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Association between tactile processing, memory performance and the organization of somatosensory cortex in participants with mild cognitive impairment

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ABBREVIATIONS

AD	Alzheimer's disease
BA	Brodmann Area
CST	cutaneous sensory thresholds
fMRI	functional magnetic resonance imaging
GOT	grating orientation task
MCI	mild cognitive impairment
MNI	Montreal Neurological Institute
MRI	magnetic resonance imaging
PAL	Paired Associates Learning
PRM	Pattern Recognition Memory
ROI	region of interest
S1	primary somatosensory cortex
SF	sensory function
VSP	visuospatial perception

1 INTRODUCTION

1.1 Clinical characteristics of mild cognitive impairment

Mild cognitive impairment (MCI) is commonly defined as a state marked by an objective impairment in one or more cognitive functions based on standardized neuropsychological tests, while people maintain the ability to complete daily activities (American Psychiatric Association, 2013; Chatzikostopoulos et al., 2022).

However, it surpasses the anticipated cognitive decline associated with normal aging (Vega & Newhouse, 2014). The evolving definition underscores not only cognitive impairment but also its relationship with daily functioning, recognizing diverse manifestations of cognitive alterations such as memory deficits, attentional problems, and altered visuospatial and executive function (Aretouli & Brandt, 2010; Johnson et al., 2009; R. C. Petersen, 2004) .

MCI is prevalent among the elderly, with a substantial proportion at risk of rapid cognitive decline (Eshkoor et al., 2015). Not all individuals with MCI progress to more severe cognitive impairment, emphasizing the distinction from dementia (Petersen, 2004). MCI is acknowledged to be critical in the continuum of cognitive aging, serving as an intermediary phase between typical cognitive functioning and significant cognitive decline (Petersen, 2004). This syndrome is the most frequent phenotype of the prodromal stage of Alzheimer's disease (AD), due to the high rate of progression to AD among MCI patients (up to 75%; Tahami Monfared et al., 2022).

The need for effective interventions and support systems for MCI is crucial given the global aging population (Casagrande et al., 2022). Efforts to detect and intervene early in MCI are vital, with research focusing on the neurobiological basis of the disorder (Saykin & Wishart, 2003).

As MCI represents a transitional state with variable trajectories, unravelling the neural correlates associated with specific cognitive domains, such as memory and sensory processing, holds promise for early detection and targeted interventions for MCI and to predict its progression to AD (Anderson, 2019; Saykin & Wishart, 2003). Moreover,

exploring the organization of somatosensory cortex adds a novel dimension, bridging tactile perception and cognitive performance in the context of MCI, potentially illuminating early biomarkers and therapeutic avenues. This dissertation aimed to analyze the intricate relationship between tactile processing, memory performance, and the organization of somatosensory cortex in participants with MCI, contributing to the evolving landscape of knowledge that informs both clinical practice and theoretical frameworks in the realm of cognitive neuroscience.

1.2 Episodic memory in participants with mild cognitive impairment

Episodic memory, the ability to recall specific events, situations, and experiences, is particularly affected in MCI and early AD (Chatzikostopoulos et al., 2022; Irish et al., 2011). Individuals with MCI show significant deficits in various aspects of episodic memory, including delayed recall, associative memory, and visual memory (Almeida et al., 2021; Hale et al., 2006). These impairments are evident years before clinical AD diagnosis, with decline in episodic memory often being the earliest detectable symptom (Albert, 2011; Salmon, 2012). Longitudinal studies have shown that individuals with isolated mild episodic memory impairment often progress to clinical AD within a few years (Almkvist et al., 1998). This decline in episodic memory, especially related to visuospatial function, is a key indicator of the disease progression to AD (Seo et al., 2021).

Episodic memory refers to the ability to remember specific events or experiences (Dickerson & Eichenbaum, 2010), and it can be divided into verbal and non-verbal episodic memory (Allen & Fortin, 2013). Visuospatial episodic memory as a specific category of nonverbal memory includes information on position and the visual content of an event (Dias et al., 2018). Studies have shown that deficits in visuospatial memory are stronger and appear earlier than deficits related to visual memory in patients with MCI or AD compared to healthy elderly participants (Mapstone et al., 2003). The remarkable impairment of visuospatial abilities is associated with higher risk of progression from amnestic subtype of MCI (aMCI) to AD (Berente et al., 2022). Recent neurophysiological and imaging studies have revealed that changes in visuospatial functions can be detected in the early stages of AD, making it an emerging biomarker for the disease (Mandal et al., 2012).

1.3 Visuospatial episodic memory related to the visuospatial process deficits in mild cognitive impairment

Researchers have shown that individuals with MCI and AD exhibit increased brain activation during visual or visuospatial tasks, suggesting compensatory mechanisms (Prvulovic et al., 2002; Thulborn et al., 2000; Yetkin et al., 2006). Functional magnetic resonance imaging (fMRI) studies involving location matching tasks have reported increased brain activation in patients with MCI and AD compared to healthy elderly individuals. In healthy older adults, positional matching tasks activate the middle layer occipital where gyrus, praecuneus, inferior parietal lobe (IPL), and middle frontal gyrus (MFG). In patients with MCI, inese regions, except IPL, show activations, along with additional activations in the superior parietal lobule (SPL), MFG, superior fusiform frontal gyrus, and hippocampus. In AD, additional activations are found in several brain regions, including the left superior temporal gyrus, praecuneus, inferior frontal gyrus, right insula, precentral gyrus, bilateral postcentral gyrus, and posterior cingulate gyrus (Yetkin et al., 2006).

In individuals with MCI, impairments in visuospatial functions are specific to the dorsal inferior parietal lobe (IPL), whereas both the dorsal IPL and ventral superior parietal lobule are impaired in AD (Derbie et al., 2022). These deficits are linked to difficulties in orienting to visual stimuli, egocentric and allocentric representations, and visuospatial perception (Derbie et al., 2022). Furthermore, persons with MCI demonstrate increased fMRI responses in the posterior hippocampal, para-hippocampal, and fusiform regions, potentially as a compensatory mechanism (Hämäläinen et al., 2007). These compensatory responses suggest that MCI and AD patients require more brain activity to perform tasks compared to individuals without cognitive deterioration (Derbie et al., 2022; Egerházi et al., 2007; Yetkin et al., 2006). From this perspective, Some scholars (Vannini et al. 2007) argued that compensatory mechanisms may mask the starting degenerative process by determining functional changes, and as the disease worsens, compensatory activity in other areas gradually increases. These findings highlight the need to identify modifiable risk factors for altered visuospatial processing, aiming to develop the effective interventions for visuospatial episodic memory problems related to visuospatial process deficits in participants with MCI (Hamilton et al., 2021; Kravitz et al., 2013).

The visual and visuospatial process system is supported by two distinct pathways, the ventral and dorsal streams, which process object information and spatial information (Kravitz et al., 2013). These pathways work together to form the perception of the spatial environment and object movement (Martins et al., 2014) (see Fig.1 for details). However, recent evidence challenges the strict segregation of these pathways, suggesting that the ventral stream is not solely involved in object recognition, and indicating that the dorsal stream extends beyond vision or visuomotor control (Sheth & Young, 2016). The dorsal stream has also been implicated in object perception, with regions in this pathway containing object representations that play a functional role in perception (Freud et al., 2016).

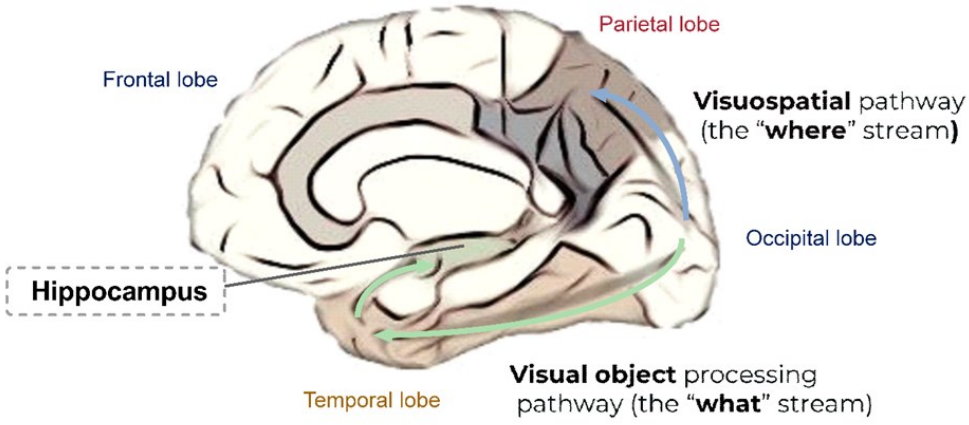


Figure 1 Neural frameworks involved in visuospatial processing. The dorsal stream (blue; the "where" stream), which includes the parietal cortex and its projections to the frontal cortex, is involved in the processing of spatial information. The ventral stream (green; the "what" stream), which includes the inferior and lateral temporal cortex and their projections to the medial temporal cortex, is involved in the processing of categorical or semantic information. Occipitotemporal cortex (OTC) visual object processing pathway (the "what" stream); Parietotemporal visuospatial pathway (the "where" stream) formation of memory. Figure redrawn from Martins et al. Neuroimage. (2014, page 302).

We hypothesize that different visual and visuospatial processes may enhance our understanding of episodic memory deficits in individuals with MCI. These pathways are implicated in different memory processes, with recruitment of different parts of the visual pathway: visual recognition memory (Pattern recognition memory: PRM) processes is related to the ventral pathway (green; the “what” stream); visual pattern and visuospatial associative learning (Paired Associate Learning test: PAL) processes are related to the dorsal pathway (blue; the “where” stream). The visual stream, comprising a network of brain regions, processes visuospatial information crucial for goal-directed movements and sensorimotor coordination (Kravitz et al., 2011). Research shows that assessing impaired PRM and PAL in individuals with amnestic MCI (aMCI) allows for clear differentiation between aMCI patients and healthy individuals (Egerházi et al., 2007). The PAL test, examining the ability to establish visuospatial associations, is particularly related to medial temporal lobe and hippocampus functions, essential for identifying MCI (Barnett et al., 2016; Yetkin et al., 2006). Understanding these distinctions between visual recognition memory and visuospatial associative learning memory can lead to better diagnostic tools and targeted therapeutic strategies for addressing different episodic memory deficits in MCI individuals.

1.4 Relationship between sensory functions and cognition in ageing and pathological aging

Ageing-associated decline in sensory functions can lead to cognitive deficits and reduced quality of life (Heft & Robinson, 2017; Li et al., 2001; Nusbaum, 1999). These declines are often due to age-related changes in the sensory organs and central nervous system processing (Nusbaum, 1999). For instance, impaired tactile sensitivity has been linked to altered cortical sensory representations and noisy neuronal processing, which may contribute to cognitive decline (Kalisch et al., 2009). Furthermore, age-related changes in neuromodulation can lead to less distinctive sensory cortical representations, affecting memory and attentional functions (Li et al., 2001). Sensory impairments, such as hearing loss and vision loss, have been associated with cognitive decline and dementia (Xiao et al., 2021). Overall, these findings highlight the importance of understanding the relationship between sensory and cognitive decline in aging.

A neuroscience-based model of ageing emphasizes the loss of brain plasticity, sensorimotor capacities and subsequent cognitive decline (Mahncke, Bronstone, et al., 2006). It has been shown that older adults display a decline in neural plasticity with physiological ageing, especially in the sensorimotor cortex (Dinse, 2006; Park & Reuter-Lorenz, 2009). However, it is also unknown whether there is a similar correlation between sensory and cognitive components in the tactile processing-related abilities of MCI patients. We assume that the tactile abilities of the somatosensory cortex are related to memory. How individuals with MCI process somatosensory information and to what extent they experience deficits of somatosensory function and how this relates to visuospatial memory, needs to be better understood.

Recent studies have shown that reduced tactile sensitivity is associated with memory decline in individuals with MCI (Löffler et al., 2024), and that cortico-cortical interactions between sensory regions are impaired in MCI (Golob et al., 2001). However, the specific contribution of each sensory system during cognitive processing remains unclear (Popovich & Staines, 2014). Passive repetitive sensory stimulation has been shown to improve perceptual abilities and induce plastic changes in the somatosensory cortex (Freyer et al., 2012). The primary somatosensory cortex (S1) has been implicated in memory tasks with tactile stimuli (Harris et al., 2002) and cooperative processing of tactile information has been observed between S1 and the posterior parietal cortex (Ku et al., 2015). Top-down suppression from the prefrontal to the primary somatosensory cortex has been shown to facilitate tactile memory (Savolainen et al., 2011). Tactile processing has been found to activate and deactivate visual cortex areas (Merabet et al., 2007). These findings suggest a complex interplay between sensory processing, cognitive decline, and the organization of the somatosensory cortex in MCI, which warrants further investigation.

1.5 Overview of tactile processing and its representation in somatosensory cortex (Brodmann areas 1, 2, and 3)

The somatosensory cortex is important in processing tactile information and is organized into distinct areas (Rowe et al., 1996). These areas are involved in various aspects of touch processing, from basic tactile discrimination to more complex functions like object recognition (Zhou & Fuster, 2000). Neurons in the somatosensory cortex

process sensory information from the hand by integrating information from large populations of receptors to extract specific features (Gardner, 1988). The system also decodes a wide range of tactile stimuli, endowing us with the capacity for object recognition, texture discrimination, sensory-motor feedback, and social exchange (Abraira & Ginty, 2013). The somatosensory cortex is involved in the short-term retention of tactile information and can respond to behaviourally associated visual and tactile stimuli (Zhou & Fuster, 2000).

S1 is characterized by its distinctive cytoarchitecture and functional modules (Ann Stringer et al., 2014; Delhaye et al., 2018), with clear functional hierarchies across its subregions (Schellekens et al., 2021) (see Figure 2). Brodmann areas BA3, BA1, and BA2 show increasing receptive field sizes, suggesting a hierarchical processing of tactile information (Schellekens et al., 2021). While BA3b and BA1 process general tactile information, BA2 specifically handles object size and shape (Hsiao, 2008). S1 and S2 exhibit distributed and overlapping representations of current stimuli, recalled information, and stimulus categories (Condylis et al., 2020). Prior information enhances tactile representation in S1, improving detection performance (Kassraian et al., 2023). Memory tasks involving tactile stimuli engage frontal-parietal networks and modulate finger representations in S1. Damage to ventrolateral and dorsomedial somatosensory association cortices results in distinct somaesthetic syndromes (Caselli, 1993). The somatosensory system interacts with other sensory modalities, suggesting shared neural networks for tactile memory (Gallace & Spence, 2009). These findings highlight the complex nature of somatosensory processing and its importance in motor control, learning, and functional recovery (Borich et al., 2015).

