex (DLPFC), plays a pivotal role in tactile recognition and decision-making.[100,101] Stoeckeletal's study[102] indicated that activation of the contralateral prefrontal and parietal lobes during tactile tasks may be associated with short-term storage of somatosensory information, while activation of the ipsilateral prefrontal lobe occurs during tactile object discrimination. Similarly, Hartmann et al,[51] employing active exploration of objects with the right hand as a task stimulus, suggested that the ipsilateral DLPFC might be involved in decoding and retrieving stored surface features from working memory. Given the disparate findings, it remains unclear whether tactile decision-making following texture recognition predominantly relies on the ipsilateral or contralateral frontal lobe. Further research is warranted to elucidate this matter.

Neural Processing of Sticky Touch

When fingertips come into contact with a sticky surface, separation generates a sticky feeling due to the mechanical stimulation caused by skin deformation, allowing the sensing of sticky information.[103] Surface stickiness, a type of object texture, undergoes tactile neural processing with S1 as the main sensory area:[104] The sticky stimulus information is then transmitted to adjacent areas (for example, S2, PPC) for high level processing. Kim's study[105] reported unexpected engagement of the Inferior Frontal Gyrus (IFG) in tactile stickiness perception, a region conventionally linked with language processing. The IFG is an important sensorimotor circuit[106] and has been linked to the motor observation-execution system,[107,108] which may explain why sticky touch elicits a response in this region. In a study by Yeon et al,[56] significant activation of the ipsilateral DLPFC and bilateral insula cortex was observed in response to sticky stimulation. Similarly, Sasaki et al[109] reported significant activation of the middle frontal gyrus and insular cortex during active grasping of a sticky ball. The involvement of these brain regions may contribute to discerning various levels of tactile stickiness. Furthermore, varying degrees of pleasant or disgusting emotions caused by the perception of sticky touch may lead to different levels of activation in the insular region.

Neural Processing of Tactile Softness

Beyond the somatosensory area,[93] brain areas related to softness discrimination include the insula, medial superior frontal gyrus, parietal operculum, putamen, cerebellum, etc. These areas constitute the brain network involved in processing softness perception.[110] Finger discrimination of object softness arises from differences in force feedback to the finger caused by surface deformation.[111] The neural signal, generated by changes in stress levels due to object touch, is transmitted to the brain, resulting in corresponding BOLD signal changes.[75] The brain network then processes this information, leading to the perception of softness. Studies have demonstrated that the intensity and spatial distribution of activation in specific brain regions can reflect the perception of stimuli in the human brain.[59] It has been observed that soft objects are typically perceived as more pleasant than hard ones,[112] suggesting a dual response of the insula to discriminative touch and affective touch. Few neuroimaging studies have explored the brain networks underlying tactile softness perception. Kitada[113] conducted passive stimulation of the right middle finger to study the brain network mechanism of softness discrimination. The results confirmed that the insula and parietal lobe are key brain regions for processing softness information of touch materials. Kim et al[114] also found similar results, indicating the involvement of the posterior insula in the right hemisphere in discriminating the hardness of objects. The difference is that Kim also reported activation of the right posterior lobe of the cerebellum. The difference between the two studies may be attributed to Kim's active touch test, while Kitada performed passive recognition. Therefore, it is demonstrated that the ipsilateral cerebellum also plays a very important role in discriminating softness through active touch. Sasakietal[109] also concluded that the cerebellum may be involved in object softness perception based on results from an active grasping study.

Differences Between Active and Passive Touch in the Discriminative Touch

In the field of discriminative touch research, active and passive touch exhibit differences in several aspects. These differences are crucial for a deeper understanding of the neural mechanisms and behavioral manifestations of tactile perception. Active touch involves a more complex neural activity network. When an individual actively touches to identify the characteristics of an object, the brain not only processes tactile information from skin receptors but also integrates proprioceptive information from the motor system and commands related to motor intentions. Research shows that the activation of S1 during active touch is significantly stronger than that of passive touch.[95] Compared with passive touch, active touch elicits more extensive and scattered brain activities in areas outside the somatosensory region, including the cerebellum, lenticular nucleus, some areas of the frontal lobe, the Supplementary Motor Area (SMA), and the parietal lobe.[95] These areas are related to motor planning, control, and coordination. Similarly, Sasaki found that in all active grasping tasks, the precentral gyrus (including M1) and the external part of the cerebellum were significantly activated.[109] These results reflect the close interaction between the motor and sensory components during active touch, such as motor planning, coordination, and sensory feedback from the skin, which is closely related to high - level cognitive functions. In contrast, passive touch mainly relies on the direct reception of external stimuli by S1 and S2.[75,92]

