Review article

Tactile discrimination as a diagnostic indicator of cognitive decline in patients with mild cognitive impairment: A narrative review

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ABSTRACT

Background: Tactile discrimination, a cognitive task reliant on fingertip touch for stimulus discrimination, encompasses the somatosensory system and working memory, with its acuity diminishing with advancing age. Presently, the evaluation of cognitive capacity to differentiate between individuals with early Alzheimer's disease (AD) and typical older adults predominantly relies on visual or auditory tasks, yet the efficacy of discrimination remains constrained.
Aims: To review the existing tactile cognitive tasks and explore the interaction between tactile perception and the pathological process of Alzheimer's disease. The tactile discrimination task may be used as a reference index of cognitive decline in patients with mild cognitive impairment and provide a new method for clinical evaluation.
Methods: We searched four databases (Embase, PubMed, Web of Science and Google scholar). The reference coverage was from 1936 to 2023. The search terms included "Alzheimer disease" "mild cognitive impairment" "tactile" "tactile discrimination" "tactile test" and so on. Reviews and experimental reports in the field were examined and the effectiveness of different types of tactile tasks was compared.
Main results: Individuals in the initial phases of Alzheimer's spectrum disease, specifically those in the stage of mild cognitive impairment (MCI), exhibit notable impairments in tasks involving tactile discrimination. These tasks possess certain merits, such as their quick and straightforward comparability, independence from educational background, and ability to circumvent the limitations associated with conventional cognitive assessment scales. Furthermore, tactile discrimination tasks offer enhanced accuracy compared to cognitive tasks that employ visual or auditory stimuli.

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Conclusions: Tactile discrimination has the potential to serve as an innovative reference indicator for the swift diagnosis of clinical MCI patients, thereby assisting in the screening process on a clinical scale.

1. Introduction

Dementia is a clinical syndrome that is linked to brain diseases, exhibiting a gradual deterioration of cognitive abilities over time, resulting in limitations in performing daily activities, engaging in social interactions, and achieving academic success [1]. Globally, approximately 50 million people are affected by dementia, and this number is approached to reach 152 million by 2050 [2]. Alzheimer's disease (AD) stands as the foremost etiological factor contributing to dementia, encompassing a substantial proportion of approximately 60–70 percent of all diagnosed cases. The most prevalent cause of dementia is AD, which accounts for 60 to 70 percent of all dementia cases [3]. The pathogenesis of AD remains complex and inconclusive [4]. Various clinical treatment options, including vaccines, antibodies, drugs, peptides targeting Aβ, as well as small molecules, compounds, and/or tau proteins, have been explored, while did not approach the clinical expectations. Especially, these approaches have not demonstrated substantial long-term clinical advantages [5]. As of now, there exists no remedy for AD utilizing the presently accessible technological resources, as the treatments merely possess the capacity to momentarily impede symptoms or the advancement of the disease. However, the identification and intervention in the prodromal or preclinical phases have the potential to impede or reverse the progression of the disease, rendering them pivotal domains of concentration in AD research [6].

Mild cognitive impairment (MCI) is a transitional state between normal brain aging and AD, serving as a precursor to various dementia and neurodegenerative diseases [7]. Both the National Institute on Aging and the Alzheimer's Disease Association (NIA-AA) and the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) have identified MCI as a pre-dementia symptomatic stage on the AD continuum [8]. Individuals diagnosed with MCI demonstrate cognitive deficits that surpass the expected levels corresponding to their age and educational background. However, they do not manifest notable deterioration in their daily activities and professional
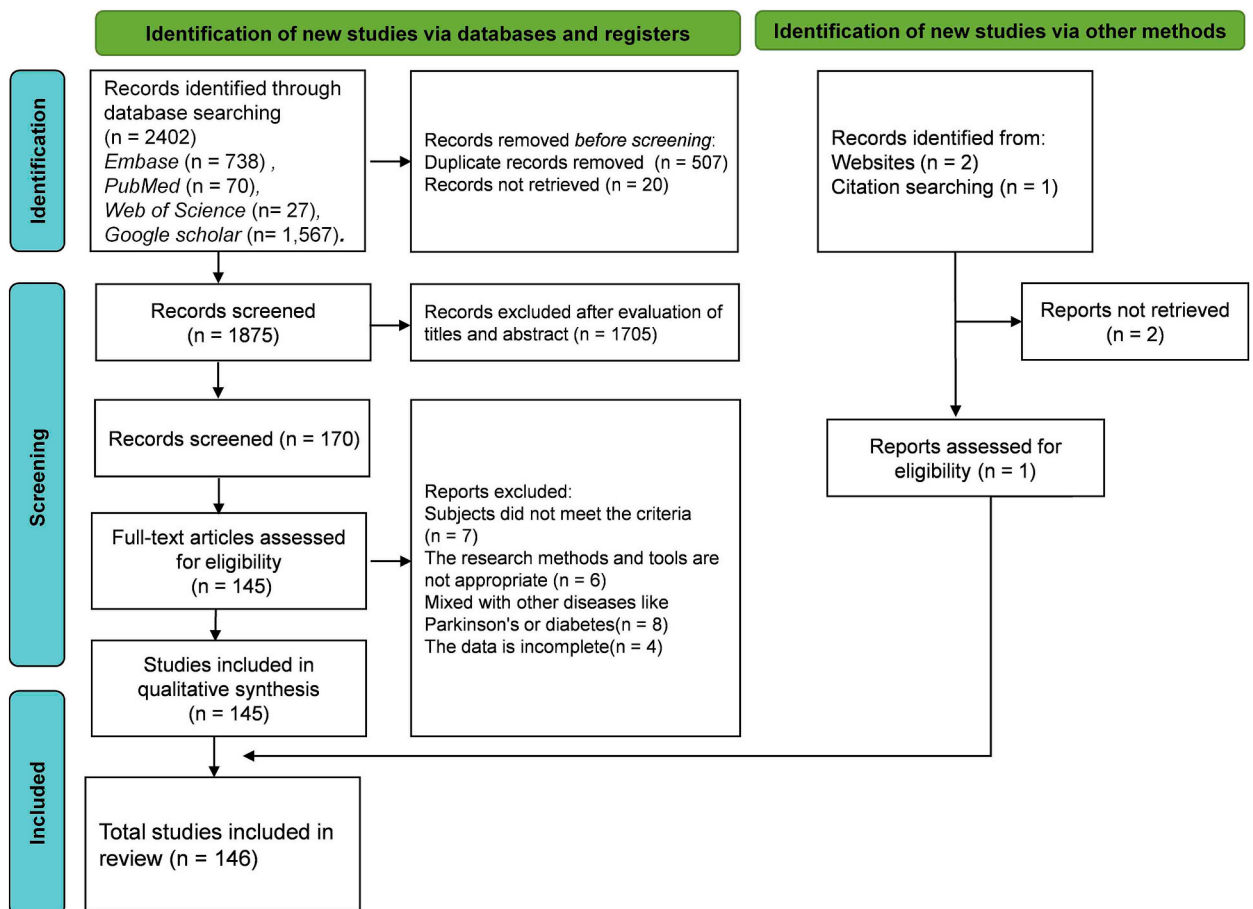