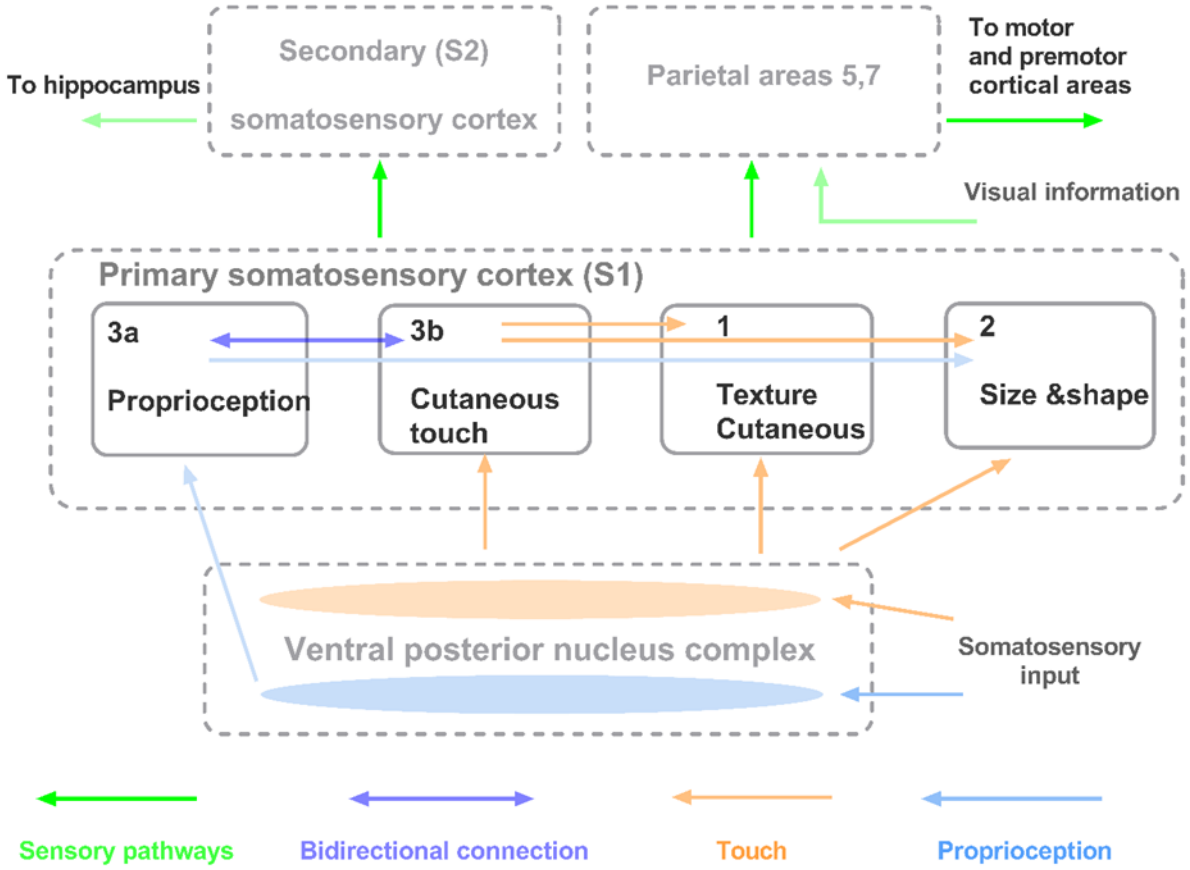


Figure 2 The hierarchical organization of somatosensory cortical areas and distinct functional roles of each Brodmann area. Figure redrawn from Delhaye et al. (2018, page 1593). Major connections between somatosensory areas. Schematic representation of the major connections between somatosensory areas in the central nervous system. Sensory input from the thalamus, then to ventral posterior nucleus (VP), primary somatosensory cortex (S1), secondary somatosensory cortex (S2), the lateral parietal cortex (LPC), and the posterior parietal cortex (PPC). S1 is located along the anterior border of the parietal lobe and comprises four cytoarchitectonically defined areas: Brodmann areas 3a, 3b, 1, and 2, with area 3b being the primary somatosensory cortex due to its significant thalamocortical input. The hierarchical organization of these areas is supported by evidence indicating that lesions in area 3b result in the loss of tactile abilities, including texture and shape discrimination and haptic object recognition, while lesions in area 1 selectively impair texture discrimination but not shape discrimination. Neurons in area 3a, located near the fundus of the central sulcus, primarily respond to proprioceptive stimuli, such as joint manipulations and muscle stretch, and possibly heat-induced pain. Lesions in area 2 impair the coordination of finger movements and the ability to discriminate the shape and size of grasped objects, highlighting the distinct functional roles of each area within the somatosensory cortex.

The somatosensory system plays an important role in tactile perception, action, and object recognition (Dijkerman & de Haan, 2007). The primary somatosensory cortex (S1) contains topographic maps of the body surface, which can be reorganized through plasticity (C. C. H. Petersen, 2007). Contrary to traditional views, S1 is involved in bilateral tactile representations and early integration of information from both sides of the body (Tamè et al., 2016).Tactile processing involves multiple cortical areas, including ventrolateral and dorsomedial somatosensory association cortices, which contribute to different aspects of somaesthetic function (Caselli, 1993). Perceptual learning can be induced through passive tactile co-activation, leading to cortical reorganization and improved spatial discrimination, but potentially impairing frequency discrimination (Hodzic et al., 2004).The somatosensory system processes various aspects of touch, including direction, softness, and shape, through specialized neural codes and mechanisms (Franzen et al., 1996). These findings highlight the complexity and adaptability of the somatosensory system in processing tactile information.

Recent research has highlighted the importance of tactile processing and somatosensory cortex alterations in MCI. The somatosensory cortex plays an important role in tactile awareness and body representation, with parallel processing streams for action and perception (Dijkerman & de Haan, 2007; Gallace & Spence, 2009). Tactile discrimination tasks have emerged as potential diagnostic indicators for MCI, offering advantages over visual or auditory tests in older populations (Xu et al., 2024). The topography of the body-surface map in the somatosensory cortex is influenced by temporal correlations of finger inputs, which may be associated with memory performance in MCI (Jones & Forster, 2015).These findings suggest that tactile processing deficits and somatosensory cortex alterations contribute to cognitive decline in MCI, providing new avenues for early diagnosis and intervention (R. C. Petersen & Morris, 2005).

1.6 Fingertip representations in S1 and related tactile and cognitive decline.

Research on fingertip representations in S1 has revealed a complex cortex organization associated with tactile and cognitive functions. Studies using high-resolution fMRI have identified somatotopic finger representations in S1 subdivisions, particularly areas 3b, 1, and 2 (Martuzzi et al., 2014; Sanchez-Panchuelo et al., 2012; Schweizer et al., 2008). Furthermore, the functional hierarchy within S1 has been demonstrated, with increasing receptive field sizes from BA3 to BA2 (Schellekens et al., 2021). These

fingertip representations with associations between tactile acuity and fingertip representation size in BA3b and BA1 have been observed in healthy individuals (Härtner et al., 2021). Importantly, finger representations in S1 exhibit plasticity, changing in response to training or task demands (Braun et al., 2000) and can be modulated by cognitive tasks (Rabe et al., 2023). These findings highlight the dynamic nature of fingertip representations in S1 and their involvement in both sensory processing and cognitive functions.

Research indicates that aging affects S1 and tactile function. Older adults show enlarged hand representations in S1 (Kalisch et al., 2009) and increased cortical excitability (Lenz et al., 2012), which are associated with decreased tactile acuity and discrimination (McIntyre et al., 2021). However, some elderly individuals retain high levels of cortical plasticity (Pellicciari et al., 2009), which may serve as a compensatory mechanism. Notably, cortical representations can be modified by experience, as demonstrated in string players (Elbert et al., 1995), suggesting potential for adaptive changes throughout life or cognition status. Increased map activation, larger topographic map areas, and reduced cortical inhibition in the primary somatosensory cortex can lead to less precise functional map readouts, impacting sensory, motor, and cognitive functions(Pleger et al., 2016; Lenz et al., 2012; Kalisch et al., 2009). These findings suggest that variability in topographic maps in the somatosensory cortex of elderly individuals is linked to both adaptive and maladaptive cognitive functions. However, previous studies have not explored how somatosensory organizational features relate to functional status in pathological aging, such as in participants with MCI. Specifically, whether different cortical features in Brodmann's area (e.g., cortical distance of fingertips or the size of the representation of the individual fingertip; the fingertip characterization parameters are detailed in the Methods section) are associated with memory performance in participants with MCI remains to be explored.

1.7 Goals and hypotheses

A neuroscience-based model of pathological ageing emphasizes the loss of brain plasticity, sensorimotor capacities and subsequent cognitive decline (Mahncke et al., 2006). It has been shown that older adults display a decline in neural plasticity with

physiological aging, especially in the sensorimotor cortex (Dinse, 2006; Park & Reuter-Lorenz, 2009), but the relationship between them remains unclear, and further comprehensive understanding of the mechanisms and processes of cognitive and sensory aging at different levels is needed.

This thesis sought to investigate the association between tactile processing, memory performance and the organization of somatosensory cortex in participants with mild cognitive impairment. We assessed sensory processing using mechanical detection thresholds (Cutaneous Sensory Thresholds; CST). Memory function was assessed using visual recognition memory (Pattern recognition memory; PRM) and visuospatial associative learning (Paired Associate Learning test: PAL) performance. Using passive tactile stimulation of the fingers in the right hand and a mapping task during functional magnetic resonance imaging (fMRI), the representation of somatosensory cortex (both cortical distance of fingertips and the size of the representation of the individual fingertip) was measured in specific Brodmann areas (within area 3, area 1 and area 2).

The main hypotheses in this study were as follows:

Hypothesis 1: Peripheral tactile sensitivity and central fingertip representation in the somatosensory cortex are associated with pattern recognition memory.

1.1 Reduced peripheral tactile sensitivity is related to poorer pattern recognition memory.

1.2 Enlarged central fingertip distance is related to poorer pattern recognition memory.

1.3 Increased central fingertip representational size is related to better pattern recognition memory.

1.4 Central fingertip representation (cortical distance or size) in the somatosensory cortex mediates the association between peripheral tactile sensitivity and pattern recognition memory.

Hypothesis 2: Peripheral tactile sensitivity and central fingertip representation in the somatosensory cortex are associated with paired associate learning memory.

2.1 Reduced peripheral tactile sensitivity is related to more paired associate learning memory errors.

2.2 Enlarged central fingertip distance is related to more paired associate learning memory errors.

2.3 Increased central fingertip representation size is related to less paired associate learning memory errors.

2.4 Central fingertip representation (cortical distance or size) in the somatosensory cortex (S1) mediates the association between peripheral cutaneous sensory threshold and paired associate learning memory errors.

2 MATERIALS AND METHODS

2.1 Participants

The study consisted of thirty-six participants aged between 49 and 79 years who fulfilled criteria for MCI (R. C. Petersen et al., 1999; Winblad et al., 2004). The inclusion and exclusion criteria followed our previously described standard protocol (Bekrater-Bodmann et al., 2019) and are presented in Table 1. The diagnostic procedure followed the current guidelines (Deuschl G & Maier W, 2017).The detailed clinical workup included comprehensive laboratory neuropsychological assessments, MRI/CT and cerebrospinal fluid (CSF) analysis, as shown in Table 1.

Table 1. Criteria for the diagnosis of MCI and diagnostic procedure

Inclusion criteria	
Participants were included if they were rated with a score of 0.5 on the Clinical Dementia Rating Scale (Morris, 1993) and fulfilled one of the following criteria:	(a) at least one z-score < -1.2 of the Consortium to Establish a Registry for Alzheimer's Disease (CERAD+) word list recall or retention, figures recall or retention performance (Welsh et al. 1994), Wechsler Memory Scale – Revised (WMS-R) immediate or delayed recall performance (Wolfsgruber et al., 2015); (b) at least one altered amyloid/tau/neurodegenerative (ATN) biomarker: reduced Aß42 (<600) or Aß-ratio (<0.55), or increased t Tau (>450) or p Tau (>61) (Dumurgier et al., 2015; Hansson et al., 2019; Jack et al., 2018) ; (c) age>60 years and MTA≥2, or age≤60 years and Medial Temporal Lobe Atrophy Score MTA≥1 (Scheltens et al., 1995)
Exclusion criteria	
The following exclusion criteria were applied to all participants:	(a) inability to complete the written forms, current dementia, other neurodegenerative diseases, stroke and other neurological disorders with neurocognitive impairments as a major feature, myocardial infarction within the last 2 years, a deficit in vitamin B12, folate or thyroid-stimulating hormone, which is not substituted for at least 3 months, lifetime prevalence of certain severe mental disorders (schizophrenia and other psychotic disorders bipolar disorder, obsessive-compulsive disorder, post-traumatic stress disorder), current severe major depression and other axis I mental disorders; (b) relevant biomedical devices (because of the MRI procedure); (c) current intake of dopaminergic, serotonergic, beta-adrenergic blocking or benzodiazepine drugs to rule out effects on general cognition.
Detailed clinical workup including	
Magnetic Resonance Imaging/Computerized Tomography study (All thirty-six participants of this study)	(a) an expert evaluation of T1-, T2-weighted and fluid attenuated inversion recovery 3T MRI images with semi-quantitative ratings of medial-temporal lobe atrophy (Scheltens score, MTA) (Scheltens et al., 1995); (b) subcortical white matter lesions (Fazekas scale) (Fazekas et al., 1987).
Cerebrospinal fluid (CSF) analysis	Cerebrospinal fluid to determine total tau (t Tau), phosphorylated tau (p Tau), Amyloid ß42 (Aß42), Amyloid ß40 (Aß40), their ratio (Aß42/Aß40, Aß-ratio), and neuron-specific enolase (Dumurgier et al., 2015; Hansson et al., 2019; Jack et al., 2018).
Laboratory neuropsychological assessments	(a) the German version of the Mini-Mental State Examination (MMSE) (Folstein et al., 1975) (b) the Consortium to Establish a Registry for Alzheimer's Disease (CERAD+) neuropsychological test battery (Welsh et al., 1994); (c) the logical memory subtests of the Wechsler Memory Scale-Revised (WMS-R) (Wolfsgruber et al., 2015) (d) an expert rating on the Clinical Dementia Rating scale (CDR) (Morris, 1993)

Participants were recruited from the Memory Clinic of the Central Institute of Mental Health (CIMH), Mannheim, Germany. All participants gave their written and informed

consent. Ethical approval of the study was provided by the Medical Ethics Committee II of the Medical Faculty Mannheim, Heidelberg, Germany (2015–543N-MA) and was conducted in accordance with the Declaration of Helsinki.

2.2 Memory performance assessed by the Cambridge Neuropsychological Test Automated Battery (CANTAB)

The CANTAB represents an advanced computerized tool for the assessment of nonverbal frontal-subcortical functioning (Robbins et al., 1994). The CANTAB is a computerized software tool developed by the University of Cambridge in 1986, and is considered to be the most valid and sensitive touch-screen test available internationally for measuring cognitive functioning (Junkkila et al., 2012).