During passive touch, the brain does not need to perform complex motor planning and control, so the activation strengthen and extent of related brain regions are limited. For example, Ackerley[115] found that when actively touching the palm and arm, a significant positive BOLD signal appeared in the left cortical network (including S1, M1, PMC, and the somatosensory association area). When passively touching the palm and arm, a significant negative BOLD signal was presented in the S1, covering most of the S1 area and extending to the M1. This difference further highlights the essential distinction in neural mechanisms between active and passive touch.

Neural Processing of Affective Touch

Touch serves as a means to express emotions such as intimacy, kindness, and tenderness. Animals can make tactile contact through head contact, licking, and grooming. Similarly, humans can transmit these emotions through gestures like hugs, caresses, and handshakes, with the brain processing emotional information in social behavior. Prolonged exposure to affective touch in children may facilitate the development of the "social brain", particularly the mentalizing network.[116] Enhancing our comprehension of the brain's functional mechanisms in response to affective touch could aid in alleviating stress, pain, anxiety, depression, and other mental health conditions. Furthermore, this understanding could offer valuable insights into disorders such as autism, depression, and chronic pain, potentially enhancing the therapeutic benefits of affective touch.

Affective touch is an act that elicits an emotional response and typically possesses social characteristics.[117,118] Social touch refers to tactile behaviors associated with social interactions and relationships, conveying emotion and fostering connections. Social touch and affective touch are often related, both involving physical contact to build relationships, convey emotions, and maintain social connections.[119,120] The encoding of this type of tactile information differs slightly from other sensory information. In addition to the somatosensory cortex, it is mainly facilitated by the insula, Anterior Cingulate Cortex (ACC), Orbitofrontal Cortex (OFC), posterior Superior Temporal Sulcus (pSTS), and other social sensation and cognition region-related representations.[52,121]

The sensory discrimination and somatosensory network activation of children and adolescents are similar to those of adults,[53] but the neural processing of affective touch varies between different ages and genders. In terms of development, human infants lack distinct brain regions for processing emotional information until around 7 months of age. Between 7 and 10 months, the functions of brain regions associated with affective touch processing gradually mature.[37–39] This suggests that the processing of affective touch develops throughout infancy. Research on individuals spanning childhood, adolescence, and adulthood[53] revealed that when a watercolor brush was used to touch the right forearm and palm, the regions of interest in the S1, S2, insula, and right pSTS were significantly activated. Activation of ipsilateral S2 was positively correlated with age whereas activation of S1 did not significantly increase with age. The study[53] also found that the sensitivity of the posterior superior temporal sulcus (pSTS) increases with age in females, but no similar trend was observed in males. This may be related to the fact that the cortical thinning of the temporal region (including STS) in females is faster than that in males.[122] Another study[123] showed that adolescents aged 15–17 exhibited the strongest activation in the insula and bilateral inferior frontal gyrus compared to young adults and older adults. Although some researchers have yielded positive results, another study suggests that the function and structure of the STS is related to an individual's experience during development.[124] Individuals who avoid touch may have a decreased activation response to affective touch. Therefore, there is currently no clear result proving a linear correlation between age and the activation response of brain areas related to affective touch.

In the neural processing of affective touch, the somatosensory cortex plays a role in recognizing tactile stimuli and is involved in distinguishing affective touch independently from other areas.[125] Consequently, the processing of the emotional aspects of touch may involve neural mechanisms that partially overlap. Case[126] used inhibitory rTMS at the S1 on the subject's right side, and found that the subject's sensory discrimination ability decreased. However, the tactile pleasure score was not changed, indicating that S1 only encodes tactile intensity and does not process tactile pleasure. Malinen et al[127] also found similar results.