Fig. 1. Flow chart of literature screening.

engagements [9]. These individuals typically face challenges in remembering events, orientation, planning, decision-making, and following instructions [10–12]. However, to make a definitive diagnosis of MCI has faced clinical challenges. MCI patients present with subtle symptoms [13], thereby requiring the utilization of medical history and validation via neuropsychological testing or alternative cognitive assessment instruments for the identification of cognitive deterioration [14]. Prominent cognitive assessment tools commonly employed encompass the Mini-Mental State Examination (MMSE), the Montreal Cognitive Assessment Scale (MoCA), and various others. However, deficiency in the sensitivity and specificity of different assessment tools for MCI diagnosis leads to no accurate uniform scale for clinical application [15]. On the other hand, there are multiple assessment processes and evaluation criteria utilized globally for the clinical diagnosis of MCI, resulting in inconsistencies in the identification, confirmation, and subsequent etiological analysis of the disease [15]. As a result, underdiagnosis or delayed diagnosis is prevalent [16], and comparing studies that employ different screening methods presents substantial challenges [15].

On the one hand, the use of tactile discrimination task to assess mild cognitive impairment has the advantages of fast, easy to compare, objective evaluation rules, and no influence of education level, so as to avoid many defects of traditional cognitive assessment scale. On the other hand, the combination of physical senses and brain cognition helps to understand the symptoms of AD patients from the somatosensory system, and provides implications for future intervention and prevention. Thus, tactile discrimination task is important for the assessment of mild cognitive impairment. In this paper, we compare and analyze the related research results of tactile perception aging and tactile cognitive tasks. The aim of this study was to explore how tactile assessment might be a potential method for identifying atypical cognitive decline in older adults.

2. Methods

We searched four databases (Embase, PubMed, Web of Science and Google scholar) up to March 2024. The search terms included "Alzheimer disease" "mild cognitive impairment" "tactile" "tactile discrimination" "tactile test" and so on. The importance of tactile in mild cognitive impairment was investigated. Reviews and experimental reports in the field were examined and the effectiveness of different types of tactile tasks was compared. Aiming at the above topics, a total of 2402 literatures were searched. Including review studies, clinical empirical studies, animal experiments and so on. Exclude irrelevant topics (e.g., involuntary movements), other diseases (e.g., diabetes, Parkinson's disease, autism, schizophrenia, etc.), inappropriate research methods and tools (e.g., electrotactile stimulation), and non-downloadable literature. Finally, 146 literatures were included. This process is completed by two people, and the third person is responsible for inspection (Fig. 1).

3. MCI and tactile abnormality

Sensory impairment has been found to exert a substantial influence on the progression of dementia and is frequently regarded as a potential contributor to cognitive decline. Extensive international research has identified hearing loss in midlife as a prominent risk factor for the onset of dementia [17]. Furthermore, multiple studies have demonstrated a notable association between hearing loss and mild cognitive impairment [18,19]. Cognitive impairment can also impact vision, as longitudinal studies have shown that visual impairment is associated with an accelerated decline in cognitive ability [20–22]. The progression of dementia and AD has been associated with changes in smell and taste. Olfactory dysfunction has been suggested as a potential indicator of functional decline related to dementia [23–25]. In individuals with MCI or AD, brain regions involved in gustatory processing, including the orbitofrontal cortex, cingulate gyrus, multimodal integration areas, amygdala, hippocampus, and other limbic system regions, are impacted [26]. Furthermore, a correlation exists between olfactory and gustatory impairments, both of which hold substantial potential as autonomous indicators of dementia [27]. Moreover, the pathological progression of AD affects tactile processing, specifically leading to notable impairments in tactile discrimination [28,29].