We are focusing on different memory functions assessed by CANTAB (Sahakian et al., 1988). Particularly, the PAL paradigm and the PRM paradigm are two tasks which engage visuospatial association and visual pattern recognition memory, respectively (see Fig. 3). The performance in both tests has been identified as a marker of cognitive decline, with a predictive accuracy of about 80% in distinguishing persons with aMCI from healthy control participants. It is also a sensitive indicator to differentiate aMCI from Alzheimer's dementia (Juncos-Rabadán et al., 2014).

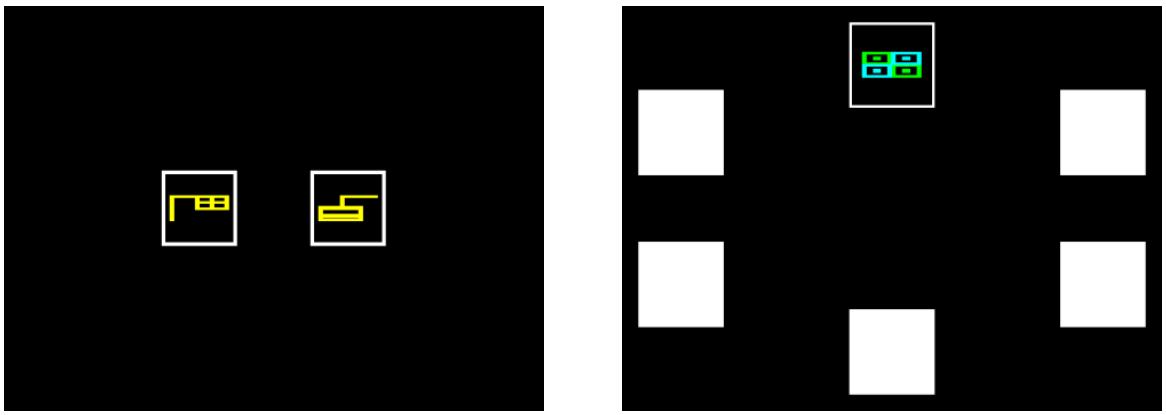


Figure 3 Memory tests. Paired Associates Learning (PAL) and Pattern Recognition Memory (PRM) from the Cambridge Automatic Neuropsychological Test Automated Battery (CANTAB). The two tasks to test visual pattern recognition memory and visuospatial associative memory are shown. In this study, the CANTAB and specifically these subtasks were used to test the different components of nonverbal memory. The participant needs to identify the pattern that was previously shown (i.e., the target pattern) in a series of patterns. In the left panel the PRM

task is presented. It is a test of visual pattern recognition memory in a 2-choice forced discrimination paradigm. In the right panel the PAL task is presented. It is a test to assess visuospatial associative memory and new learning.

2.2.1 Paired Associates Learning (PAL)

In the CANTAB, the PAL test assesses the visual episodic memory by means of a paired associates learning paradigm. This test is primarily sensitive to changes in medial temporal lobe functioning and is sensitive to damage in the medial temporal lobe area, with some input from the frontal lobes(Barnett et al., 2016).

In this test, boxes are displayed on the screen and are "opened" in a random order, each one of them containing a pattern. The patterns are then displayed in the middle of the screen of a laptop computer, one at a time, and the participant should select the box in which the pattern was originally located. If the participant makes an error, the boxes are opened in sequence again to remind the participant of the locations of the patterns. Participants respond on the touch screen of the laptop by tapping the location in which the pattern appeared. In the data presented here, participants could complete up to 5 stages, which involved learning of one, two, three, six or eight pattern-location pairings. We used the “total errors adjusted score” (a measure that is adjusted for the level of difficulty reached) as a measure for associative memory performance with higher scores indicating lower memory performance (Barnett et al., 2016).

2.2.2 Pattern Recognition Memory (PRM)

The PRM test is included in the CANTAB and is sensitive to temporal or hippocampal dysfunctions. PRM is a test of visual pattern recognition memory in a 2-choice forced discrimination paradigm. In this test, the participant is presented with a series of visual patterns, one at a time, and is required to choose between a pattern they have already seen and a novel pattern. The outcome measures of the PRM task include the number and percentage of correct trials. A higher number and percentage of correct trials are indicative of better pattern recognition memory (Karlsen et al., 2022).

2.3 Peripheral tactile sensitivity test: cutaneous sensory thresholds (CST)

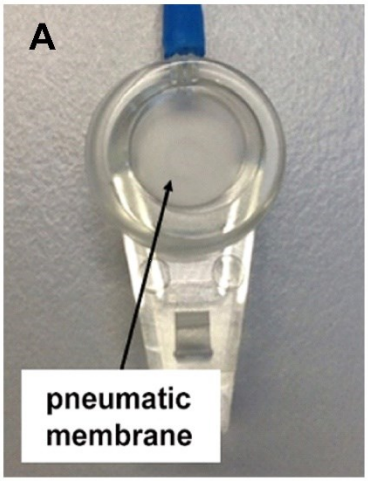
The tactile mechanical threshold was determined by stimulating the fingertip of the second digit of the right hand using von Frey filaments (Marstocknervtest, Marburg,

Germany). Testing touch forces ranged from 0.25 to 512 mN in a logarithmic scale (Löffler et al., 2024). During the test, subjects were asked to close their eyes and to verbally indicate whenever they perceived a sensation on their skin. The filaments were manually applied by the experimenter perpendicular to the subject's skin. A standard examination protocol and staircase procedure (Bell-Krotoski et al., 1995; Christensen et al., 2020) was applied resulting in a mechanical threshold, defined as the geometric mean of five below- and five above-threshold intensities. Here, lower scores reflect enhanced sensation. Due to an acute injury at the stimulation site, data on mechanical detection threshold are missing for two participants with MCI (Löffler et al., 2024).

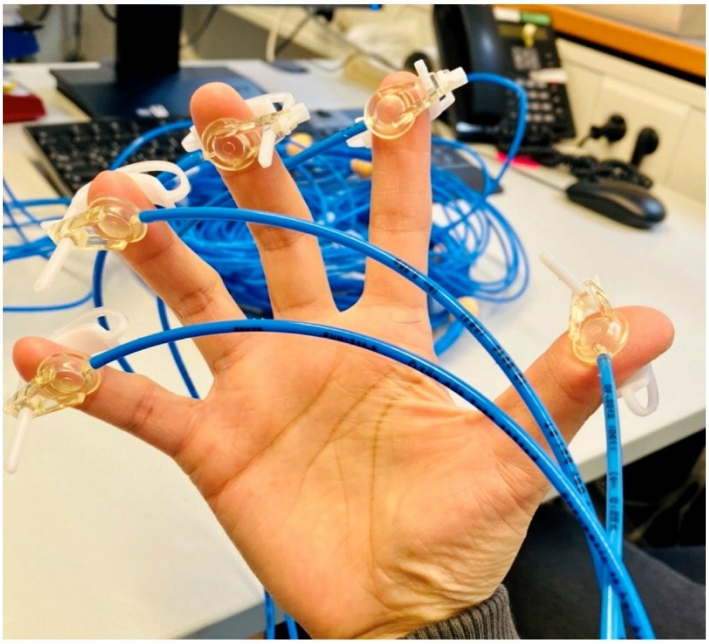
2.4 Magnetic resonance scanning procedure.

2.4.1 Functional magnetic resonance imaging task and stimulation

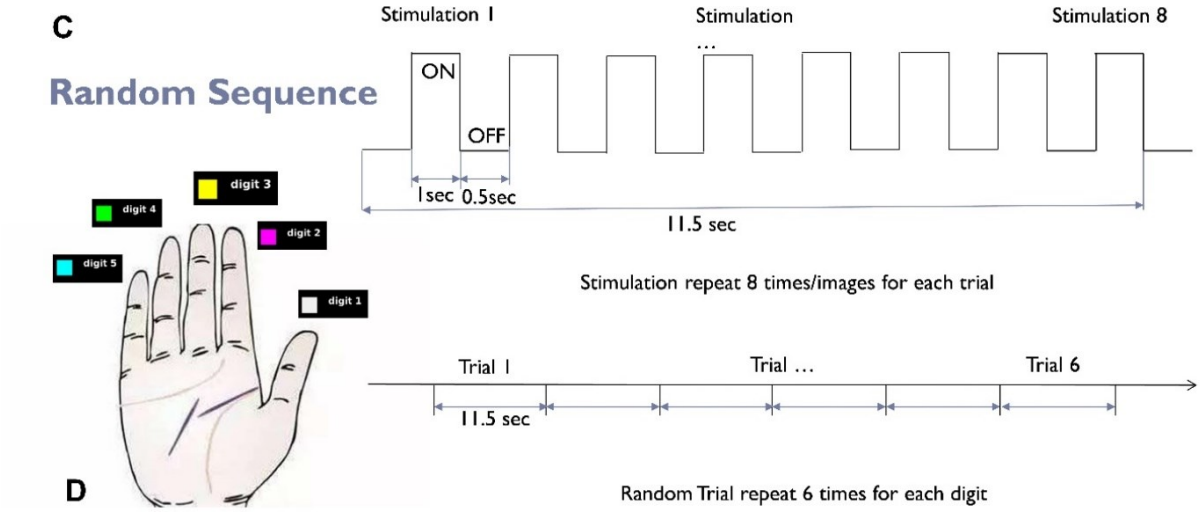
Pneumatic stimulus finger clips (MEG International Services Ltd. Coquitlam, Canada; Fig. 4a) were used for tactile stimulation. Stimulus application and display of the paradigm were electronically controlled with a custom-made pneumatic relay device (Festo AG & Co. KG, Esslingen, Germany). In the fMRI examination, all digits of the right hand were stimulated on the distal phalanx with the pressure of compressed air driving the pneumatic stimulation which was set to 3 bar (Bekrater-Bodmann et al., 2014). Stimuli were presented in a random block design which consisted of stimulation blocks (each lasting 11.5 s), interleaved by off-blocks of randomized duration between 10 and 14s (Bekrater-Bodmann et al., 2019). Stimulus presentation details are available in Fig. 4c.



B



Pneumatic finger clip,
MEG International Services
Ltd., Coquitlam, Canada



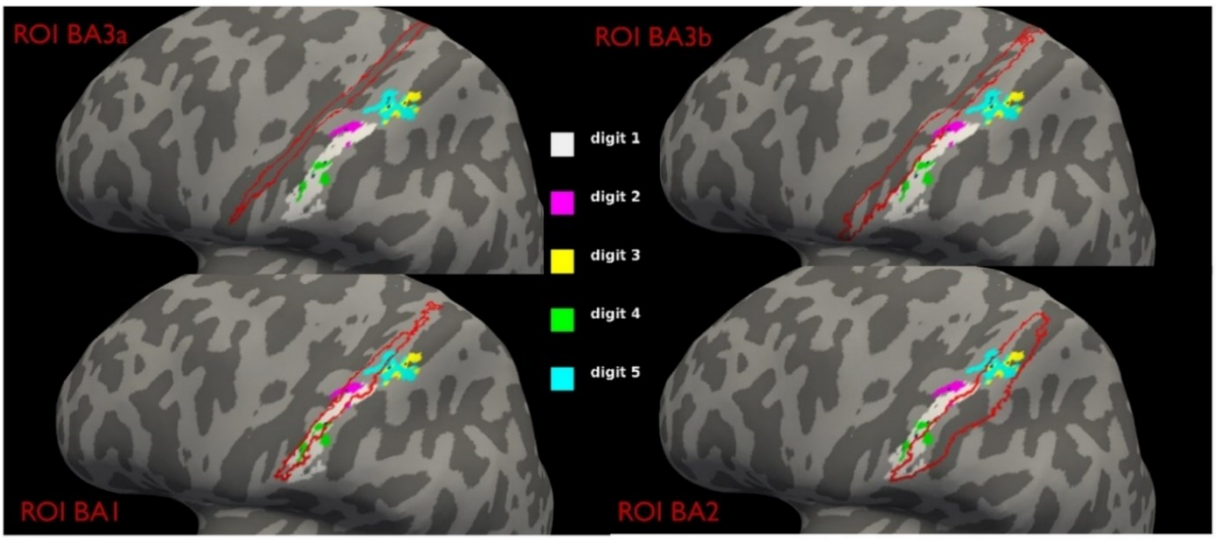


Figure 4 fMRI task and stimulation. A. Pneumatic stimulus finger clips (MEG International Services Ltd. Coquitlam, Canada). B. Stimulation of the fingers; C. functional magnetic resonance imaging random block design. D. Display of finger activations in Brodmann areas of the primary somatosensory cortex (S1). Brodmann areas as a region of interest (ROI) (BA3a, BA3b, BA1 and BA2).

2.4.2 Magnetic resonance imaging data parameters

Magnetic Resonance Imaging (MRI) data were acquired on a 3 Tesla whole body scanner (SIEMENS TRIO) with a 32-channel head coil. During the scans, participants were instructed to let their minds wander, avoid repetitive thought, keep their eyes open and focus their attention on a central fixation point displayed in the center of an MR-compatible high-resolution screen and projected on a mirror attached to the MR head coil. A structural T1-weighted 3D scan was acquired using a gradient echo sequence (voxel size 0.8x0.8x0.8 mm, field of view 250x250 mm, repetition time/echo time/inversion time TR/TE/TI =1900/2.72/900 Ms., 224 slices, flip angle 9°, with a 0.8 mm isotropic resolution). One whole-head fast gradient-echo echo-planar functional image was recorded to optimize the anatomical registration of successive functional images targeting the left somatosensory cortex. Functional MRI (fMRI) was acquired using a gradient-echo echo-planar imaging technique with field of view (FOV) = 220 x 220 mm, in-plane resolution 1.2×1.2 mm (22 slices, slice thickness= 1.8 mm, TR/TE=1500/22 Ms., flip angle 90°, acquisition order interleaved even).

2.4.3 Magnetic resonance imaging data preprocessing

All imaging data were processed using FreeSurfer Software version 6.0 (Fischl et al., 2002). First, starting from T1-weighted brain scans, the cortical surface was automatically reconstructed and the white matter and pial surfaces were demarcated (Desikan et al., 2006; Destrieux et al., 2010), which were then used to define regions of interest for subsequent functional analysis and digit somatotopic mapping.