In research, social touch[123,128] is often represented by touching a subject with true hands (skin-to-skin contact). The tactile stimulation used in affective touch usually includes soft brushes, feathers.[55,65] Using soft brushes may induce a relatively simple tactile sensation with relatively weak emotional color. In some experimental situations, the brushing

of a brush may be regarded as a standardized and relatively neutral tactile stimulation, which may induce an affective reaction. The touch site typically located on hairy skin. This is related to the emotional function of CT fibers and their distribution on hairy skin.[129] Skin-to-skin contact often carries more emotional and social functions, especially in intimate interactions, which may make it easier to generate affective resonance, and parts of the brain regions related to emotions and social cognition will be more actively involved in processing tactile stimuli. In contrast, true hands are more likely to induce the prosocial nature of touch, while tools such as soft brushes can eliminate the interpersonal effect. This distinction is crucial to our understanding of the neural processing mechanisms underlying affective touch. Strauss's study[65] found that touching the dorsal side of the subject's left forearm with the experimenter's hand caused a stronger tactile pleasure than brush strokes. They detected that the S1 and S2 extended to a stronger bold signal in the superior temporal cortex. Ebisch[130] stimulated subjects' right hands through animate target (human hand), inanimate target (fake hand), and massage brushes, and also found that the touch of human hands produced a higher degree of pleasure.

If skin-to-skin touch originates from oneself, the social nature between people will also disappear. Boehme et al[121] instructed subjects to touch their left forearm with their right index finger. They found that deactivation occurred in the insula, ACC, superior temporal gyrus, amygdala, parahippocampal gyrus, and prefrontal area, and the deactivation expanded to brain regions encoding low-level sensory representations, including the thalamus and brainstem. Touching the forearm triggers distinct BOLD signal responses in various brain regions including the somatosensory cortex, insula, superior temporal gyrus, and others, suggesting diverse mechanisms underlying interpersonal social touch processing.

For instance, the study by Schaefer et al[128] reported that when the palm was touched by the experimenter's hand, S1, bilateral S2, M1, bilateral Premotor Cortex (PMC), inferior frontal gyrus, insula, and other regions were significantly activated. In addition, they found that the BOLD reaction in S1 was negatively correlated with empathy personality traits, personal pain, and perspective-taking abilities.

The prosocial nature of touch was studied using similar methods. Prosocial behavior, characterized by positive behavior benefiting others, is typically driven by empathy and concern for the rights, feelings, and well-being of others. This encompasses behaviors such as helping, sharing, comforting, and cooperating, ultimately contributing to mood enhancement and stress reduction.[131] For example, one study demonstrated that holding hands among lovers instills a sense of safety and comfort while reducing the connection between the anterior part of the insula and the ACC.[132] In a study conducted by Schaefer et al,[64] subjects' palms were touched with true hands and rubber hands, resulting in activation of the contralateral sensorimotor cortex, PMC, inferior frontal gyrus, and anterior insula. Post touch, the activation of S1 and S2 regions was suppressed when participants chose to exhibit prosocial behavior. Notably, higher S1 activation during touch correlated with more significant S1 deactivation during prosocial behavior decision-making, leading subjects to display increased selflessness and generosity in the dictator game. Consequently, the inhibition of somatosensory cortex activity after touch may promote altruistic behavior.

It is crucial to highlight that the tactile stimulation site in some of the aforementioned studies is the palm, generally considered an area where non-CT fibers are distributed. CT fibers, responsible for conducting affective touch and social interaction stimuli, are primarily found in hairy skin.[28–31] Schaefer's work demonstrated that sensory processing of glabrous skin touch can induce pleasurable sensations and elicit altruistic prosocial behaviors. This body of research indicates that social touch can enhance cognitive and emotional processing, fostering empathy, altruism, generosity, and happiness, with the involvement of the somatosensory cortex. Another study, focusing on touching palms with real hands[133] confirmed that tactile stimulation of the palm elicits a strong response in the insula. Touch on the glabrous area of the palm is capable of inducing a pleasant feeling of touch, ultimately resulting in detectable activation in the insular cortex. Perini et al[134] speculated that the insula may receive mixed input from CT and Aβ fibers from the arms and palms, which is another reason for the observed activation of the insula during palm stimulation. In addition, Sailer[135] observed that the striatum, OFC, and putamen were activated during 40 minutes watercolor brush stimulation, and proposed that the participation of these regions influenced subjective reward values of the stimulation, which may promote sustained social contact interaction.

Tactile Neural Processing in Disease States

Disease states, such as autism, chronic fibromyalgia, anorexia nervosa, stroke, etc., may affect normal touch processing functions, leading to disrupted or absent tactile sensations. These tactile impairments not only reduce the quality of life

but also increase patients' psychological stress and feelings of social distance. Understanding the central mechanisms responsible for these tactile abnormalities is crucial to better understanding and managing these issues, ultimately enhancing quality of life and offering patients improved diagnostic and treatment options.