Tactile perception interacts with the pathological processes of Alzheimer's disease. On the one hand, tactile discrimination is impaired by the pathological processes of Alzheimer's disease. This may be related to astrocytes. Astrocytes are involved in a variety of structural, metabolic and homeostasis functions, and are involved in the control of cerebral blood flow[30]. The loss of normal astrocyte function may be the main cause of neurodegeneration [31,32]. Signs of astrocyte reactivity appear in the very early stages of age-related cognitive decline [33]. Most of the evidence supporting the early emergence of reactive astrocytes comes from postmortem tissue studies that show alterations in glial fibrillary acidic protein (GFAP) and/or some other astroglia-associated protein and mRNA species in individuals with mild cognitive impairment (MCI) or preclinical AD [34–37]. Using 11C-deuterium-L-deprenyl (11C-DED), Nordberg and his colleagues revealed that astrocyte reactivity was significantly elevated in many cortical and subcortical regions in living MCI patients compared to age-matched healthy controls [38]. The early emergence of astrocyte reactivity in Alzheimer's disease may provide a key upstream mechanism for many complex and highly correlated pathological processes, including neuro-inflammation, synaptic dysfunction, cerebrovascular pathology, and hypometabolism [37]. It has been found that loss of astrocyte dependent long-term enhancement (LTP) in the somatosensory cortex (SSCx) in 8-month-old presenilin-2 amyloid precursor protein (PS2 APP) mice is associated with complete impairment of tactile recognition memory consolidation, which is dependent on SSCx function and plasticity [39]. This suggests that long-term synaptic plasticity, which is dependent on astrocytes, is reduced in somatosensory circuits, predicting the loss of specific tactile memory. Many examples of astrocyte plasticity have been demonstrated in the whisker-thalamic-barrel-body sensory system in rodents, and astrocytes have been proposed to play an important role in fundamental processes such as cortical sensory map organization [40] and interaction with neural networks [41] to enhance their computational performance. Therefore, the plasticity of astrocytes may have a key influence on somatosensory function [42]. During injury or inflammation, reactive astrocytes may cause homeostasis disorder[43], suggesting that the somatosensory abnormalities in

the pathological course of Alzheimer's disease may be caused by astrocytes. Studies have found that MCI and AD patients exhibit abnormal somatosensory information processing, leading to a decrease in tactile shape discrimination compared to age-matched control [44]. Notably, a previous study highlights a significant decrease in the tactile angle discrimination ability of individuals with MCI compared to normal older adults [45].

Tactile stimulation, on the other hand, improved AD symptoms in both human patients and mice. Massage is classified as a tactile sensory stimulus and has been used to intervene in patients with AD [46,47]. It has been found that stimulation of peripheral tactile nerves through massage can improve affective behavior disorders in patients with possible early AD [48]. Moreover, neonatal tactile stimulation improved cognitive, motor skills, and anxiety-like symptoms in both pregnancy-stressed and non-stressed adult APP mice, changes that were associated with reduced Aβ plaque formation [49]. The application of TS in adult APP mice reduced AD-like behavioral symptoms and pathology in adult APP mice [50].

The research specifically examines tactile discrimination as it offers several advantages in understanding the impact of cognitive impairment on sensory perceptions as following:

First, the interconnection between the human hand and brain plays a vital role in two fundamental and pertinent functions, namely the exploration of the physical environment and the intentional modification of specific components. These functions heavily depend on the accurate perception of mechanical occurrences when objects make contact with the hand. The pivotal factor in facilitating this perception lies in the ability of mechanosensory afferents, which regulate the hairless skin on the palm, to operate as a collective group of units [51].

Second, in relation to sensory afferents, tactile sensation encompasses the widest spectrum and offers a plethora of information. The predominant etiology of acquired hearing impairment commonly stems from cochlear damage [52]. Visual impairment among individuals with AD frequently implicates the retina [53]. Olfactory and gustatory afferents depend on olfactory receptor cells [54] and taste buds [55], respectively. In contrast, the preliminary phase of tactile sensory processing encompasses cutaneous sensory neurons [56], which are widely distributed throughout the human body [57] and exert a substantial influence on everyday activities. Notably, the ventral region of the finger houses a dense population of sensory neurons within the skin [58], thereby leading to enhanced tactile sensitivity and discrimination abilities.

Third, the sense of touch, considered a fundamental mode of perception, offers distinct advantages in terms of neural processing within the nervous system [59]. The tactile system encompasses both the peripheral and central nervous systems, including tactile receptors, afferent fibers, the spinal cord, and the cerebral cortex [60,61]. The transmission and processing of tactile signals involve multiple brain regions, with the somatosensory cortex playing a crucial role as the primary higher center for tactile information processing [62,63], along with the involvement of the parietal lobe and prefrontal cortex [64]. These brain regions are closely related with cognitive functions, such as: attention, memory, and decision-making. Previous study tried to use a tactile discrimination learning paradigm borrowed from an animal model to compare neuropsychological mechanisms between AD patients and Parkinson's disease (PD) sufferers. The results showed that the former had suffered an impairment in the ability of tactile original learning (TOL) and also a more persistent errors in the test of tactile reversal of original learning (TRL) than the latter [65].