The preprocessing of the structural image served to identify the anatomical position of the primary S1 cortex (Fischl et al., 2002, 2004) in the left hemisphere of each participant separately, yielding subject-specific cytoarchitectonic probability maps (Fischl et al., 2008) useful to restrict the analysis to Brodmann area 3b, area 3a, area 2 and area 1 (i.e. the four regions-of-interest considered in the following analysis) . These four

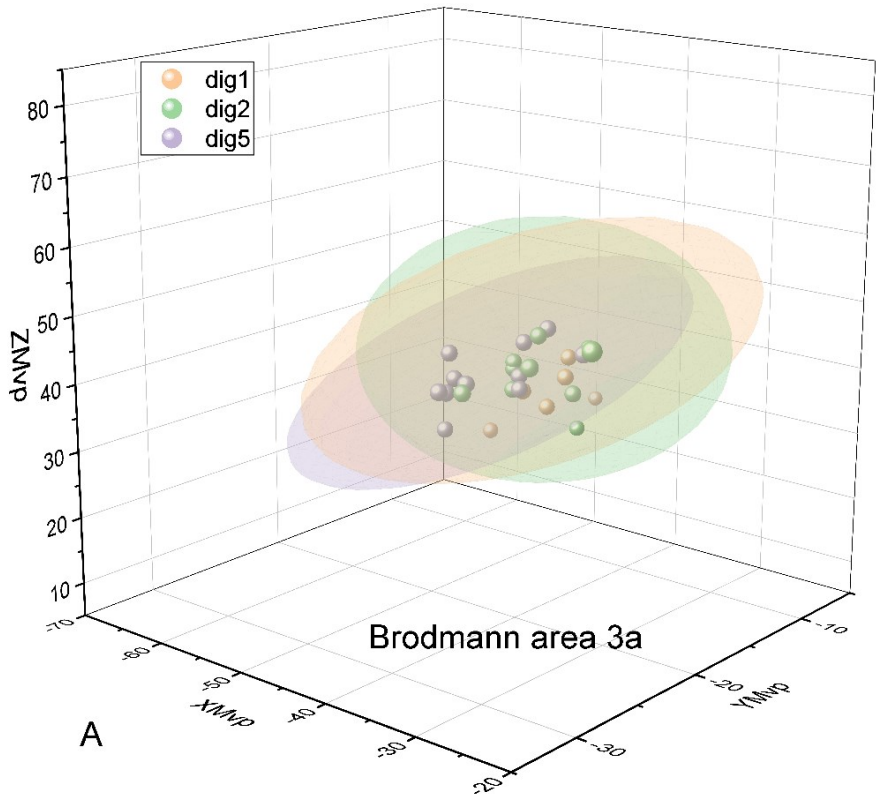
regions-of-interest were selected because of their relevance in somatotopic representation of the hand using pressure stimuli (Choi et al., 2016; Janko et al., 2022; Pfannmöller et al., 2016).

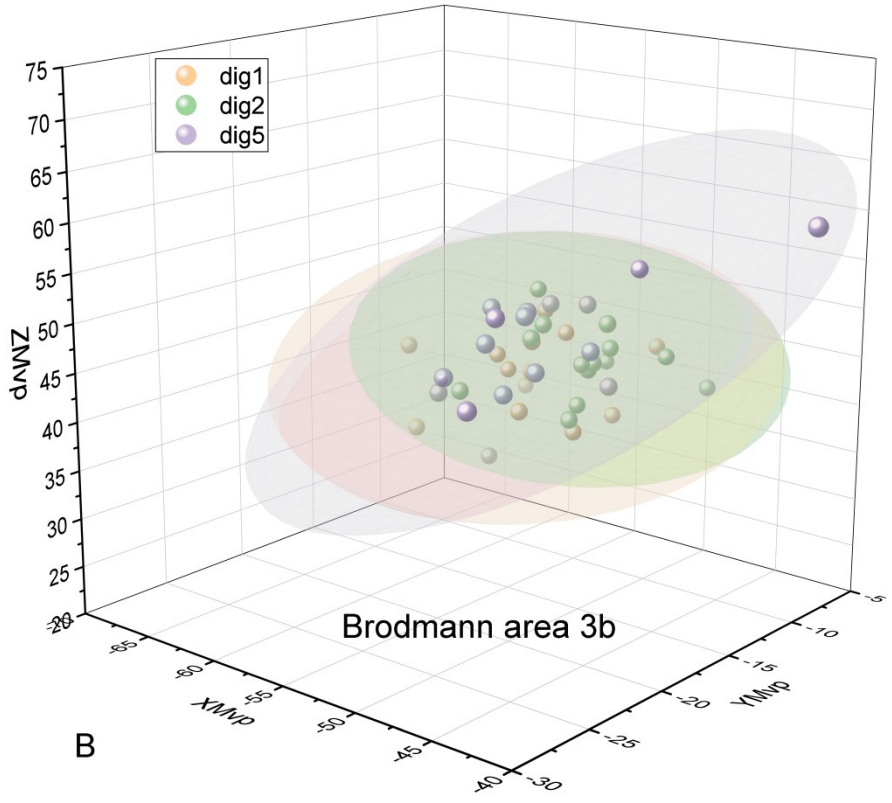
Table 2: MNI coordinates for peak activations of the first, second and fifth digit fingertips in participants. MNI coordinates for peak activations of the right fingers. All peak activations are presented in the left hemisphere. MNI = Montreal Neurological Institute. x y z = A standard set of 3 coordinates in x, y and z directions developed at the Montreal Neurological Institute (MNI) should be reported as spatial locations in the brain.

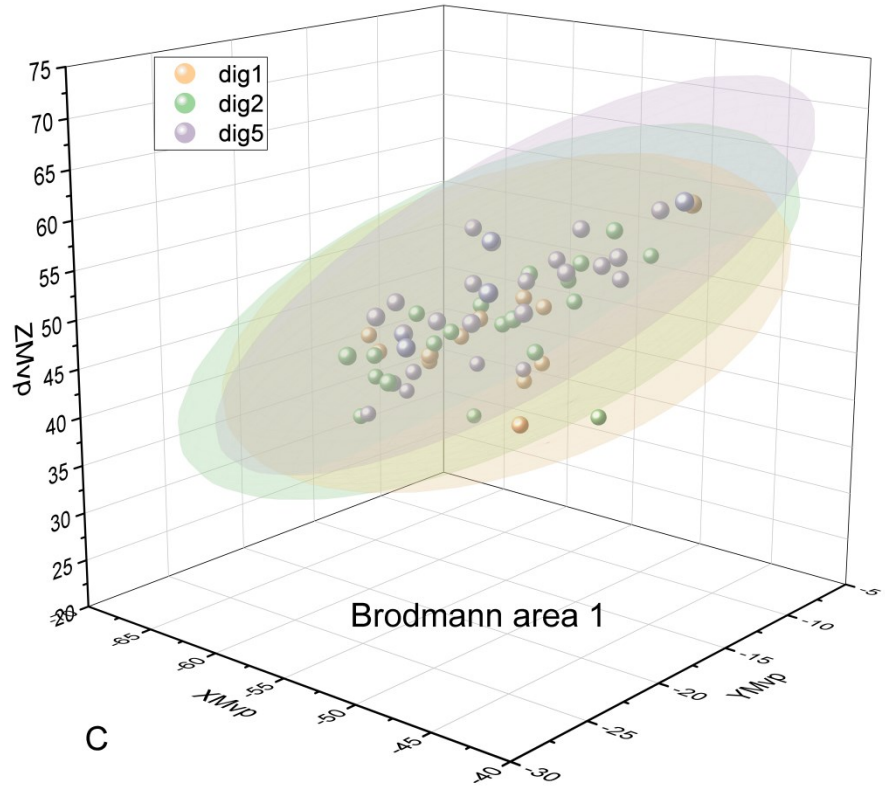
Brodmann area	**ID**	**X**	**Y**	**Z**	**X**	**Y**	**Z**	**X**	**Y**	**Z**
		First digit (sample size n=20)			**Second digit** (sample size n=25)			**Fifth digit** (sample size n=25)		
Brodmann area 2 (BA2)	1	---	---	---	---	---	---	---	---	---
	2	-52.72	-24.11	47.01	-44.79	-28.35	58.63	-44.79	-28.35	58.63
	3	---	---	---	---	---	---	-50.64	-18.62	40.42
	4	-58.12	-17.75	41.35	-47.55	-34.37	56.06	-47.46	-31.52	57.08
	5	---	---	---	-46.78	-22.51	48.61	-45.93	-23.25	48.86
	6	-58.85	-21.26	43.67	-46.64	-36.77	59.68	-45.92	-36.84	59.88
	7	-46.52	-23.54	48.62	-39.6	-36.31	59.57	-39.6	-36.31	59.57
	8	-48.58	-29.54	47.12	-44.74	-32.87	50.05	-41.42	-34.24	59.49
	9	-56.41	-19.13	45.3	-53.36	-10.42	39.76	-53.31	-10.6	41.06
	10	-48.7	-26.87	49.19	-51.03	-25.15	50.01	-48.7	-26.87	49.19
	11	-36.41	-34.77	65.99	-48.7	-23.61	48.65	---	---	---
	12	---	---	---	-55.18	-21.95	39.2	---	---	---
	13	-50.84	-22.97	49.07	-50.54	-23.38	47.78	-50.84	-22.97	49.07
	14	-41.39	-28.49	50.39	-56.58	-13.76	40.51	-44.23	-25.78	50.23
	15	-44.64	-29.87	57.36	-46.2	-28.81	57.17	-46.2	-28.81	57.17
	16	---	---	---	---	---	---	---	---	---
	17	-53.07	-19.96	34.85	-50.15	-27.02	40.57	-39.34	-35.32	50.72
	18	-48.56	-21.72	40.4	-49.13	-21.2	39.85	-40.31	-28.89	51.14
	19	-51.53	-16.77	44.28	-53.65	-15.24	43.5	-53.65	-15.24	43.5
	20	-55.15	-17.34	43.06	---	---	---	-55.33	-16.86	44.3
	21	-57.51	-16.36	42.87	-57.51	-16.36	42.87	-57.63	-16.18	41.67
	22	-54.5	-18.49	41.73	-49.9	-15.92	47.65	---	---	---
	23	---	---	---	-58.61	-13.81	35.96	-56.01	-15.66	32.67
	24	-38.77	-39.34	59.97	-38.55	-39.32	61.05	-39.22	-39.12	64.11
	25	---	---	---	-49.24	-21.82	41.91	-49.24	-21.82	41.91
	26	---	---	---	-39.17	-38.57	56.15	-58.19	-21.95	41.53
	27	-33.93	-27.16	70.18	-33.93	-27.16	70.18	-33.84	-28.02	70.59
	28	---	---	---	-54.19	-25.3	43.69	-55.15	-24.79	43.17
	29	---	---	---	---	---	---	---	---	---
	30	-49.23	-22.35	55.86	---	---	---	---	---	---

	31	-45.35	-27.78	54.27	-39.9	-28.71	55.77	-38.28	-33.18	63.25
	32	---	---	---	-46.73	-27.9	46.31	-42.37	-34.07	52.29
	33	---	---	---	---	---	---	-43.12	-22.69	55.5
	34	-50.52	-22.8	48.93	-48.52	-24.17	56.23	-41.5	-28.21	54.87

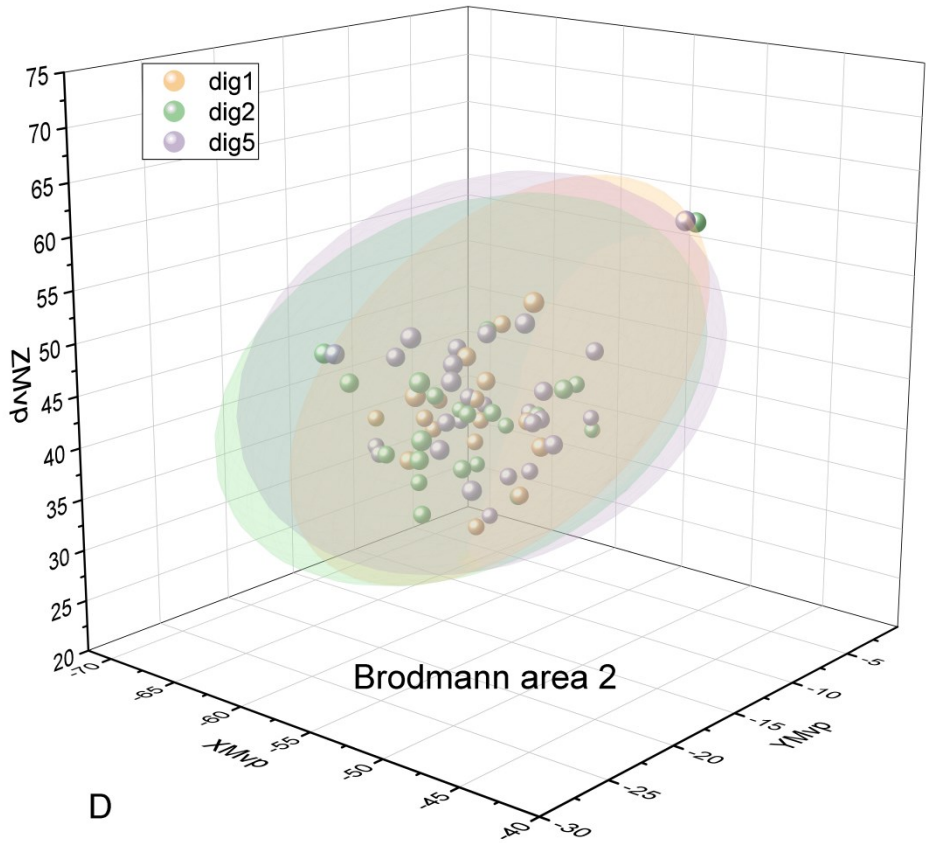
2.4.4 Somatotopic representation






dig1
dig2
dig5
ZMNI
XMNI
YMNI
Brodmann area 1

C


dig1
dig2
dig5
ZMNI
XMNI
YMNI
Brodmann area 2

D

Figure 5 Scatterplots based on the peak voxels for the first digit (yellow), the second digit (green) and fifth digit (purple) for participants based on regions of interest (ROIs) (A) Brodmann area 3a (B) Brodmann area 3b (C) Brodmann area 1 (D) Brodmann area 2. Peak voxels are grouped by ellipses with a confidence interval of 95%.

2.4.5 Associations of digit representations in the somatosensory cortex with memory performance

FreeSurfer version 6.0 functional analysis pipeline was used to investigate the mapping of the digits in the somatosensory cortex. Data from each participant were analysed separately. The detailed functional magnetic resonance imaging data analysis includes the pipeline of simultaneous registration, motion correction, and digit somatotopy surface projection.

The somatotopic mapping of the five digits was extracted from the individual participants' functional data after the preprocessing via FreeSurfer. We estimated the size of each fingertip representation and fingertip distance across all pairs of digits for each of the four Brodmann areas. Accordingly, for each Brodmann area, digit representations values were available from the preprocessing via FreeSurfer, encompassing both fingertip representation size and distance between each pair of digits. Thus, the matrix of digit representations that included the digit somatotopic mapping (both fingertip representation size and distance between each pair of digits) for each of the four Brodmann areas was obtained after the preprocessing.

Spearman correlation was employed to ascertain which fingertip representation values had a significant association with memory and tactile mechanical sensitivity (a significance level of 0.05 was used for all analyses). Then, we chose the fingertip representation values that were significantly associated to both memory and tactile mechanical sensitivity in the following analyses (univariate regression models and mediation analysis).

2.5 Statistical analysis

Analyses were carried out using SPSS version 26 (Armonk, NY: IBM Corp.). Continuous variables were checked for normal distribution using Kolmogorov–Smirnov tests.

Descriptive characteristics of each variable are reported as mean and standard deviation (SD) for continuous variables and frequency and percentages for categorical variables.