Neural Processing of Touch in ASD

Autism Spectrum Disorder (ASD), which is not a disease in the traditional sense, is a neurodevelopmental disorder primarily characterized by impairments in social interaction and communication. Its basic characteristics include persistent impairment of social interaction, restricted interests, and repetitive behaviors.[136–138] ASD can result in abnormal responses to sensory input, affecting the sensory processing of touch.[139,140] Presently, the neural mechanism underlying abnormal tactile processing in ASD individuals has not yet been determined.[141] Employing an fMRI-based tactile stimulation test can reveal the key brain regions and neural mechanisms responsible for these abnormalities in ASD individuals. fMRI studies of tactile processing in ASD individuals often employ hairy skin for tactile stimulation, observing differences in brain response compared to typically developing participants (control group).

Kaiser et al[62] used a watercolor pen to brush at a speed of 7 cm/s on the arms (CT fiber-targeted sites) and palms (non-CT targeted sites) of ASD individuals. The individuals exhibited robust responses to both CT touch and non-CT touch in the S1 cortex. However, responses specific to CT touch in the bilateral insula, insular opercular area, right pSTS, bilateral temporoparietal junction of the inferior parietal lobule, right fusiform gyrus, right amygdala, and the ventrolateral prefrontal cortex, including the inferior frontal gyrus and precentral gyrus, were reduced. Interestingly, the severity of ASD is inversely correlated with brain signal response. Perini et al[63] exclusively stroked the forearms of ASD individuals with a wool brush. Results indicated that the affective touch experience of typically developing individuals in behavioral tests surpassed that of ASD participants. Moreover, individuals did not exhibit right pSTS activation, a response observed in normal individuals when receiving stimulation. These results suggest that fMRI-detected brain activation signals using touch as the stimulation paradigm can serve as indicators to assess the severity of autism. Changes in neural coupling between brain areas (such as the insula and pSTS) and affective touch in ASD, may be related to their avoidance of social touch and decreased affective touch perception.[63]

Some scholars speculate from the perspective of functional connectivity that sensory processing abnormalities may be caused by abnormal connections between major sensory regions such as S1 and the brain networks involved in transmitting and processing sensory information. However, Cechmanek's research[49] challenges this hypothesis, revealing no significant difference in the functional connectivity of the somatosensory cortex between adolescent participants with ASD and a typically developing control group. Similarly, Frost-Karlsson's results[142] showed no significant difference in brain activation between ASD individuals and typically developing control subjects when their forearms are touched. Notably, Cechmanek analyzed resting-state data from ASD individuals, without specifically incorporating sensory stimulation. Consequently, it cannot fully represent the tactile processing mechanism of ASD. Future research could conduct a correlation analysis between functional connectivity and behavioral measurements, comparing differences in functional connectivity between typically developing control subjects and ASD individuals under sensory stimulation, such as touch. Additionally, the subjects in Frost-Karlsson's study were all adults, using skin-to-skin contact. Behavioral studies suggest that adults with autism and typically developing individuals can experience similar pleasant touches.[143] In contrast, both Kaiser's and Perini's studies involved adolescent subjects who were touched with brushes. The differences in results may be linked to different age distribution of subjects and whether the task stimuli contain social tendencies. Therefore, further studies are needed to understand the developmental patterns of tactile perception and processing in ASD individuals as they age. Furthermore, a study[144] found that among ASD individuals, females had significantly lower tactile pleasure scores than males, and exhibited more complex patterns in the perception and processing of touch and emotions. This further indicates that gender and emotional factors play an important role in tactile processing.

In summary, the tactile perception and social interaction impairments in ASD individuals may be due to the insensitivity of regions such as the insula and pSTS to CT-targeted touch, which play a crucial role in affective touch processing. Kaiser's research also confirmed this, showing children and adolescents with ASD experience interruptions when processing the affective touch of CT fibers, impacting the development of the social brain.[62] Specifically, the insula is not only the brain region for processing affective touch but is also involved in multiple functions such as body