Furthermore, when considering the methodology of clinical examinations, various tests are used for assessing sensory functions, such as the smell stick test for olfactory examination [66], the University of Pennsylvania Odor Identification Test (UPSIT) for olfactory assessment, pure tone audiology as the gold standard for clinical evaluation of hearing loss, and optical coherence tomography (OCT) for visual examinations [53,67]. However, tactile discrimination testing offers superior sensitivity and convenience compared to these tests. Unlike its counterparts, tactile discrimination testing does not necessitate elaborate equipment or intricate procedures, rendering it applicable in diverse community and clinical contexts.

Hence, this study aims to elucidate the underlying factors contributing to the diminished tactile discrimination abilities observed in individuals with MCI, by examining the altered patterns of tactile discrimination processing in this population.

4. Assessment of tactile and cognitive functions

In recent times, there has been a notable surge in scholarly attention towards haptic research across the domains of cognitive psychology, engineering psychology, and psychiatry. Tactile discrimination, in particular, pertains to the capacity to perceive, retain, and assess the form, texture, temperature, and other characteristics of an object through the sense of touch at the fingertips [29]. The principal objective of tactile discrimination lies in the detection, identification, and recognition of external stimuli, thereby facilitating swift decision-making and subsequent behavioral guidance for individuals [68].

Tactile sensation emerges as the primary sensory system during human development [69]. Prior to birth, the fetus exhibits increased exploration of the uterine wall in response to maternal touch during the later stages of gestation. Skin-to-skin interactions during infancy play a crucial role in the formation of self-awareness [70]. Disruptions in tactile input during this developmental period can have profound implications for an individual's social functioning in adulthood [71]. The initial maturation of the haptic system facilitates individuals' rapid adjustment to their surroundings and the acquisition of a substantial repertoire of tactile encounters. These encounters exert a profound impact on the development of the brain, cognitive capacities, and establish a fundamental basis for subsequent motor control, spatial perception, and social interaction in later stages of life [69,72,73]. The act of touch serves as an indicator of the degree of emotional closeness between individuals. It has been observed that individuals who are emotionally connected, regardless of their relationship status, exhibit a greater propensity to engage in frequent physical contact with others [74]. Conversely, individuals grappling with mental health concerns have reported a reduced frequency of touch and diminished perception of its effects [75]. Conversely, the frequency of touch has been found to significantly impact our subjective perception of the tactile experience [76].

The perception of tactile sensation is facilitated by a dual conduction and coding system. Aβ afferent fibers play a crucial role in transmitting the sensory attributes of touch, allowing us to discern the dimensions, form, and consistency of objects in our surroundings. These fibers are primarily responsible for the discriminative aspects of touch [68]. Furthermore, within the hairy skin of the human body, a distinct cluster of unmyelinated C-tactile (CT) afferent fibers exists, which actively contribute to the social function of touch by detecting and relaying emotional information. The examination of older adults' reactions to affective touch has the potential to contribute to the timely identification of AD. From a cognitive impairment standpoint, the processing of tactile stimuli activates multiple cerebral areas and necessitates higher-order cognitive operations, including the integration of tactile input and the utilization of short-term memory [29]. Moreover, the observation of older adults' responses to discriminative touch may reveal deviations in cognitive domains such as comprehension, executive function, and working memory.

Due to the considerable importance of touch in early developmental stages, it is justifiable to posit that tactile perception plays a crucial role in the development and operation of both developing and mature organisms [73]. Consequently, tactile perception possesses the potential to function as an innovative marker for early differentiation between individuals with MCI and typical older adults, thereby offering a dependable benchmark for clinical screening measures. Moreover, conducting additional research on tactile modifications in individuals with MCI can enhance our comprehension of the role played by the somatosensory system in the manifestation of symptoms in those with AD. Such comprehension can offer valuable insights for the development of future interventions and preventive measures.

5. Relevant studies of identifying MCI by tactile discrimination

Tactile perception encompasses the interaction between peripheral sensory processes and central cognitive mechanisms, as showed in Fig. 2, to detect and perceive objects, as well as to recognize and evaluate their dimensions, morphology, and surface attributes [77, 78]. Substantial evidence supports the notion that tactile perceptual abilities diminish with advancing age [79–81]. The influence of age on perceptual evaluation abilities, which encompass cortical neuronal tuning properties, lateral inhibition, attention, and working memory, appears to be more pronounced than its impact on stimulus-driven sensitivity, which involves skin features and receptor density [77]. Additionally, research has demonstrated that the tactile processing of geometric properties, such as shape and size, often necessitates the integration of both cutaneous and kinesthetic inputs [82]. In certain instances, the identification of object shapes can be accomplished by the skin indentations that conform to the fingertip, whereas the comprehension of shapes with contours extending beyond the fingertip predominantly depends on kinesthetic input [83].