To examine associations between the sensory, memory domains, we computed Spearman correlation coefficients between tactile sensitivity, digit representation variables and memory performance, assessed from the PAL and PRM tests (The PERCENTRANKS function in SPSS software has been used to convert numerical values into percentiles in their Spearman correlation).

Univariate regression models (PLS regression) and mediation analysis (PLS path model: PLS-SEM, bootstrapping) were conducted using SmartPLS Statistics (Version 4.0, SmartPLS GmbH, Oststeinbek, Germany).

To identify independent determinants of memory, univariate regression models were calculated for each of the two memory measures, using PAL and PRM score as outcome. Tactile sensitivity and digit representation variables were analysed to determine the respective associations with memory. For the regression models, coefficients (β), 95% confidence intervals (CI) and R^2 along with the p-value for the model are reported. A significance level of 0.05 was used for all analyses.

Mediation analyses (Wang et al., 2022), which test whether the covariance between two variables can be explained by a third variable (the mediator), were conducted to assess the directional association of tactile sensitivity and memory performance. We assessed the mediation effect of the organization of somatosensory cortex on the association between the tactile sensitivity and memory performance. Mediation analysis was run in SmartPLS software (Hair et al., 2019), version 4.0 using the “PLS-SEM” model, with nonparametric bootstrapping and 5,000 iterations to estimate direct and indirect effects and P-values between variables.

3 RESULTS

3.1 Clinical characteristics of participants with MCI

Of the total number of thirty-six participants, two participants were excluded from the analyses because they had incomplete fMRI data sets due to the motion artefacts exceeding the defined criteria. The characteristics of the remaining thirty-four participants are presented in Table 3.

Table 3. Demographic and sample characteristics, memory, peripheral tactile sensitivity, and central fingertip representation in S1 measures of participants.

Characteristics	Mean	SD	Median (Mdn)	IQR	Minimum	Maximum	Sample size (n)
Demographic							
Age (years)	68.59	8.49	71.00	13.00	49.00	79.00	34
Gender (female)			15 (44.12%)				34
Education (years)	14.44	3.38	13.25	5.50	10.00	22.00	34
MMSE	26.97	1.90	27.00	2.25	22.00	30.00	34
Memory function							
PRM	81.5	11.84	83.33	10.42	58.33	100	34
PAL errors	74.65	40.54	70.5	65	6	151	34
Peripheral tactile sensitivity							
CST	2.26	2.75	1.36	2.49	0.18	13	32
Central fingertip representation							
D1-D5 distance Area 3b	17.23	5.73	17.68	5.69	3.89	25.65	10
D5 size Area 2	42.71	32.05	34.22	59.42	5.69	106.14	27

Abbreviations: SD=standard deviation, Mdn=median, IQR=interquartile range, n=number. MMSE = mini mental state examination (global cognition test assesses general cognitive functioning). Memory function PRM: pattern recognition memory, PAL memory: paired associates learning; subtests of the Cambridge Neuropsychological Test Automated Battery, CANTAB, Cambridge Cognition, Cambridge, United Kingdom. Peripheral tactile sensitivity CST: cutaneous sensory thresholds as assessed with von-Frey filaments. Central fingertip representation variable in S1 as evaluated by fMRI-measurement of activation maxima within Brodmann areas of the right fingers. All peak activations are presented in the left hemisphere. D1-D5 distance Area 3b: the fingertip cortical distance in mm calculated between first digit (D1) and fifth digit (D5) in Brodmann area 3b; D5 size Area 2: the cortical representation size of fifth digit fingertip in Brodmann area 2 (only the cluster with max peak activation) in mm^2.

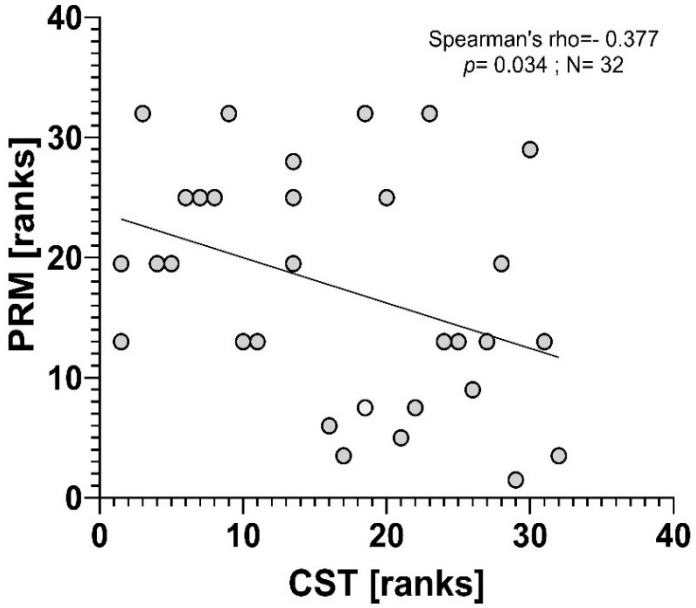
3.2 Correlations between tactile processing and pattern recognition memory

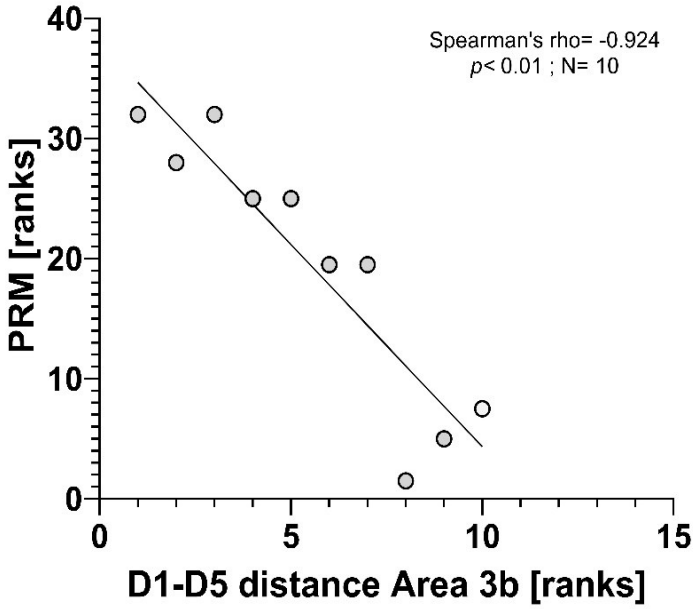
3.2.1 Correlations between peripheral tactile sensitivity, central fingertip representation in S1 and PRM performance.

Table 4. Correlations between peripheral tactile sensitivity, cortical representation in S1 and PRM performance.

Spearman correlation	**Statistical data**	**Memory**	**Peripheral tactile sensitivity**	**Central fingertip representation in S1**	
matrix	Spearman's rho	PRM	CST	D1-D5 distance Area 3b	D5 size Area 2
PRM	Correlation Coefficient	1.000	-.377	-.924	.684
	P-value	- - -	0.034	< 0.01	< 0.01
	N	34	32	10	27

Abbreviations: P=Probability (P) value, N=number. Memory function PRM: pattern recognition memory; sub-tests of the Cambridge Neuropsychological Test Automated Battery, CANTAB, Cambridge Cognition, Cambridge, United Kingdom. Peripheral tactile sensitivity CST: cutaneous sensory thresholds as assessed with von-Frey filaments. Central fingertip representation variable in S1 as evaluated by fMRI-measurement of activation maxima within Brodmann areas of the right fingers. All peak activations are presented in the left hemisphere. D1-D5 distance Area 3b: the fingertip cortical distance in mm calculated between first digit (D1) and fifth digit (D5) in Brodmann area 3b; D5 size Area 2: the cortical representation size of fifth digit fingertip in Brodmann area 2 (only the cluster with max peak activation) in mm^2.


Spearman's rho=- 0.377
p= 0.034 ; N= 32
PRM [ranks]
CST [ranks]
0
10
20
30
40


Spearman's rho= -0.924
p< 0.01 ; N= 10
PRM [ranks]
D1-D5 distance Area 3b [ranks]
0
5
10
15
20
30
40

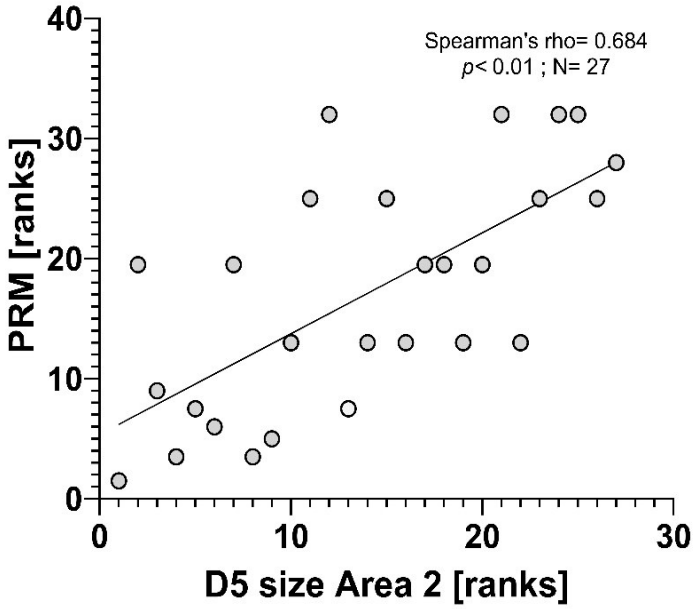

Spearman's rho= 0.684
p< 0.01 ; N= 27
PRM [ranks]
D5 size Area 2 [ranks]
0
10
20
30
40

Figure 6 The association of peripheral tactile sensitivity, central fingertip representation in S1 and pattern recognition memory performance. Due to non-normality of the data for peripheral tactile sensitivity central fingertip representation variable and transformation did not correct this deviation, we tested spearman correlations among variables based on ranked data. Abbreviations: N=number. Memory function PRM: pattern recognition memory; sub-tests of the Cambridge Neuropsychological Test Automated Battery, CANTAB, Cambridge Cognition, Cambridge, United Kingdom. Peripheral tactile sensitivity CST: cutaneous sensory thresholds as assessed with von-Frey filaments. Central fingertip representation variable in S1 as evaluated by fMRI-measurement of activation maxima within Brodmann areas of the right fingers. All peak activations are presented in the left hemisphere. D1-D5 distance Area 3b: the fingertip cortical distance in mm calculated between first digit (D1) and fifth digit (D5) in Brodmann area 3b; D5 size Area 2: the cortical representation size of fifth digit fingertip in Brodmann area 2 (only the cluster with max peak activation) in mm^2.

In participants with MCI, Pattern Recognition Memory performance, assessed by PRM test, was significantly negatively related with peripheral tactile sensitivity (rho= -0.377, p=0.034, n=32) and D1-D5 distance (rho= -0.924, p< 0.01, n=10), and positively related with D5 size (rho= 0.684, p< 0.01, n=27). Table 4 and Figure 6 show the detailed Spearman correlation matrix.

3.2.2 Regression analyses from peripheral tactile sensitivity, central fingertip representation in S1 to pattern recognition memory

The results of the validation data using nonparametric bootstrapping with 5,000 iterations with the “PLEM” model analyses of peripheral tactile sensitivity and central fingertip representation in S1 variables on pattern recognition memory are depicted in Table 5.

Table 5. Results of the regression analyses for relationships of peripheral tactile sensitivity, central fingertip representation in S1 variables and pattern recognition memory.

Relationship	Beta	95% CI [LL, UL]		SD	T-value	P-value	Effect	R-square
CST -> PRM	-0.407	-0.666	-0.101	0.155	2.634	0.008	negative	0.166
Distance -> PRM	-0.777	-0.98	-0.611	0.097	7.98	< 0.001	negative	0.603
Size -> PRM	0.612	0.348	0.803	0.119	5.161	< 0.001	positive	0.374

Abbreviations: B=Beta Coefficient, SE=Standard deviation, T=t - Statistics, P=Probability (P) value, CI=Confidence Interval, when reporting confidence intervals (CI), use the format 95% CI [LL, UL] where LL is the lower limit of the confidence interval and UL is the upper limit. R-square=the proportion of variance in the dependent variable that can be explained by the independent variable. N=number. Memory function PRM: pattern recognition memory; sub-tests of the Cambridge Neuropsychological Test Automated Battery, CANTAB, Cambridge Cognition, Cambridge, United Kingdom. Peripheral tactile sensitivity CST: cutaneous sensory thresholds as assessed with von-Frey filaments. Central fingertip representation variable in S1 as evaluated by fMRI-measurement of activation maxima within Brodmann areas of the right fingers. All peak activations are presented in the left hemisphere. Distance: the fingertip cortical distance in mm calculated between first digit (D1) and fifth digit (D5) in Brodmann area 3b; Size: the cortical representation size of fifth digit fingertip in Brodmann area 2 (only the cluster with max peak activation) in mm^2. Note: The predict effects and P-values were estimated using nonparametric bootstrapping with 5,000 iterations with the "PLEM" Model in Smart PLS software, version 4.2.0.

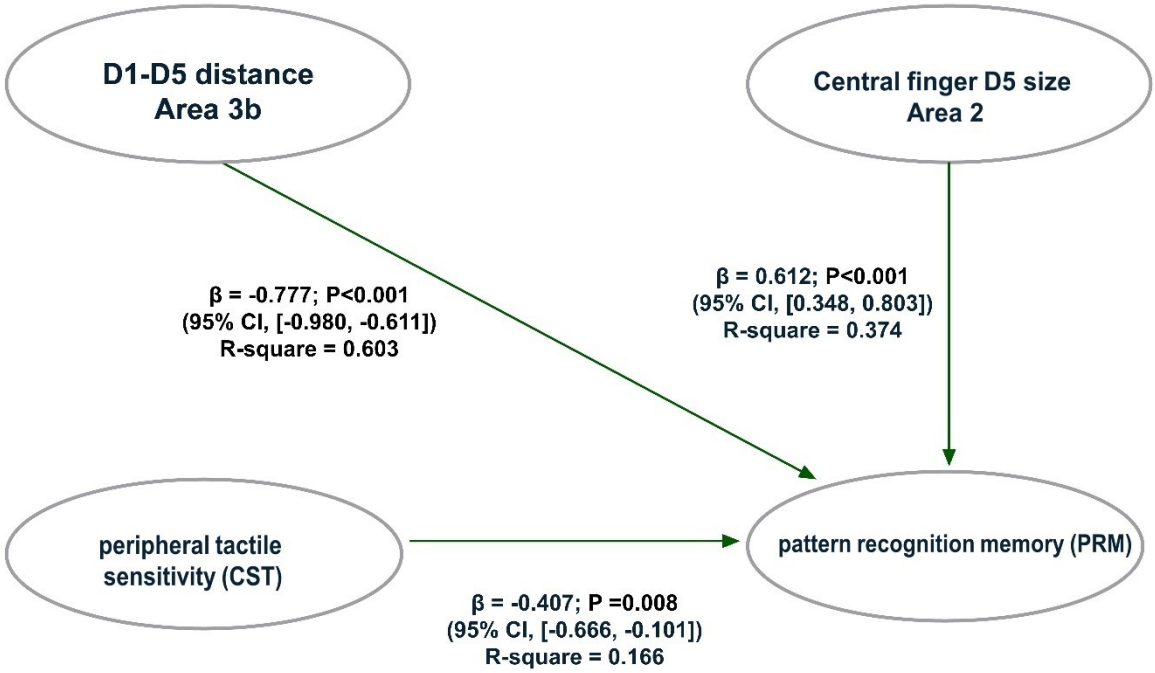


Figure 7 The association of peripheral tactile sensitivity, central fingertip representation in S1 and pattern recognition memory performance. Abbreviations: β=Beta Coefficient, SE=Standard deviation, T=t - Statistics, P=Probability (P) value, when reporting confidence intervals, use the format 95% CI [LL, UL] where LL is the lower limit of the confidence interval and UL is the upper limit. R-square: the proportion of variance in the dependent variable that can be explained by the independent variable. N=number. Memory function PRM: pattern recognition memory; sub-tests of the Cambridge Neuropsychological Test Automated Battery, CANTAB, Cambridge Cognition, Cambridge, United Kingdom. Peripheral tactile sensitivity CST: cutaneous sensory thresholds as assessed with von-Frey filaments. Central fingertip representation variable in S1 as evaluated by fMRI-measurement of activation maxima within Brodmann areas of the right fingers. All peak activations are presented in the left hemisphere. Distance: the

fingertip cortical distance in mm calculated between first digit (D1) and fifth digit (D5) in Brodmann area 3b; Size: the cortical representation size of fifth digit fingertip in Brodmann area 2 (only the cluster with max peak activation) in mm^2. Note: The predict effects and P values were estimated using nonparametric bootstrapping with 5,000 iterations with the “PLEM” Model in Smart PLS software, version 4.2.0.