perception and pain modulation.[145] Abnormal function of the insula may lead to impairments in processing tactile information in ASD individuals, further influencing their tactile perception quality and affective touch experience. The pSTS also plays a vital role in the social perception network and emotional recognition, especially in detecting and interpreting social signals of human intent.[146] Research shows that the pSTS can help individuals understand other's social signals, such as facial expressions and body movements,[147] and it is particularly important in processing affective touch. Dysfunction of the pSTS may cause ASD individuals to inaccurately perceive the emotional information conveyed through touch, leading to increased social avoidance behavior. A study pointed out that the pSTS connectivity patterns in ASD individuals is immature, negatively correlated with the severity of autistic symptoms, and has a weak or non-existent correlation with anatomical measurements. However, due to the high heterogeneity of ASD, this mechanism is only one of the potential explanations, and the specific mechanism requires further verification. Patil pointed out in a review that the differences in sensory processing in ASD individuals may stem from multiple mechanisms, including Altered Neural Connectivity, Sensory Gating Dysfunction, Atypical Sensory Modulation, Imbalance in Sensory Excitation and Inhibition, and Atypical Multisensory Integration.[148] These potential mechanisms explain the complex patterns and individual differences in tactile processing in patients ASD individuals.

In recent years, with the development of multimodal neuroimaging techniques, such as the combination of fMRI and Diffusion Tensor Imaging, has provided new opportunities to explore the mechanisms of tactile impairments in individuals with ASD. Currently, due to the inconsistency in the resting-state functional connectivity results in ASD individuals, future research could combine methods such as Granger causality analysis and dynamic functional connectivity under tactile conditional stimulation to further explore the mechanisms of tactile processing in ASD individuals. These research findings are expected to support the development of neuroimaging-based assessment tools and provide a theoretical foundation for the formulation of personalized treatment plans.

Neural Processing of Touch in AN

Anorexia nervosa (AN) is a condition in which individuals exhibit excessive control of diet and a strong fear of weight gain. The incidence rate in women is higher than that in men. This leads to image disturbance,[138] resulting in dissatisfaction with body shape and weight, leading to cognition, emotional and sensory disorders. Although the mechanism leading to body image disturbance is currently unclear, it is postulated to be associated with the inability to conduct correct body sensory evaluation as confirmed by Davidovic et al.[54] In the study, a wool brush was used to stroke the dorsum of the right forearm of AN patients (producing an affective touch). Behavioral tests demonstrated a significantly lower level of pleasure derived from tactile stimuli in AN patients compared to healthy subjects. Brain imaging revealed similar activation intensity in the S1, S2, and insula regions for both groups. However, healthy individuals exhibited significantly higher activation in the bilateral occipital lobes, a brain region associated with visual processing and body image perception. This difference in brain activity suggests a potential neurophysiological basis for the observed discrepancies in body image perception between AN patients and healthy individuals. Similarly, AN patients showed reduced activity in the contralateral caudate nucleus, which was ascribed to the patient's inability to correctly evaluate pleasant tactile stimuli. Frost-Karlsson et al[142] started with social contact and touched the left arm with the subject's own right hand. They reported that during self-touch, the AN group exhibited significant changes in S1, pSTS, claustrum, cingulate gyrus, insula and hippocampus gyrus activation was higher compared to that of healthy controls. In general, considering that the behavior of self-touch is predictable and planned, the brain attenuates the response generated by perceiving self-touch.[121]

In summary, AN patients have abnormal tactile perception and processing, especially the inability to generate pleasant perception in response to the external affective touch.[149] When receiving external stimuli, AN patients show decreased activation in the occipital lobe and caudate nucleus. AN patients exhibit increased activation in S1, pSTS, and the insula, and are unable to deactivate brain activity in response to self-touch. This may contribute to distorted self-body predictions and a reduced perception of body shape, potentially serving as a central mechanism underlying body image disturbances. Previous studies have found that females are more sensitive to information about their own bodies than males.[150] Some studies have shown that during the same-sex body perception task, healthy males have stronger activation in the left lateral occipital cortex than healthy females.[151] Therefore, AN females may have a less distinct or

more vulnerable body schema of their own, which makes them more prone to internalized distorted perception of their own bodies. This may be the reason why the incidence rate in females is higher than that in males.