5.1. Bottom-up afferent process

Four mechanoreceptive afferent systems situated in the skin have been identified as the source of sensory feedback [56]. Prior studies have suggested that the comprehension of tactile shape perception can be attributed to the amalgamation of skin mechanoreceptor functionalities [84,56]. Nevertheless, the process of aging brings about numerous anatomical and morphological alterations in the hands and fingers [44]. Skin aging is characterized by the emergence of wrinkles and the decline in firmness and elasticity [85]. The aforementioned alterations have the potential to exert an adverse influence on the interconnection between the integumentary system and neural pathways [86]. Additionally, the decline in both the abundance of mechanoreceptors within the skin and the velocity of peripheral nerve conduction is observed as individual's age [87–89]. From a pragmatic standpoint, diminished tactile sensitivity in older individuals can give rise to a range of challenges, encompassing difficulties in tactile object recognition and
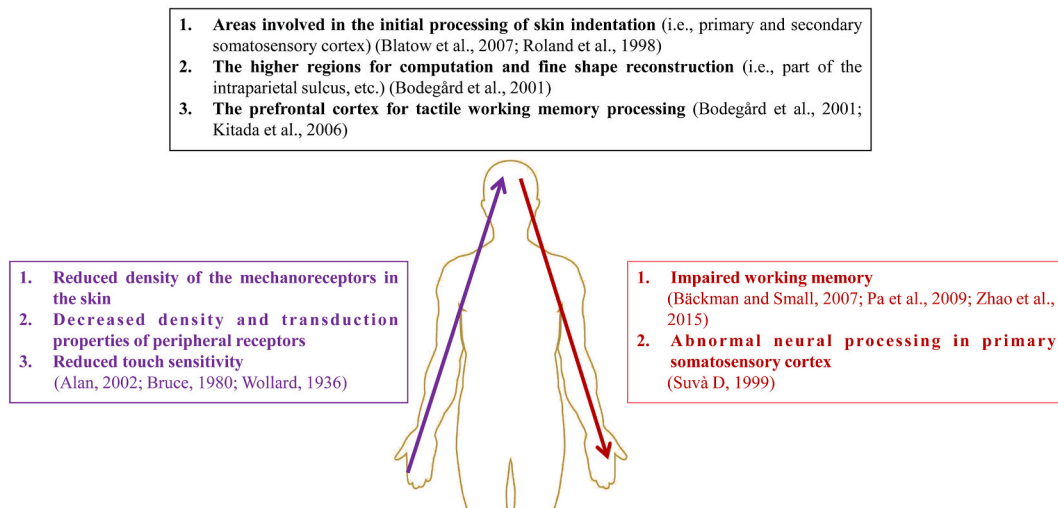

Fig. 2. Tactile processing patterns in patients with MCI (Picture edited from: www.ver.com).

impaired perception of objects in contact with the skin [90,91]. The observed effects can potentially be ascribed to age-related declines in the density and transduction characteristics of peripheral receptors, including Merkel receptors, Pacinian corpuscles, and Meissner corpuscles [90]. Nevertheless, there remains a dearth of research investigating tactile perception in older adults with mild cognitive impairment, necessitating future investigations to ascertain potential disparities in tactile afferent systems between individuals with MCI and cognitively healthy older adults.

5.2. Top-down transmission process

The process of tactually distinguishing between two objects entails the comparison of sensory input received from the touched object with stored information in the cognitive system regarding the other object. This process elicits activation in a widely distributed central neural network, primarily involving regions responsible for initial processing of skin indentation (e.g., the primary and secondary somatosensory cortex) [92,93], as well as higher-level regions involved in computational and precise shape reconstruction (e. g., portions of the intraparietal sulcus) [94], and the prefrontal cortex for tactile working memory processing [94,95]. Furthermore, emotional states have the potential to modulate sensory processing at an individual level [96]. Consequently, it is plausible to consider that emotional factors may also exert an influence on tactile cognition in individuals diagnosed with MCI.

Although there exists a considerable amount of literature documenting somatosensory dysfunction in animal models of AD [97,98], the evidence supporting similar pathology in human patients is limited. A commonly observed phenomenon in the AD neuroimaging literature is the preservation of primary sensory cortices, specifically the primary sensorimotor cortices, until the later stages of the disease progression [99–102]. However, the existing functional neuroimaging literature lacks sufficient consideration of a significant confounding variable that consistently and significantly impacts the processing of somatosensory stimuli: higher-order cognitive functions [103]. Individuals diagnosed with AD demonstrate varying levels of impairment in attention and processing speed [104, 105], indicating deficits in various aspects of cognitive control during the initial phases of the illness. The neural processing of somatosensory stimuli, including the functional gating of redundant somatosensory and auditory information, and their interplay, has been discovered to be linked with these cognitive functions [106–112]. Considering cognitive factors, it becomes apparent that AD significantly affects neural processing in the primary somatosensory cortex, although these effects are obscured by the variability in individual cognitive decline [103].

It has found that plaques could be observed in the primary motor cortex of patients diagnosed with mild to moderate AD [113]. Subsequently, other researchers examined the reaction of primary and secondary somatosensory regions to median nerve stimulation in individuals with MCI and AD. Their findings indicated that MCI patients displayed a higher level of response in the contralateral secondary somatosensory cortex (cSI) compared to both healthy older adults and AD patients This suggests that the secondary somatosensory cortex (SII) is affected in MCI patients, indicating that it may serve as an early marker of brain function abnormalities leading to AD [114].