The results show that peripheral tactile sensitivity CST has a significantly negative association relationship with pattern recognition memory (B =-0.407, t = 2.634, P = 0.008) with the predict model explaining 16.6% of the variance. The fingertip cortical distance has a significantly negative association with on pattern recognition memory (B =-0.777, t = 7.98, P < 0.001), with the predictive model explaining 60.3% of the variance. The fingertip cortical representation size has a significant positive association with relationship with pattern recognition memory (B =0.612, t = 5.161, P < 0.001), with the predictive model explaining 37.4% of the variance. Table 5 and Figure 7 show the detailed validation data matrix.

3.2.3 Size of the central fingertip representation in Area 2 mediated the association of peripheral tactile sensitivity and pattern recognition memory

We conducted mediation analyses to identify whether the central fingertip representation in S1 (central fingertip distance and the representation size of the individual fingertip) mediated the association between CST for peripheral tactile sensitivity and pattern recognition memory (PRM) memory. Table 6, Table 7 and Figure 8 show the detailed mediation statistic matrix.

The central fingertip distance did not significantly mediate the association between tactile sensitivity and memory function in the PRM test (β=-0.162, P=0.338, 95%CI = -0.532 to 0.155) (See Table 6 and Figure 8).

Table 6. Mediation analysis (cortical distance) of the association between tactile processing and PRM performance.

Hypotheses: Cortical distance mediates the relationship between peripheral tactile (CST) and PRM memory.

Statistic data	**Beta**	**95% CI [LL, UL]**		**SD**	**T-value**	**P-value**	**Effect**	Proportion mediated
Direct effect	-0.436	-0.736	-0.064	0.188	2.326	0.020	negative	
Total effect	-0.598	-0.934	-0.031	0.253	2.363	0.018	negative	
Indirect effect	-0.162	-0.532	0.155	0.169	0.959	0.338	n.s.	27.09%

Abbreviations: B=Beta Coefficient, SD=Standard deviation, T=t - Statistics, P=Probability (P) value, CI=Confidence Interval, when reporting confidence intervals (CI), use the format 95% CI [LL, UL] where LL is the lower limit of the confidence interval and UL is the upper limit. R-square=the proportion of variance in the dependent variable that can be explained by the independent variable. N=number. Memory function PRM: pattern recognition memory; sub-tests of the Cambridge Neuropsychological Test Automated Battery, CANTAB, Cambridge Cognition, Cambridge, United Kingdom. Peripheral tactile sensitivity CST: cutaneous sensory thresholds as assessed with von-Frey filaments. Central fingertip representation variable in S1 as evaluated by fMRI-measurement of activation maxima within Brodmann areas of the right fingers. All peak activations are presented in the left hemisphere. Distance: the fingertip cortical distance in mm calculated between first digit (D1) and fifth digit (D5) in Brodmann area 3b; Size: the cortical representation size of fifth digit fingertip in Brodmann area 2 (only the cluster with max peak activation) in mm^2. Note: The predict effects and P values were estimated using nonparametric bootstrapping with 5,000 iterations with the “PLEM” Model in Smart PLS software, version 4.2.0.

Moreover, we performed a mediation analysis to clarify the proportion of the correlational effects of peripheral tactile sensitivity (CST) on PRM memory mediated by central fingertip representation size (see Table 7). The “PLEM” Model in Smart PLS software was performed, in which peripheral tactile sensitivity (CST) and central fingertip representation size were the predictors and PRM was the outcome (see Table 7 and Figure 8).

The total effect was the estimate peripheral tactile sensitivity (CST) on PRM (beta =-0.407), and the direct effect was the effect estimated from the “PLEM” Model in Smart PLS software adjusting for central fingertip representation size (beta=-0.237). The indirect effect was obtained by subtracting the direct effect from the total effect (beta=-0.171); the mediated proportion was 42.01%.

Table 7. Mediation analysis (cortical size) of the association between tactile processing and pattern recognition memory performance.

Hypotheses: Cortical size mediates the relationship between peripheral tactile (CST) and PRM

Statistic data	**Beta**	**95% CI [LL, UL]**		**SD**	**T-value**	**P-value**	**Effect**	Proportion mediated
Direct effect	-0.237	-0.508	0.082	0.153	1.544	0.123	n.s.	
Total effect	-0.407	-0.666	-0.101	0.155	2.634	0.008	negative	
Indirect effect	-0.171	-0.334	0.000	0.084	2.028	0.043	negative	42.01%

Abbreviations: B=Beta Coefficient, SD=Standard deviation, T=t - Statistics, P=Probability (P) value, CI=Confidence Interval, when reporting confidence intervals (CI), use the format 95% CI [LL, UL] where LL is the lower limit of the confidence interval and UL is the upper limit. R-square=the proportion of variance in the dependent variable that can be explained by the independent variable. N=number. Memory function PRM: pattern recognition memory; sub-tests of the Cambridge Neuropsychological Test Automated Battery, CANTAB, Cambridge Cognition, Cambridge, United Kingdom. Peripheral tactile sensitivity CST: cutaneous sensory thresholds as assessed with von-Frey filaments. Central fingertip representation variable in S1 as evaluated by fMRI-measurement of activation maxima within Brodmann areas of the right fingers. All peak activations are presented in the left hemisphere. Distance: the fingertip cortical distance in mm calculated between first digit (D1) and fifth digit (D5) in Brodmann area 3b; Size: the cortical representation size of fifth digit fingertip in Brodmann area 2 (only the cluster with max peak activation) in mm^2. Note: The predict effects and P values were estimated using nonparametric bootstrapping with 5,000 iterations with the “PLEM” Model in Smart PLS software, version 4.2.0.

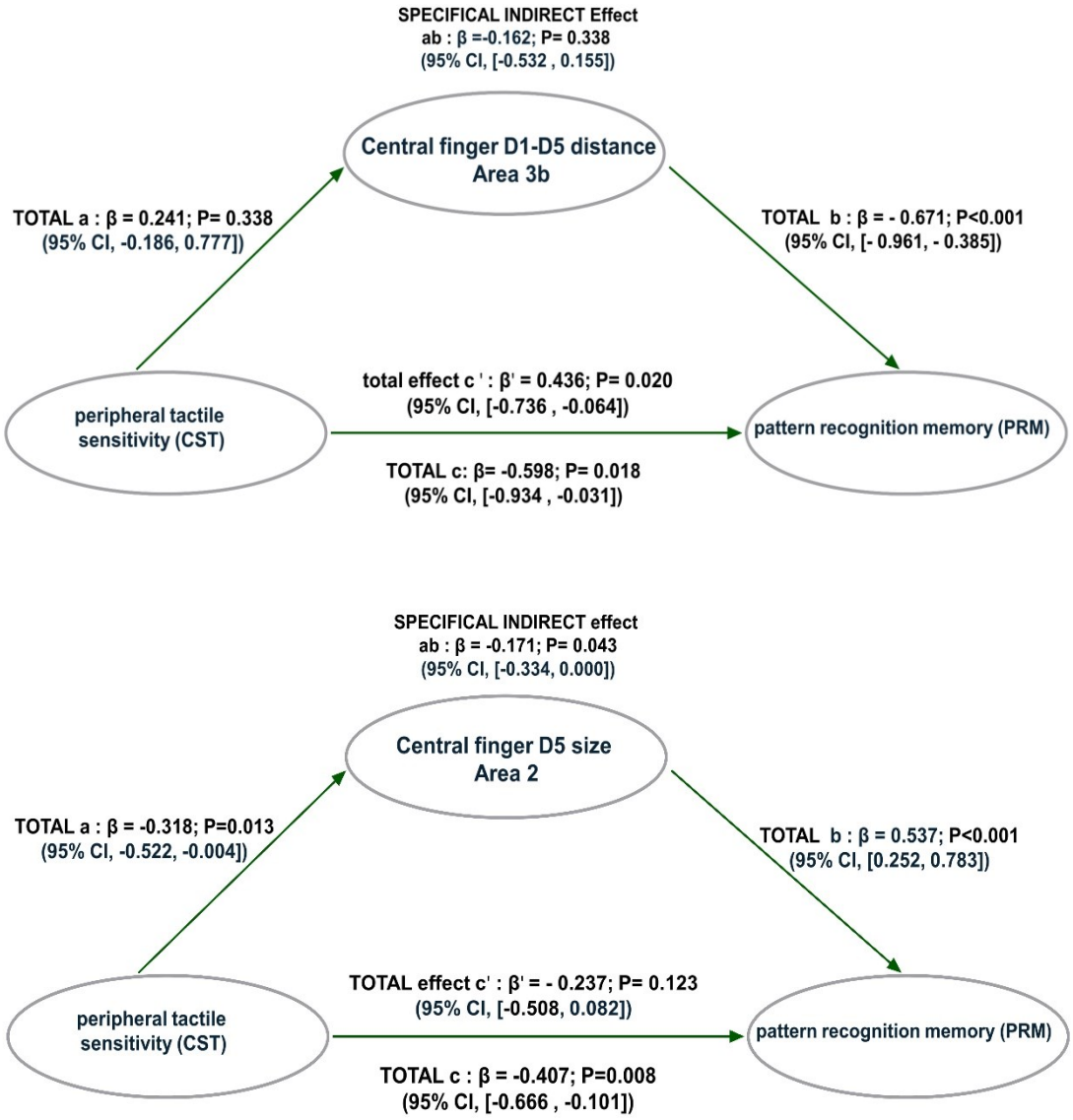


Figure 8 Mediation analysis of the association between tactile processing and memory performance. Abbreviations: β=Beta Coefficient, P=Probability (P) value, when reporting confidence intervals, use the format 95% CI [LL, UL] where LL is the lower limit of the confidence interval and UL is the upper limit. R-square: the proportion of variance in the dependent variable that can be explained by the independent variable. N=number. Memory function PRM: pattern recognition memory; sub-tests of the Cambridge Neuropsychological Test Automated Battery, CANTAB, Cambridge Cognition, Cambridge, United Kingdom. Peripheral tactile sensitivity CST: cutaneous sensory thresholds as assessed with von-Frey filaments Central fingertip representation variable in S1 as evaluated by fMRI-measurement of activation maxima within Brodmann areas of the right fingers. All peak activations are presented in the left hemisphere. D1-D5 distance Area 3b: the fingertip cortical distance in mm calculated between first digit (D1) and fifth digit (D5) in Brodmann area 3b; D5 size Area 2: the cortical representation size of fifth

digit fingertip in Brodmann area 2 (only the cluster with max peak activation) in mm^2. Note: The indirect and direct effects and P values were estimated using nonparametric bootstrapping with 5,000 iterations with the “PLEM” Model in Smart PLS software, version 4.2.0.

Finally, the P-value of the indirect effect was significant, and we found evidence that the relationship between peripheral tactile sensitivity (CST) and PRM was mediated by central fingertip size (β=-0.171, P=0.043, 95%CI -0.334 to 0.000) (see Figure 8).

Combining the above results, one mediation model was identified: size of the central fingertip representation in Area 2 mediated the association of peripheral tactile sensitivity and pattern recognition memory.

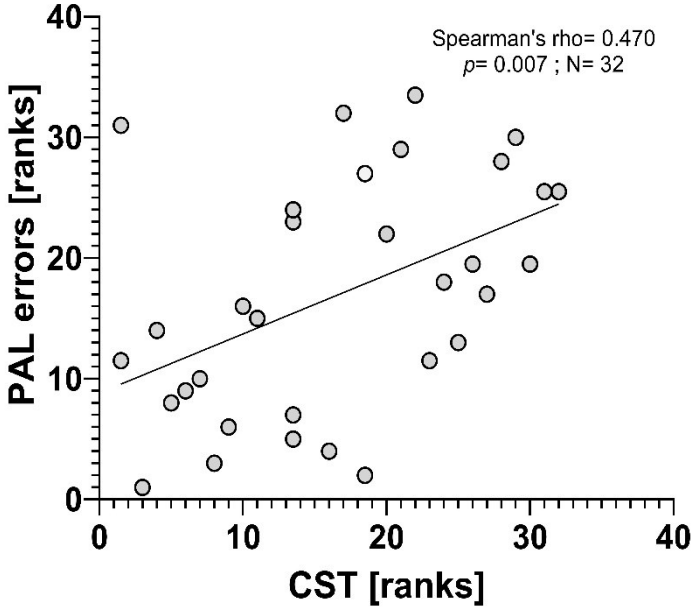
3.3 Correlations between tactile processing and paired associate learning memory

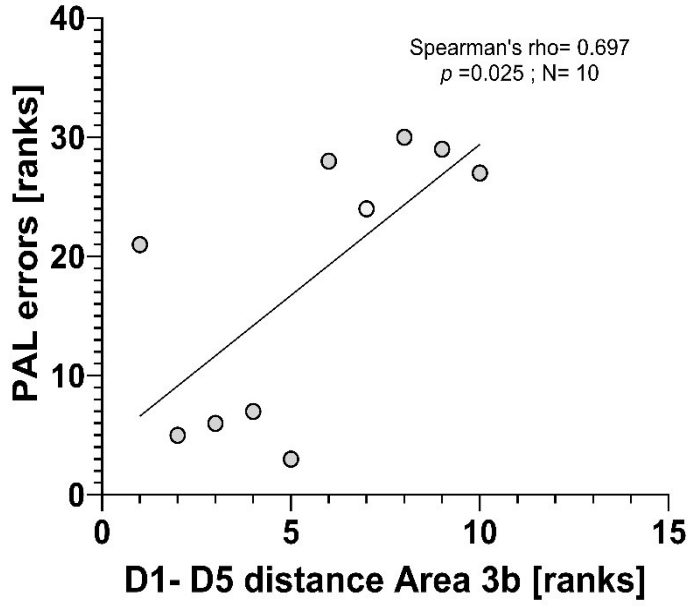
3.3.1 Correlations between peripheral tactile sensitivity, central fingertip representation in S1 and PAL performance

Table 9. Correlations between peripheral tactile sensitivity, central fingertip representation in S1 and PAL performance.