Tactile Neural Processing in Stroke Patients

Nearly half of stroke patients experience varying degrees of sensory impairment, which are driven by changes in the brain's functional networks.[152–154] De Bruyn et al[48] recruited 19 acute-phase stroke patients with the tactile disorder and used resting-state fMRI to investigate the relationship between brain functional connectivity and severity of somatosensory impairment of the upper extremity in the acute-phase stroke. It was found that the strength of functional connectivity between and within hemispheres was inversely associated to the severity of somatosensory deficits. In other words, the strength of functional connectivity was lower in patients with severe somatosensory deficits. In the study by Goodin et al[47] it was found that the cause of impaired tactile function in stroke patients may be associated with decreased functional connectivity from the S1 of the hemisphere on the lesion side to the contralateral S1, temporal, parietal, and occipital regions (ie, interhemispheric connections). The aforementioned studies have demonstrated the correlation between tactile impairment and functional connectivity strength. This highlights the importance of functional brain network integrity in the maintenance of somatosensory function. In future, studies should investigate the mechanisms of tactile impairment in stroke patients, and the role of treatment in reestablishing functional connectivity between brain regions.

Tactile Neural Processing in Other Diseases

In addition to the common disorders associated with typical tactile impairments, chronic fibromyalgia (FM) and Major Depressive Disorder (MDD) can make patients avoid social contact, due to altered neural processing of touch in the brain. When subjected to the same tactile stimuli, brain activation in patients with FM was comparable to that of healthy individuals, but the assessment of pleasure from touch was lower compared with that of healthy individuals. Unlike healthy individuals, patients exhibited deactivation of the contralateral posterior insula when receiving tactile stimuli.[155] This study found normal early sensory processing in FM patients, but abnormal sensory assessment linked to posterior insula deactivation. Compared to healthy controls, MDD patients showed greater aversion to human contact and lower touch pleasure scores. Lower BOLD responses in the nucleus ambiguus, caudate nucleus, and nucleus accumbens during touch stimulation are detected in patients using fMRI.[156] This suggests that abnormal striatal function during the tactile processing stage may be a central mechanism underlying social aversion and isolation in MDD patients. There are gender differences in the cortical structure of MDD patients.[157] The incidence rate of MDD is higher in female than in male.[158] Research has found that[157] the surface areas of the right superior frontal, medial orbitofrontal gyrus, inferior frontal gyrus triangle, superior temporal gyrus, middle temporal, lateral occipital lobe, and inferior parietal lobule in female MDD patients are smaller than those in male. Structural abnormalities can lead to functional abnormalities. Therefore, there may be a complex tactile processing mechanism in MDD, and future research should also focus on the differences in tactile neural processing in patients with different genders and disease courses.

In summary, researchers have revealed the processing mechanisms of haptics in disease states through the design of task-based or resting-state fMRI experimental paradigms. The aforementioned studies indicate that the above disorders presenting with tactile deficits on neurofunctional imaging are associated with diminished BOLD response or functional connectivity strength. Moreover, it has been shown that the somatosensory cortex, pSTS, and other regions are potential the targets of neuromodulation therapy, and the intensity of the BOLD signal in the target brain regions and alterations in functional connectivity between the corresponding brain areas may serve as outcomes. By elucidating both the common characteristics of disease occurrence and development and the unique changes observed, we can establish more precise directions for disease treatment and rehabilitation efforts. In addition to the biological and clinical factors discussed above, socioeconomic status may also affect tactile processing. Although we did not find substantial evidence directly linking socioeconomic status to tactile processing in the literature reviewed, it is considered that socioeconomic status may indirectly influence sensory processing.[159] Factors such as healthcare, life experiences, and environmental stress, which are usually influenced by socioeconomic status, may play a role in sensory development and regulation. Further research is needed to investigate how these factors influence tactile processing. Furthermore, although our current

understanding of the developmental trajectories of tactile processing in ASD and other disorders is limited, the evidence presented and the speculative mechanisms discussed highlight the need for further research. Longitudinal fMRI studies, along with multimodal approaches integrating genetic, behavioral, and neural measures, are essential to fully elucidate the complex relationship between age, tactile processing, and the pathophysiology of these disorders. This will not only enhance our understanding of the underlying mechanisms but also pave the way for more effective diagnostic and therapeutic interventions.

The Interaction Between Touch and Pain

Pain is an experience related to actual or potential tissue damage that contains multiple sensory, affective, cognitive and motor components.[160] While both touch and pain are somatosensory sensations detected by specialized receptors on the skin, the precise brain region that encodes the perception of pain has not yet been definitively identified.[161] The processing of painful information and innocuous tactile information is generally considered to exhibit similar hierarchical structures in the somatosensory system of the human brain.[40] Both perception thresholds of pain and touch influence brain functional connectivity. A previous study showed[162] that a higher frequency of the Default Mode Network (DMN) connection correlates with higher sensitivity of a person's response to pain. Moreover, the smaller the fluctuation of functional connectivity, the higher the person's response sensitivity to touch. Brain areas that process two types of sensory information are highly similar,[32,163,164] including S1, S2, insular, prefrontal cortex, Cingulate Cortex and other brain regions involved in somatosensory, emotional, cognitive and other functions.[165,166] The brain areas activated by pain also respond to tactile stimuli, and vice versa, with neural activity reflecting perceived stimulus intensity. Research has shown[165] that compared with painful stimulation, contralateral S1 is activated to a higher degree under tactile stimulation, while S2 is activated to a similar degree under both stimuli.