Furthermore, both active and passive tactile shape recognition have been shown to elicit activation in the anterior supramarginal gyrus (SG) and intraparietal sulcus (IPS) cortex [94]. The subparietal cortex (IPC), encompassing the intraparietal sulcus (IPS), angular gyrus (AG), and supramarginal gyrus (SG), is known to play a critical role in spatial memory and has been proposed as a distinct neuroimaging indicator for predicting the transition from MCI to AD [115]. Furthermore, previous research has demonstrated notable variations in the folded aperture of the parieto-occipital fissure and the intraparietal sulcus in both hemispheres of the brain among older adults without cognitive impairment, individuals with MCI, and patients with AD [116]. Specifically, MCI patients exhibit a measurement that is 1 mm wider in comparison to healthy control (HC) patients, whereas AD patients display a measurement that is 2 mm wider in comparison to MCI patients [116].

The role of working memory systems is essential in the maintenance, manipulation, and decision-making processes of short-term information, such as somatosensory discrimination [94,95,117]. Impairment in working memory function has been identified as one of the initial symptoms of AD [118–120], and it has been utilized as an indicator for the early detection of cognitive decline in individuals with AD [121,122]. Patients diagnosed with mild cognitive impairment (MCI) demonstrate pathological alterations in brain regions associated with working memory, such as frontal lobe atrophy [123,124] and dysfunction [125,126]. Consequently, these changes lead to impairments in the cognitive processes involved in working memory [127–130]. Specifically, when individuals rely solely on touch to compare two distinct stimuli, they must effectively encode and retrieve information about the characteristics of the initial stimulus from their working memory, subsequently utilizing this information to make a comparison with the data obtained from the second stimulus [117].

Prior research has demonstrated that individuals with AD exhibit notably inferior performance compared to typical older adults in tasks involving visual and auditory working memory, such as letter recall tasks, Hayling tasks, and the Brown-Peterson procedure [131–134]. These findings imply that visual and auditory working memory may serve as prognostic indicators for the transition from a healthy state to AD. Traditionally, neuropsychological tests used for assessing AD heavily rely on vision and/or hearing, such as MMSE and MoCA. However, it is important to note that individuals who experience severe vision or hearing loss, also known as dual sensory loss or blindness, cannot be effectively assessed using the aforementioned measures [117]. Consequently, the creation of a tactile cognitive test would be advantageous in addressing the constraints of current screening tools and could function as an additional benchmark alongside clinical scales. Presently, the repertoire of tactile discrimination tasks encompasses two-point tactile discrimination, texture discrimination, tactile angle discrimination tests, and additional assessments. Nevertheless, it is important to note that certain tests within this array are exclusively appropriate for experimental investigations rather than clinical examinations.

6. Typical tactile assessment tasks

6.1. Two-point tactile discrimination

The two-point discrimination (TPD) test is a cutaneous sensory assessment utilized for quantifying an individual's tactile acuity [135]. Initially, TPD was thought to be exclusively influenced by alterations in the density of peripheral innervation within the tested area, particularly after peripheral nerve injury [136]. Nevertheless, the examination of tactile acuity has subsequently broadened to encompass not only the functioning of peripheral innervation domains but also the somatotopic organization of the sensory cortex via the spinal cord pathway [137]. This enhanced comprehension provides an explanation for the occurrence of alterations in tactile acuity among certain individuals, even in the absence of any peripheral nerve injury [138]. The TPD threshold is extensively employed as a metric for evaluating higher-level perceptual abilities in both clinical and research environments.

A study has showed that 36 young participants, with an average age of 21.1 ± 0.8 years, were recruited to evaluate tactile acuity [139] (Fig. 3A). To accomplish this, a custom-made two-point tactile stimulation device (Takei; Niigata, Japan) with computer-controlled stimulation conditions was employed. This device facilitated meticulous regulation of multiple stimulation parameters, such as needle spacing, needle elevation rate, needle penetration depth, stimulus presentation time, and stimulus interval. During the conducted experiment, a total of eight distinct stimulus distances, spanning from 1.0 to 4.5 mm with intervals of 0.5 mm, were randomly administered on the pad of the participants' right index finger. The participants were given explicit instructions to indicate whether they perceived a single point of contact or two points of contact. In instances where they were confident that both dots were touched, they responded by indicating two dots. Conversely, if they were uncertain or only sensed one dot, they responded with one dot. It is important to acknowledge that this measurement approach may be vulnerable to the influence of repeated measurements and perceptual learning, thereby presenting certain operational challenges.

In a study, the examination of the efficacy of a novel approach for assessing tactile acuity in dynamic touch was deemed more advantageous compared to static touch [140] (Fig. 3B). The research sample consisted of 42 individuals aged 60–70 years, who were positioned in armchairs and had their right hand positioned in a cushioned alcove, adopting a standardized relaxation posture. Participants were given instructions to shut their eyes, don noise-canceling headphones, and utilize the distal phalanx of their right index finger to examine a slender polymethylmethacrylate sheet that was purposefully crafted for the research endeavor.