Spearman correlation	**Statistic data**	**Memory**	**Peripheral tactile sensitivity**	**Central fingertip representation in S1**	
matrix	Spearman's rho	PAL errors	CST	D1-D5 distance Area 3b	D5 size Area 2
PAL	Correlation Coefficient	1.000	.470	.697	-.626
	P-value	- - -	0.007	0.025	< 0.01
	N	34	32	10	27

Abbreviations: P=Probability (P) value, N=number. Memory function PAL: paired associate learning; sub-tests of the Cambridge Neuropsychological Test Automated Battery, CANTAB, Cambridge Cognition, Cambridge, United Kingdom. Peripheral tactile sensitivity CST: cutaneous sensory thresholds as assessed with von-Frey filaments. Central fingertip representation variable in S1 as evaluated by fMRI-measurement of activation maxima within Brodmann areas of the right fingers. All peak activations are presented in the left hemisphere. D1-D5 distance Area 3b: the fingertip cortical distance in mm calculated between first digit (D1) and fifth digit (D5) in Brodmann area 3b; D5 size Area 2: the cortical representation size of fifth digit fingertip in Brodmann area 2 (only the cluster with max peak activation) in mm^2.


Spearman's rho= 0.470
p= 0.007 ; N= 32
PAL errors [ranks]
CST [ranks]
0
10
20
30
40


Spearman's rho= 0.697
p =0.025 ; N= 10
PAL errors [ranks]
D1- D5 distance Area 3b [ranks]
0
5
10
15
20
30
40

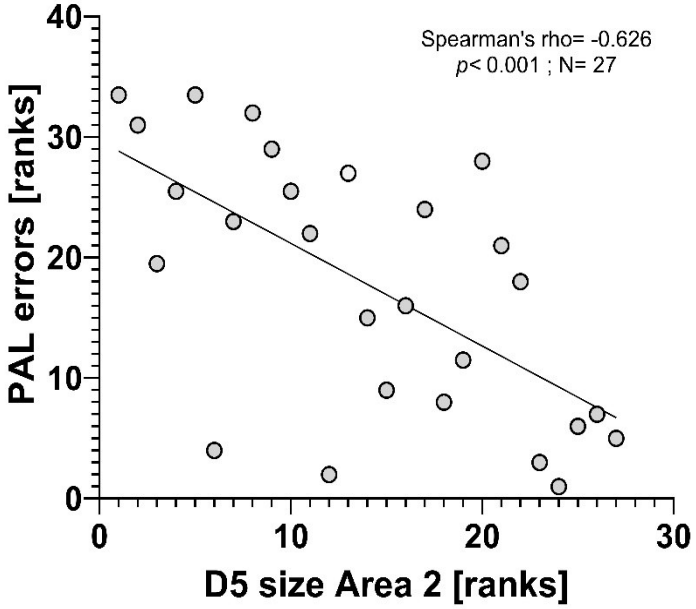

Spearman's rho= -0.626
p< 0.001 ; N= 27
PAL errors [ranks]
D5 size Area 2 [ranks]
0
10
20
30
40

Figure 9 The association of peripheral tactile sensitivity, central fingertip representation in S1 and PAL memory performance. Since non-normality of the data for peripheral tactile sensitivity central fingertip representation variable and transformation did not correct this deviation, we tested spearman correlations among variables based on ranked data. Abbreviations: N=number. Memory function PAL: paired associate learning; sub-tests of the Cambridge Neuropsychological Test Automated Battery, CANTAB, Cambridge Cognition, Cambridge, United Kingdom. Peripheral tactile sensitivity CST: cutaneous sensory thresholds as assessed with von-Frey filaments. Central fingertip representation variable in S1 was evaluated by fMRI-measurement of activation maxima within Brodmann areas of the right fingers. All peak activations are presented in the left hemisphere. D1-D5 distance Area 3b: the fingertip cortical distance in mm calculated between first digit (D1) and fifth digit (D5) in Brodmann area 3b; D5 size Area 2: the cortical representation size of fifth digit fingertip in Brodmann area 2 (only the cluster with max peak activation) in mm^2.

In participants with MCI, associative memory performance assessed by PAL was significantly negatively related with peripheral tactile sensitivity (rho=-0.470, p=0.007, n=32). It was also significantly positively related with cortical D1-D5 distance (rho= 0.697, p=0.025, n=10) and was significantly negatively related with cortical D5 size sensitivity (rho= -0.626, p< 0.01, n=27). Table 9 and Figure 9 show the detailed Spearman correlation matrix.

3.3.2 Regression analyses from peripheral tactile sensitivity and central fingertip representation in S1 was utilized to paired associate learning memory

Table 10 and Figure 10 depict the validation results (nonparametric bootstrapping, 5,000 iterations) for the PLEM model analyses of peripheral tactile sensitivity and central fingertip representation in S1 variables on PAL.

Table 10. Results of the validation data regression analyses for relationships of peripheral tactile sensitivity, central fingertip representation in S1 and PAL performance.

Relationship	Beta	95% CI [LL, UL]		SD	T-value	P-value	Effect	R-square
CST -> PAL	0.368	0.225	0.597	0.095	3.874	< 0.001	positive	0.136
Distance -> PAL	0.736	0.485	0.932	0.118	6.216	< 0.001	positive	0.541
Size -> PAL	-0.626	-0.852	-0.318	0.139	4.517	< 0.001	negative	0.392

Abbreviations: B=Beta Coefficient, SE=Standard deviation, T=t - Statistics, P=Probability (P) value, CI=Confidence Interval, when reporting confidence intervals (CI), we use the format 95% CI [LL, UL]

where LL represents the lower limit of the confidence interval and UL the upper limit. R-square=the proportion of variance in the dependent variable that can be explained by the independent variable. N=number. Memory function PAL: paired associate learning memory; sub-tests of the Cambridge Neuropsychological Test Automated Battery, CANTAB, Cambridge Cognition, Cambridge, United Kingdom. Peripheral tactile sensitivity CST: cutaneous sensory thresholds as assessed with von-Frey filaments. Central fingertip representation variable in S1 was evaluated by fMRI-measurement of activation maxima within Brodmann areas of the right fingers. All peak activations are presented in the left hemisphere. Distance: the fingertip cortical distance in mm calculated between first digit (D1) and fifth digit (D5) in Brodmann area 3b; Size: the cortical representation size of fifth digit fingertip in Brodmann area 2 (only the cluster with max peak activation) in mm^2. Note: The predict effects and P values were estimated using nonparametric bootstrapping with 5,000 iterations with the "PLEM" Model in Smart PLS software, version 4.2.0.

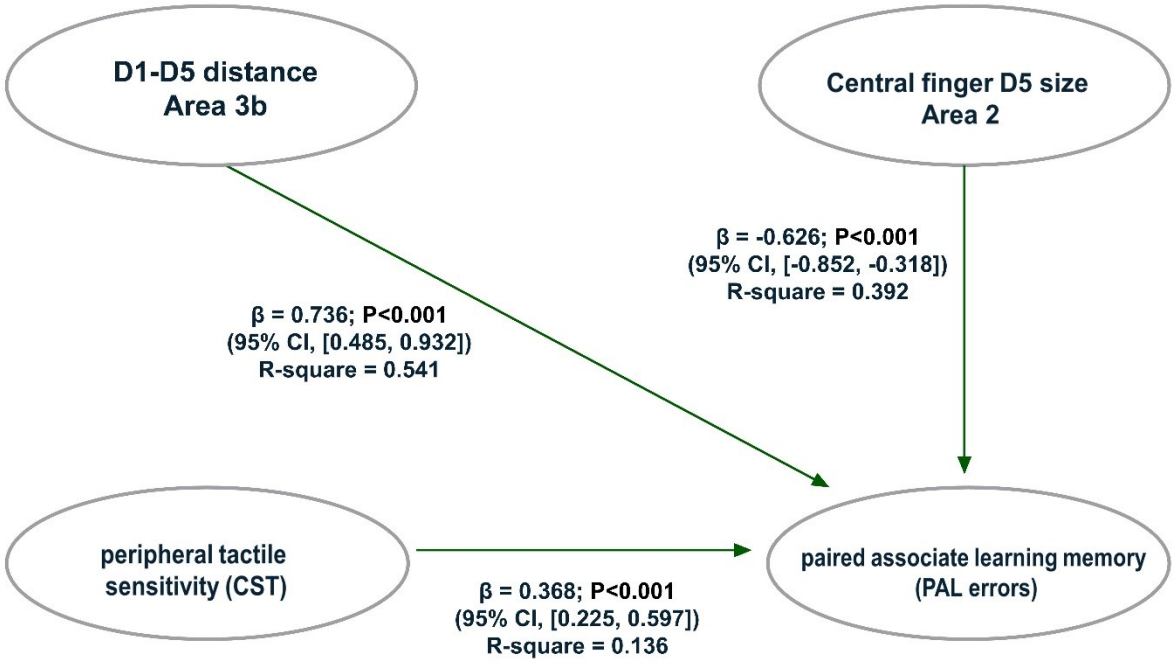


Figure 10 The association of peripheral tactile sensitivity, central fingertip representation in S1 and PAL performance. Abbreviations: β=Beta Coefficient, SE=Standard deviation, T=t - Statistics, P=Probability (P) value, CI=Confidence Interval. When reporting confidence intervals, we use the format 95% CI [LL, UL] where LL represents the lower limit of the confidence interval and UL the upper limit. R-square: the proportion of variance in the dependent variable that can be explained by the independent variable. N=number. Memory function PAL: paired associate learning memory; sub-tests of the Cambridge Neuropsychological Test Automated Battery, CANTAB, Cambridge Cognition, Cambridge, United Kingdom. Peripheral tactile sensitivity CST: cutaneous sensory thresholds was assessed with von-Frey filaments. Central fingertip representation variable in S1 was evaluated by fMRI-measurement of activation maxima within

Brodmann areas of the right fingers. All peak activations are presented in the left hemisphere. Distance: the fingertip cortical distance in mm calculated between first digit (D1) and fifth digit (D5) in Brodmann area 3b; Size: the cortical representation size of fifth digit fingertip in Brodmann area 2 (only the cluster with max peak activation) in mm^2. Note: The predict effects and P values were estimated using nonparametric bootstrapping with 5,000 iterations with the "PLEM" Model in Smart PLS software, version 4.2.0.

The results show that peripheral tactile sensitivity CST has a significant positive relationship with pattern recognition memory (B =0.368, t = 3.874, P < 0.001), with the predictive model explaining 13.6% of the variance. The fingertip cortical distance has a significantly positive relationship with PAL performance (B =0.736, t = 6.216, P < 0.001), with the predict model explained 54.1% of the variance. The fingertip cortical representation size has a significantly negative relationship with PAL performance (B =0.626, t = 4.517, P < 0.001), with the predict model explained 39.2% of the variance. Table 10 and figure 10 show the detailed validation data matrix.

3.3.3 Central fingertip representation did not mediate the association of peripheral tactile sensitivity with paired associate learning memory

Table 11. Mediation analysis (cortical distance) of the association between tactile processing and PAL performance.

Hypotheses: cortical distance mediates the relationship between peripheral tactile (CST) and PAL memory

Statistic data	**Beta**	**95% CI [LL, UL]**		**SD**	**T-value**	**P-value**	**Effect**	Proportion mediated
Direct effect	0.517	0.084	0.869	0.189	2.740	0.006	positive	
Total effect	0.665	0.407	0.975	0.133	5.015	< 0.001	positive	
Indirect effect	0.147	-0.127	0.555	0.174	0.848	0.397	n.s.	22.11%

Abbreviations: β=Beta Coefficient, SE=Standard deviation, T=t - Statistics, P=Probability (P) value. When reporting confidence intervals, we use the format 95% CI [LL, UL], where LL represents the lower limit of the confidence interval and UL the upper limit. R-square: the proportion of variance in the dependent variable that can be explained by the independent variable. N=number. Memory function PRM: pattern recognition memory, PAL memory: paired associates learning; subtests of the Cambridge Neuropsychological Test Automated Battery, CANTAB, Cambridge Cognition, Cambridge, United Kingdom. Peripheral tactile sensitivity CST: cutaneous sensory thresholds as assessed with von-Frey filaments.

Central fingertip representation variable in S1 was evaluated by fMRI-measurement of activation maxima within Brodmann areas of the right fingers. All peak activations are presented in the left hemisphere. D1-D5 distance Area 3b: the fingertip cortical distance in mm calculated between first digit (D1) and fifth digit (D5) in Brodmann area 3b; D5 size Area 2: the cortical representation size of fifth digit fingertip in Brodmann area 2 (only the cluster with max peak activation) in mm^2. Note: The indirect and direct effects and P values were estimated using nonparametric bootstrapping with 5,000 iterations with the "PLEM" Model in Smart PLS software, version 4.2.0.