The specific identification of finger sensations triggered by painful cold and heat stimuli could be encoded by low-threshold tactile neurons in the skin, in collaboration with nociceptive neurons. Specialized modules within the S1 region effectively handle tactile and pain signals distinctly. A study on squirrel monkeys,[167] found that there are separate activation modules for processing touch, nociceptive cold and heat stimulation in the S1 area. The activation of nociceptive cold stimuli occurs in BA3a, the BA 3b-1 junction, and BA 2. The response areas to noxious thermal stimulation are in BA 3b, BA3b-1 junction, BA 1–2 junction and BA 2 area. Chen et al[168] also reported activation regions in response to finger thermal pain stimulation in BA3b, BA3a, BA1, and BA2 of squirrel monkeys, and stronger BOLD signals in BA3b and BA2 were observed.

The insula also modulates thermal pain processing, especially the operculo-insula.[169] It is considered to be the only brain region where direct electrical stimulation can produce pain. Obvious thermosensory and nociceptive dysfunction will appear after injury. In a study examining nociceptive thermal pain and stabbing pain sensations on the dorsum of the right hand,[170] researchers discovered multiple somatic representations of pain in the operculo-insular area. This finding suggests that this region serves as a site for perceptual integration and can also influence emotional responses and behavior according to the affected body part. In addition to differences in thermal and cold pain perception, differences in the performance of mechanical stabbing pain on glabrous and hairy skin have been detected. In general, the pain intensity at the human individual hairy skin is significantly stronger compared with that of glabrous skin. Interestingly, the average BOLD signal response observed in the S1 and S2 regions during stinging stimulation is significantly stronger for glabrous skin compared to hairy skin.[171] This discrepancy may be attributed to the differences in the number and types of sensory receptors present in these distinct skin types. Glabrous skin encodes more tactile information of stimulation, while hairy skin conducts more emotional information including itching, resulting in differences in the perception of external stimuli received by the somatosensory cortex between the two types of skin. Activation of the M1 were observed in both squirrel monkeys and human individuals[166,172] when receiving painful stimuli. Although few studies have shown distinct movements directly associated with pain or touch, painful stimulation, in contrast to tactile stimulation, may evoke the inclination for potential escape actions, whether consciously or unconsciously. Thus, in pain stimulation studies, areas such as M1, PMC, and SMA typically display significant BOLD signals.[173]

Studies demonstrate that the perception and processing of pain involve some aspects of the neural circuitry of the touch component. Thus, touch and pain can interact with each other. In daily life, individuals often engage in the

spontaneous behavior of rubbing a painful body area, suggesting a potential analgesic effect of touch. A study has shown[174] that touch massage activates the pregenual anterior cingulate cortex, which is believed to play an important role in advanced functions related to pain processing.[175] This area is activated by both opioid analgesia and placebo, suggesting it may be involved in touch-induced analgesia mechanisms. Similarly, the periaqueductal gray (PAG) matter, which receives input from the ACC, plays a crucial role in the descending pain system and is associated with pain relief.[176,177] In women, social support from their partner, such as holding partner's hand, can reduce pain.[178,179] This may be related to reduced pain-related activation in areas such as the insula, ACC, orbitofrontal cortex, and DLPFC. fMRI studies have suggested that multimodal sensory cortices functionally influence each other and show plasticity.[172,180] Future studies should explore the brain mechanism underlying the interaction between pain and tactile stimulation to reveal the central processing mechanism of pain information and provide new ideas and methods for clinical pain relief.