The experiment comprised a forced-choice discrimination task in which participants were required to ascertain whether the first or second sheet exhibited a greater band spacing. A total of eight sheets, differing in spacing by 0.2 mm, were presented 15 times, while two sheets with a more pronounced 0.4 mm spacing difference were presented 6 times. Consequently, participants were tasked with comparing a total of 132 pairs of spacing. The entire assessment had a duration of approximately 1.5 h, with a 5-min intermission provided after every 15 min of testing. However, it is imperative to acknowledge that this methodology has not been implemented on individuals diagnosed with MCI and lacks empirical evidence within that specific demographic. Additionally, the duration of measurement may prove excessively lengthy and potentially challenging for elderly participants, thereby diminishing its suitability as a clinical assessment tool.
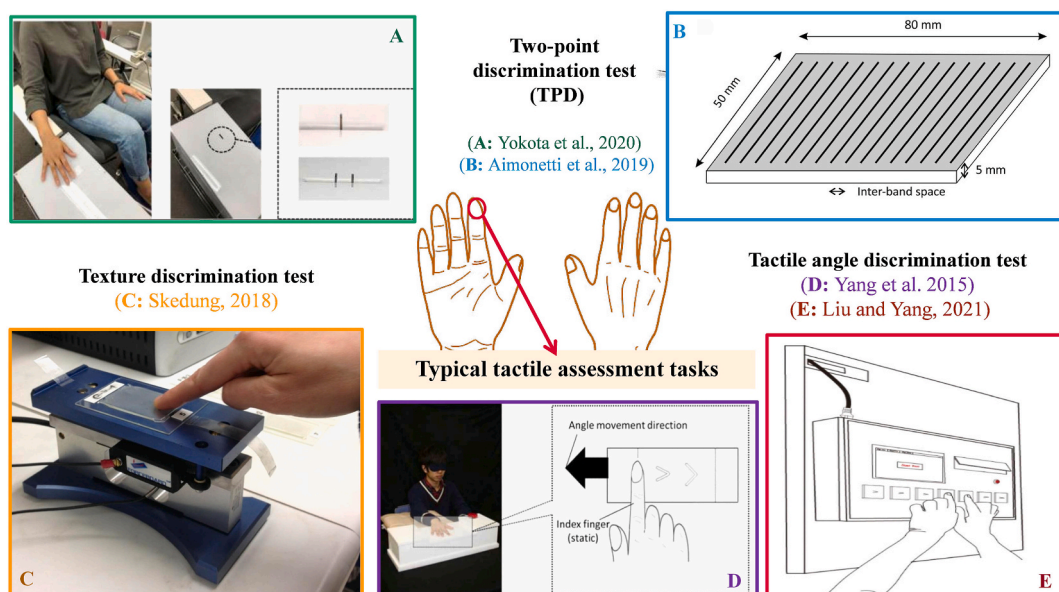

Fig. 3. **Typical tactile assessment tasks.** (**A**, **B**) Two-point discrimination test. (**C**) Texture discrimination test. (**D**, **E**) Tactile angle discrimination test.

6.2. Texture discrimination test

A novel approach for quantifying tactile sensitivity has been established, which was employed a texture discrimination test to assess individuals' tactile perceptual capabilities via blind active exploration of systematically varying microtextured surfaces and a same-different paradigm [141] (Fig. 3C). During the experimental procedure, participants were blindfolded and engaged in a tactile task involving the repetitive tapping of surfaces using their dominant hand's index finger. The presentation of stimuli followed a constant stimulus approach, wherein a control stimulus (Ref100) was initially presented, followed by a subsequent test stimulus. Participants were explicitly instructed to discern whether the second surface differed or remained the same in comparison to the control stimulus. Each surface was subjected to six random comparisons with the control surface, resulting in a cumulative total of 36 comparisons per participant.

The research revealed a notable decrease in neural texture recognition ability among older participants. This approach not only quantifies the decline in tactile discrimination in the elderly but also enables the evaluation of outcomes following rehabilitation interventions. Finger rubbing is identified as a crucial perceptual indicator for precise texture discrimination, presenting a promising avenue for enhancing diminished tactile perception. However, it is imperative to acknowledge that this measure is deficient in data that compares individuals with MCI to cognitively healthy older adults. Consequently, the specific cause of the decline in texture discrimination remains uncertain, as it is unclear whether it is solely a result of aging or if it is influenced by the presence of AD pathology. Therefore, additional research is warranted to explore potential disparities in texture discrimination between individuals with MCI and cognitively healthy older adults.

6.3. Tactile angle discrimination test

A new test called the Angle Discrimination Test was proposed and applied to subjects with MCI and AD [45] (Fig. 3D). The researchers deemed angle perception to be a pivotal factor in the development of tactile shape. To mitigate the impact of visual feedback, the subjects were equipped with an eye patch during the experiment. They extended their right index finger towards the contact point of a test apparatus, comprising a square plate featuring angular projections. These square plates were affixed to a conveyor belt that consistently moved beneath the subject's finger at a speed of 5.0 mm/s. The subjects were instructed to verbally disclose the angles with greater values through a compelled selection technique. The study observed that every pair of angles consisted of a reference angle of $60°$ and eight comparison angles, which varied from $4°$ to $50°$ greater than the reference angle. The findings indicated a decrease in tactile angle discrimination among both MCI patients and AD patients when compared to a control group of healthy elderly individuals. Furthermore, the mean accuracy and angle discrimination thresholds were significantly lower in AD patients in comparison to both the control group and MCI patients.

Above study presents empirical evidence supporting the efficacy of the Angle Discrimination Test in discerning variations in tactile angle discrimination among individuals with cognitive impairment and those who are cognitively intact in the elderly population. Moreover, it underscores the potential of tactile angle discrimination as a highly responsive marker for detecting cognitive decline in patients diagnosed with MCI and AD. Similar study has been conducted to explore the tactile angle discrimination ability in individuals with subjective cognitive decline (SCD), amnestic mild cognitive impairment (aMCI), AD, and normal older adults [117]. The researchers posited that there are abnormalities in the processing of tactile information that manifest during the stage of subjective cognitive decline and persist as cognitive impairment advances.