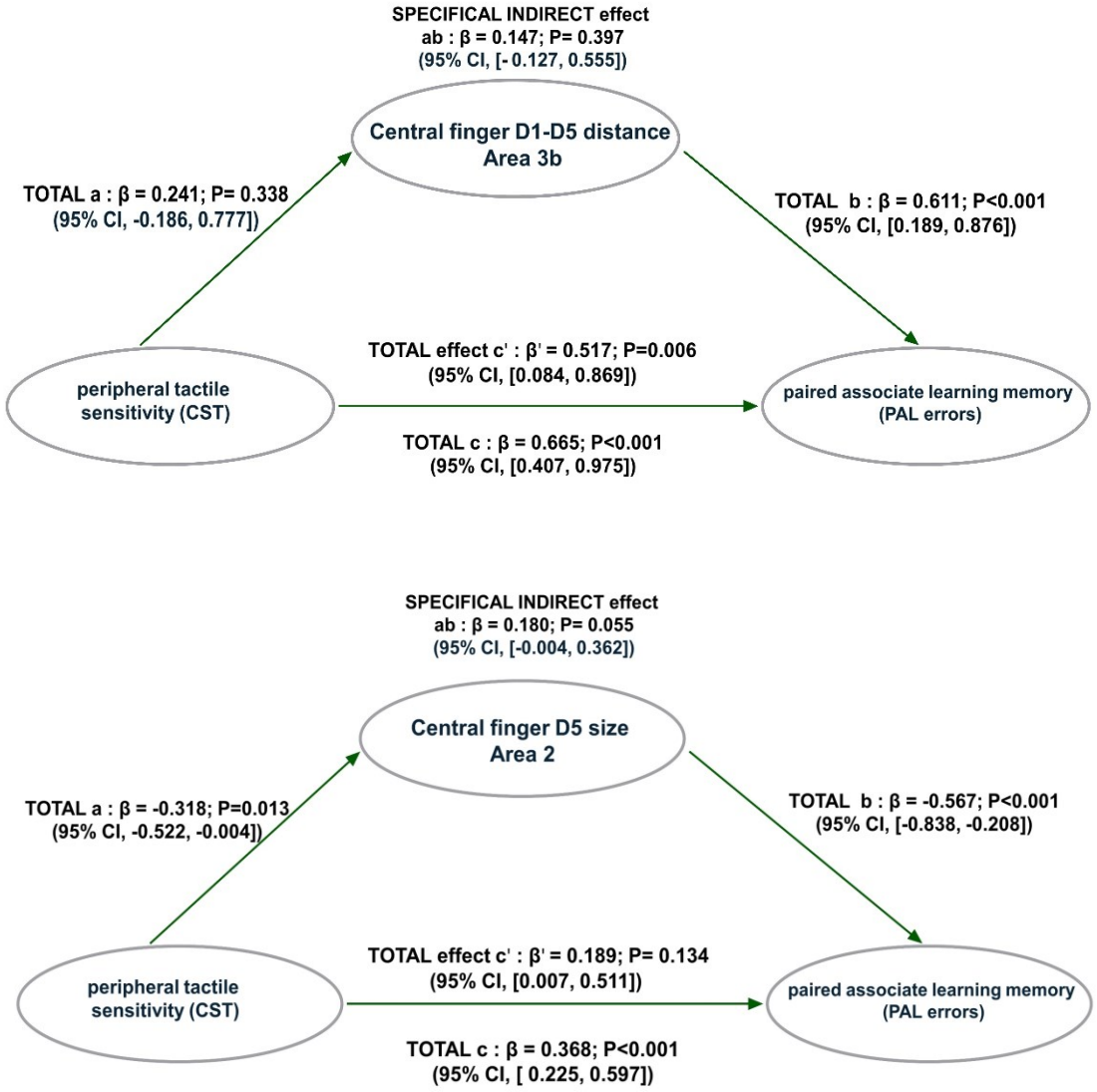


Figure 11 Mediation analysis of the association between tactile processing and memory performance. Abbreviations: β=Beta Coefficient, SE=Standard deviation, T=t - Statistics, P=Probability (P) value. When reporting confidence intervals, we use the format 95% CI [LL, UL], where LL represents the lower limit of the confidence interval and UL the upper limit. R-square: the proportion of variance in the dependent variable that can be explained by the independent

variable. N=number. Memory function PRM: pattern recognition memory, PAL memory: paired associates learning; subtests of the Cambridge Neuropsychological Test Automated Battery, CANTAB, Cambridge Cognition, Cambridge, United Kingdom. Peripheral tactile sensitivity CST: cutaneous sensory thresholds was assessed with von-Frey filaments. Central fingertip representation variable in S1 was evaluated by fMRI-measurement of activation maxima within Brodmann areas of the right fingers. All peak activations are presented in the left hemisphere. D1-D5 distance Area 3b: the fingertip cortical distance in mm calculated between first digit (D1) and fifth digit (D5) in Brodmann area 3b; D5 size Area 2: the cortical representation size of fifth digit fingertip in Brodmann area 2 (only the cluster with max peak activation) in mm^2. Note: The indirect and direct effects and P values were estimated using nonparametric bootstrapping with 5,000 iterations with the "PLEM" Model in Smart PLS software, version 4.2.0.

Table 12. Mediation analysis (cortical size) of the association between tactile processing and paired associate learning memory.

Hypotheses: Cortical size mediates the relationship between peripheral tactile (CST) and PAL memory

Statistic data	**Beta**	**95% CI [LL, UL]**		**SD**	**T-value**	**P-value**	**Effect**	Proportion mediated
Direct effect	0.189	0.007	0.511	0.126	1.497	0.134	n.s.	
Total effect	0.368	0.225	0.597	0.095	3.874	< 0.001	positive	
Indirect effect	0.180	-0.004	0.362	0.094	1.923	0.055	n.s.	48.91%

Abbreviations: β=Beta Coefficient, SD=Standard deviation, T=t - Statistics, P=Probability (P) value. When reporting confidence intervals, we use the format 95% CI [LL, UL], where LL represents the lower limit of the confidence interval and UL the upper limit. R-square: the proportion of variance in the dependent variable that can be explained by the independent variable. N=number. Memory function PAL memory: paired associates learning; subtests of the Cambridge Neuropsychological Test Automated Battery, CANTAB, Cambridge Cognition, Cambridge, United Kingdom. Peripheral tactile sensitivity CST: cutaneous sensory thresholds was assessed with von-Frey filaments. Central fingertip representation variable in S1 was evaluated by fMRI-measurement of activation maxima within Brodmann areas of the right fingers. All peak activations are presented in the left hemisphere. D1-D5 distance Area 3b: the fingertip cortical distance in mm calculated between first digit (D1) and fifth digit (D5) in Brodmann area 3b; D5 size Area 2: the cortical representation size of fifth digit fingertip in Brodmann area 2 (only the cluster with max peak activation) in mm^2. Note: The indirect and direct effects and P values were estimated using nonparametric bootstrapping with 5,000 iterations with the "PLEM" Model in Smart PLS software, version 4.2.0.

We conducted mediation analyses to identify whether the central fingertip representation in S1 (central fingertip distance and the representation size of the individual fingertip) mediated the association between CST and PAL errors. Table 11, Table 12 and Figure 11 show the detailed mediation statistic matrix.

It was found that the central fingertip distance (β=0.147, P=0.397, 95%CI: -0.127 to 0.555) did not significantly mediate the association between CST and PAL errors (see Table 11 and Figure 11).

The representation size of the individual fingertip partly mediated the association of peripheral tactile sensitivity with paired associate learning memory errors (β=0.180, P=0.055, 95%CI: -0.004 to 0.362). However, the P-value of the indirect effect was insignificant, and lacked sufficient evidence to demonstrate that the effect of peripheral tactile sensitivity (CST) on PAL was mediated by central fingertip representation size (see Figure 11 and Table 12).

4 DISCUSSION

4.1 Summary of the results

We found that peripheral tactile sensitivity and central fingertip representation (both fingertip cortical distance and size) were associated with both PAL and PRM memory in our MCI participants. In addition, mediation analyses showed that only fingertip cortical size mediated the associations between tactile sensitivity and PRM memory performance and partially showed a trend toward mediating likelihood for the association between tactile sensitivity and PAL memory performance.

4.2 Correlations between peripheral tactile sensitivity and central fingertip representation of somatosensory cortex and pattern recognition memory

Our study demonstrated a significant relationship between peripheral tactile sensitivity and pattern recognition memory in participants with mild cognitive impairment (MCI). Reduced tactile sensitivity, indicated by higher CST performance, was associated with worse PRM outcomes, and was confirmed through Spearman correlation analysis. Regression modelling using PLS-SEM with nonparametric bootstrapping further supported this finding, showing that peripheral tactile sensitivity explained a significant proportion of the variance in PRM performance. Additionally, central fingertip representation, particularly cortical distance (explained variance: 60.3%) and size (explained variance: 37.4%), were strongly associated with PRM performance. These results highlight the importance of both peripheral sensory input and central somatosensory cortical factors in cognitive function.

Previous central fingertip representation investigations in healthy humans showed a correlation between peripheral tactile acuity and fingertip representation distance in area 3b (Härtner et al., 2021). Our hypothesis is that enlarged central fingertip distance would be related to worse pattern recognition memory, and it could be shown in area 3b in our participants with MCI. However, the mediation analysis did not show that fingertip representation distance mediated the association between peripheral tactile sensitivity and PRM. The lack of mediation effect for cortical distance, despite its direct

correlation with PRM memory, suggests distinct mechanisms underlying different somatosensory features.

Mediation analyses revealed that fingertip cortical size, but not cortical distance, mediated the association between peripheral tactile sensitivity and PRM performance. This identified the relationship: central fingertip representation size (Area 2) mediates the relationship between peripheral tactile sensitivity and PRM, which underscores the critical role of central somatosensory fingertip cortical size in connecting sensory input to memory processes. By identifying cortical size as a mediator, our study points to a potential intervention target for mitigating memory deficits in individuals with MCI. Specifically, the role of the BA2 region, which mediates object recognition and integrates sensory input with cognitive functions, was highlighted in our results. These findings align with the sensory deprivation hypothesis, which posits that cortical reorganization compensates for reduced sensory input and supports cognitive processes. Future research should investigate the potential modifiability of BA2 function as a target for therapeutic interventions to improve related or specific memory performance.

Given that somatosensory cortical size of fifth digit was more strongly associated with the cognitive phenotype (PRM) compared to the second digit, our results further highlight the relationship between the fifth digit cortical representation, peripheral tactile threshold and memory performance. Previous studies observed that sensory processes in sensory impairment resulted in higher neural activity in response to the reduced input, and higher neural activity was associated with more nerve density in animal or human studies(Merabet & Pascual-Leone, 2010; Wong, 1995).

Previous study investigation reported that lower associative memory performance was significantly related to reduced tactile sensitivity in participants with MCI (Löffler et al., 2024). Our study extends the understanding for memory performance by highlighting peripheral and central tactile impairment as a risk factor not only for associate learning memory but also for pattern recognition memory decline. Reduced tactile sensitivity is positively related to negative cognitive performance. Our current results align with a previous longitudinal study that identified reduced touch perception as a predictor of dementia in older adults (Brenowitz et al., 2019).

4.3 Correlations between peripheral tactile sensitivity and central fingertip representation of somatosensory cortex and paired associate learning memory

In contrast to PRM, the relationship between tactile processing and paired associate learning demonstrated distinct patterns. While reduced peripheral tactile sensitivity was significantly associated with poorer PAL performance, enlarged fingertip cortical distance correlated with more PAL errors, and increased cortical size correlated with fewer PAL errors. However, mediation analyses did not reveal fingertip representation distance as a significant mediator between tactile sensitivity and PAL. Cortical size only partially showed a trend toward mediation for the association between tactile sensitivity and PAL memory performance which led to the rejection of the hypothesis: central fingertip representation (cortical size) in somatosensory cortex (S1) did not mediate the association of peripheral tactile sensitivity and paired associate learning memory. These results suggest that while central somatosensory factors contribute to PAL performance, additional mechanisms, possibly involving dorsal somatosensory pathways, may play a more substantial role.

Our work extends previous studies on central somatosensory representation in persons with cognitive impairments which have rarely explained the association between somatosensation and memory decline(Löffler et al., 2024). Our present results are in line with results of previous neural pathway study, which reported Paired Associate Learning test: PAL memory processes may relate to both visual pattern (ventral stream) and visuospatial associative learning (dorsal stream, contained somatosensory cortex tactile processing) (Martins et al., 2014).This suggests that the association between peripheral touch and PAL is not only related to the factors of the BA2 neural pathway for object recognition, but also likely related to other central somatosensory factors in the dorsal processing of visuospatial. It also reasonably explains why the central tactile representation of BA2 in our mediation analysis of peripheral tactile and PAL memory only showed a certain mediation trend, and was not significant. Future research needs to pay more attention to the close relationship between the dorsal somatosensory pathway or other visuospatial pathway related factors and PAL memory.

4.4 Implications from peripheral tactile sensitivity, central fingertip representation in S1 to memory functions

The observed associations between tactile sensitivity, fingertip representation in the somatosensory cortex (S1), especially PRM memory suggest that central tactile processing dysfunction may serve as a marker for neurodegenerative pathology (Stephen et al., 2010). Since the brain is a highly plastic organ that shows adaptive as well as maladaptive plasticity (Flor et al., 1995), it might be an optimal target for innovative interventions that utilise principles of neuroplasticity to delay or even reverse cortical and behavioural age-related changes (Goh & Park, 2009). Neuroplasticity-oriented programmes, involving intensive sensory, cognitive, or motor stimulation, have demonstrated the potential to enhance neuromodulator systems, encourage advantageous neuroplasticity in cortical representations, and enhance neurocognitive function which deteriorates with age (Anguera et al., 2013; Mahncke, Connor, et al., 2006; Mishra et al., 2013) .

For instance, the training of perceptual and sensorimotor functions in virtual reality environments affects specific memory performance (Brooks and Rose 2003). If the training was designed to tune peripheral perceptual and sensorimotor abilities, and monitoring poor central tactile processing, identifying brain regions that play a role in recovery may help to optimise trials of fMRI biofeedback interventions, and measurement of plasticity reserve by fMRI would appear to be a promising predictor of clinical outcomes (Laura et al., 2018).

4.5 Limitations of this study and future work

Due to the cross-sectional nature of the analyses, our study is also subject to limitations. We cannot determine the temporal and causal relationships of sensory abilities with memory. Considering the limited number of participants in the sample, our results should therefore be considered as preliminary exploration of functional specialization in sensory behaviour and brain function.

We have found a correlation between the pressure sensitivity of touch and memory. There are other characteristics of touch, such as direction and angle. These aspects

may have different correlations with other memories or cognitions. These are areas that need to be discovered in the future.

This study investigated potential mechanisms through which tactile processing and somatosensory cortex activation are associated with increased risk for cognitive decline. However, our study did not resolve whether tactile processing and somatosensory cortex activation are causally related to dementia, or whether tactile processing, somatosensory cortex activation and dementia share the same common neurodegenerative aetiology. Further research is needed to confirm the mechanisms underlying the association between tactile processing, somatosensory cortex activation and dementia.

5 SUMMARY

Aging is often characterized by cognitive decline and sensory functions may play an important part in the brain changes associated with it. In this study we examined the role of the organization of somatosensory cortex in the association between sensory changes and mild cognitive impairment (MCI).

In this study we examined 34 individuals with mild cognitive impairment and assessed sensory function using peripheral tactile sensitivity. Cognitive function was assessed using associative memory performance (PAL) and pattern recognition memory (PRM). We employed magnetic resonance imaging to assess the cortical representation of the fingertips in primary somatosensory cortex in different Brodmann areas. Peripheral tactile sensitivity and central fingertip representation (both fingertip cortical distance and size) were associated with PAL and PRM memory in our MCI participants. In addition, mediation analyses showed that the size of the cortical representation of the fingertip mediated the association between tactile sensitivity and PRM performance, and showed a trend towards significance in mediating the association between tactile sensitivity and PAL performance.

In this study we observed a close association between cortical changes, tactile sensitivity and memory decline in individuals with mild cognitive impairment. These data suggest that interventions aimed at improving tactile sensitivity might be useful in improving the cortical representation of sensory processes and thus might lead to improved memory function. This might be a promising strategy for treatment of cognitive decline leading to dementia.

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