Summary and Future Outlook

Currently, fMRI-based studies have made significant progress in the field of tactile neural processing. These studies not only deepen our understanding of tactile perception but also provide new perspectives for future neuroscience studies. An examination of the literature above suggests that tactile processing for various features engages distinct networks independently. The somatosensory cortex is the primary higher brain area for processing tactile information.[181] After reaching the S1 area, touch signals are initially sorted in BA 3b. BA 2 processes size and shape,[91,182] while texture discrimination occurs in S2 and the posterior parietal cortex.[183,184] Softness is recognized by the insula and parietal areas. Social touch, which conveys rich emotional information, is processed through S1 conduction to several regions such as the insula, pSTS, and amygdala. Brain regions that process touch and nociception information are highly similar, differing in the activation of M1, PMC, and SMA regions as reported in studies of nociception. For individuals with disorder such as ASD, reduced activation of regions such as the insula and pSTS or reduced strength of functional connectivity between brain regions has been demonstrated to be one of the reasons promoting the development of tactile disorders by fMRI.

The current advancements lay a solid foundation for extending the use of fMRI in clinical settings and research related to touch. This holds significant promise for exploring neural processing patterns in tactile perception under both normal and pathological conditions, as well as for predicting disease progression.[47,63,142,155,156] These results can insight further research to further examine the role of various brain regions in tactile processing. However, in recent years, research on fMRI-based tactile neural processing still faces the following problems: ①Current research results on tactile neural processing presents a relatively simplified functional modular perspective of somatosensory cortex, making it difficult to outline the complexity of the tactile system; ②The diversity and complexity of tactile stimuli make it difficult to simulate the tactile experience that occurs in the real world in clinical trials; ③fMRI can efficiently reveal the activity of a single tactile stimulus, but the process of multisensory integration is relatively complex and incompletely understood; ④Limited by the principles of hemodynamic response generation, the peak of the BOLD signal detected by fMRI usually occurs after 3–6 s of nerve stimulation.[43,185] Although tactile neural processing involves rapid nerve conduction courses, fMRI may not effectively capture the precise details of these processes.

In future research, addressing current challenges necessitates the establishment of more intricate tactile models and standardized tactile stimulation procedures. Developing research paradigms that comprehensively simulate various tactile properties, such as texture and hardness, will bring us closer to replicating complex tactile stimuli encountered in real-world scenarios. It is essential to thoroughly investigate the anatomical basis and functional network involved in transmitting stimulus signals from the thalamus to ultimately form sensations in the cortex. This comprehensive approach will lead to a more precise understanding of the neural mechanisms underlying tactile processing. In further research, researchers should investigate the interplay between tactile information and other sensory inputs to understand the brain's overall perceptual function. They can also examine the involvement of different brain regions in processing diverse information and study the patterns of connectivity within related brain networks. Moreover, integrating fMRI with higher temporal and spatial resolution techniques like Electroencephalogram (EEG) and functional Near-Infrared Spectroscopy (fNIRS) could be instrumental in advancing future research endeavors.

Notably, translating these findings into clinical practice remains to be a significant challenge. Some studies have demonstrated that tactile training has positive effects on improving interhemispheric balance.[186] Future studies should aim to establish better rehabilitation programs for related diseases from the perspective of tactile stimulation of neuroplasticity. Besides, many therapies related to tactile stimulation such as massage,[187] manual therapy,[188] cupping therapy,[189] and Guasha[190] in complementary and alternative medicine need to be explored to determine the mechanism of tactile stimulation, and promote the treatment and rehabilitation management of diseases.

Abbreviation

LTMRS, Low-Threshold Mechanoreceptors; CT fibers, C-tactile afferent fibers; S1, Primary Somatosensory Cortex; fMRI, functional Magnetic Resonance Imaging; BOLD, Blood Oxygenation Level-Dependent; S2, Secondary Somatosensory Cortices; BA, Brodmann Area; D1, the thumb; D2, the index finger; D4, the ring finger; D5, the little finger; M1, Primary Motor Cortex; PPC, Posterior Parietal Cortex; IFG, Inferior Frontal Gyrus; ACC, Anterior Cingulate Cortex; OFC, Orbitofrontal Cortex; pSTS, posterior Superior Temporal Sulcus; PMC, Premotor Cortex; SMA, Supplementary Motor Area; ASD, Autism Spectrum Disorder; AN, Anorexia Nervosa; FM, Fibromyalgia; MDD, Major Depressive Disorder; DMN, Default Mode Network; EEG, Electroencephalogram; fNIRS, functional Near-Infrared Spectroscopy; OP, Parietal Operculum; DLPFC, Dorsolateral Prefrontal Cortex; rTMS, repetitive Transcranial Magnetic Stimulation; PAG, periaqueductal gray; FC, functional connectivity.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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