In order to examine this matter, the researchers implemented alterations to the experimental design, specifically by manipulating the dimensions of the reference and comparison angles, as well as incorporating a third alternative in the forced selection procedure, enabling participants to assess the equality of the angles. The findings revealed that individuals with SCD exhibited superior average accuracy in comparison to those with aMCI and AD, yet their performance was inferior to that of cognitively healthy older adults. Nonetheless, SCD patients demonstrated a higher mean threshold for discriminating angles in comparison to cognitively healthy older adults, suggesting a decline in their ability to discern tactile stimuli. The results showed that the mean angle discrimination thresholds of SCD patients were higher than those of normal older adults and lower than those of aMCI and AD patients.

Moreover, the receiver operating characteristic (ROC) curve analysis revealed a larger area under the curve (AUC) for the angle discrimination threshold in comparison to MMSE score. This finding suggests that tactile angle discrimination could potentially offer benefits in the early detection of AD.

However, the study had several limitations. The limited sample size of the study restricts the ability to apply the findings to a broader population. The forced-choice method employed in the study necessitated prolonged engagement, which may pose challenges for older individuals who may struggle with sustained focus. Furthermore, the experimental apparatus utilized in the study was not automated or portable, and its intricate operation rendered it impractical for clinical implementation. These limitations underscore the necessity for additional research employing larger sample sizes and the creation of tactile assessment tools that are more user-friendly and portable, facilitating their seamless integration into clinical environments.

Another study has been conducted to improve the tactile angle discrimination test by introducing an angular sorting experiment using a new apparatus [142] (Fig. 3E). The experimental procedure entailed the utilization of an eye patch by the participants to eliminate visual feedback. Two reference angles, representing the smallest and largest angular stimuli, were established as fixed points. Additionally, five distinct angular stimuli were presented to the participants in a random manner. The participants employed their right index finger to discern and compare each angular stimulus, subsequently arranging them in ascending order from smallest to largest using their left hand. The findings of this study demonstrated a significant positive correlation between the angle sorting test and the angle discrimination test, suggesting that the angle sorting method may serve as a viable means to assess angle discrimination

thresholds. Furthermore, a comparative analysis between college students and retired older adults unveiled that the latter group exhibited diminished angle discrimination capabilities in contrast to their younger counterparts.

The researchers underscored the merits of the angular sorting task, which entailed active tactile exploration and manipulation of surfaces and objects by the hand, resulting in a more objective and authentic perception in contrast to passive touch. Additionally, the angular sorting task exhibited a reduced time requirement, necessitating approximately 3–5 min for completion. However, it is imperative to acknowledge that this study exclusively focused on the examination of angle discrimination thresholds in normal older adults and young college students. The assessment of the angular sorting task's validity in evaluating angle discrimination thresholds in individuals with MCI and AD remains unexplored. Consequently, additional research is warranted to ascertain the suitability and efficacy of this approach within clinical populations.

7. Conclusion

The timely intervention and treatment of patients with MCI is of utmost importance. Nevertheless, existing clinical scales frequently fail to consider sensory impairment as a potential risk factor for cognitive decline and dementia. Given its crucial role in early development, tactile sensation may have a substantial impact on the identification of abnormalities in somatosensory processing among individuals with MCI and AD. The perception and differentiation of tactile stimuli, known as tactile discrimination, depend on extensively distributed neural networks within the brain. These networks encompass various regions, including the primary and secondary somatosensory cortex, the intraparietal sulcus, and the prefrontal cortex, all of which are susceptible to the pathological mechanisms associated with AD. Deviations in tactile discrimination may serve as an indicator of an expedited deterioration in sensory function among individuals with MCI and AD, in contrast to older adults without cognitive impairments.

The utilization of tactile discrimination as a screening modality for individuals with MCI presents numerous merits. This approach remains unaffected by factors such as visual acuity or educational attainment, thereby establishing its worth as an invaluable instrument capable of mitigating the constraints associated with current methodologies. Through the observation of tactile alterations in MCI patients, valuable insights can be gleaned regarding the role of the somatosensory system in the manifestation of symptoms related to AD. Such comprehension holds the potential to foster the advancement of interventions and preventative measures targeting AD. Incorporating tactile discrimination assessments into the early identification of patients with MCI can yield valuable insights into cognitive decline and contribute to the formulation of comprehensive intervention and prevention strategies.

Data availability

No data was used for the research described in the article.

CRediT authorship contribution statement

Jinan Xu: Writing – original draft, Methodology, Data curation. **Yuqi Sun:** Resources, Methodology, Data curation. **Xianghe Zhu:** Software, Methodology, Data curation. **Sipei Pan:** Software, Resources, Methodology, Formal analysis, Data curation. **Zhiqian Tong:** Writing – review & editing, Supervision, Funding acquisition, Data curation, Conceptualization. **Ke Jiang:** Writing – review & editing, Software, Project administration, Methodology, Formal analysis, Data curation.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Zhiqian Tong reports financial support was provided by Oujiang Laboratory.

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