Aging of Path Integration Ability and Its Neural Mechanisms

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Abstract

Path integration denotes the spatial navigation capacity whereby an individual continuously integrates sensory cues during locomotion to update self-position. Amidst escalating population aging, whether the behavioral performance of path integration and its neural signatures can predict early-stage neurodegenerative diseases has emerged as a prominent research focus. Investigations conducted in real and virtual reality environments have demonstrated that path integration capacity progressively deteriorates across the continuum from normal to pathological aging. This capacity depends on the cooperative activity of grid cells and other spatial cell populations, and the structural and functional degradation of key nodal structures—including the entorhinal cortex and hippocampus—constitutes the neural signature underlying age-related decline in path integration. The present article seeks to elucidate the differential patterns of behavioral decline and the specific neural mechanisms of path integration during aging, thereby furnishing robust theoretical underpinnings for the development of aging assessment diagnostic systems and targeted interventions.

Full Text

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Abstract: Path integration refers to an individual' s ability to continuously update their position by integrating sensory cues during movement. Against

the backdrop of accelerating population aging, whether the behavioral manifestations and neural characteristics of path integration can predict early neurodegenerative diseases has become a research hotspot. Studies based on real or virtual reality environments demonstrate that path integration ability progressively declines from normal aging to pathological aging. This ability relies on the collaborative functioning of grid cells and other spatial cells, with structural and functional deterioration of key nodal regions such as the entorhinal cortex and hippocampus constituting the neural signature of path integration decline during aging. This article aims to deepen understanding of the behavioral decline patterns and specific neural mechanisms of path integration during aging, thereby providing a solid theoretical foundation for developing aging assessment diagnostic systems and targeted interventions.

Keywords: path integration, spatial navigation, aging, Alzheimer' s disease, neural mechanisms

Classification Codes: B842; B845

According to the latest data from the National Bureau of Statistics, China' s elderly population exceeded 280 million by the end of 2024, marking a severe aging challenge. Accompanying this demographic shift, the incidence and mortality rates of related diseases have risen significantly, with Alzheimer' s disease (AD) being a typical representative (Rostagno, 2022). Normal or pathological aging typically brings cognitive decline, such as slowed information processing and memory deterioration, a phenomenon defined as cognitive aging (Loaiza, 2024). Traditional cognitive aging research has focused on fundamental cognitive abilities like memory, executive function, and attention (Puthusseryppady et al., 2024; Stark & Stark, 2017). However, recent studies suggest that spatial navigation ability appears more sensitive to aging and holds promise as an early diagnostic marker for aging-related cognitive dysfunction (Ekstrom & Hill, 2023; Zhou et al., 2023).

Spatial navigation is a crucial cognitive function through which organisms orient themselves by integrating self-motion cues with environmental reference cues (Ekstrom & Hill, 2023). Path integration (PI) is a core component of spatial navigation, referring to the function by which organisms continuously update and track their position by integrating self-motion cues from the vestibular system, proprioceptors, and visual system in real-time (Loomis et al., 1993; Segen et al., 2022). The foraging behavior of desert ants provides a classic example of PI (see Figure 1 [Figure 1: see original paper]A): after leaving the nest along a winding route to find food, ants return directly to the nest in a straight line, indicating they continuously integrate their own movement information (such as step counting and direction) to calculate their relative position to the nest (Merkle & Wehner, 2009).

Increasing evidence demonstrates that PI is vulnerable to both normal and pathological aging, showing early and significant decline (Koike et al., 2024), potentially stemming from its specific response to entorhinal-hippocampal cir-

cuit degeneration. Consequently, PI is considered a potential biomarker for early neurodegenerative diseases (孔祥祯, 蒲艺, 2023). Based on this evidence, this study aims to examine PI decline patterns and specific neural characteristics during normal and abnormal aging processes, addressing four key aspects: 1) analyzing PI performance differences among healthy older adults, AD risk populations, and clinical patients across various task paradigms; 2) elucidating PI neural mechanisms at both micro-neuronal and macro-brain region levels; 3) analyzing specific neural mechanisms underlying PI decline during normal and pathological aging based on the reviewed mechanisms; and 4) objectively evaluating current research limitations and future directions. This article seeks to deepen understanding of changes in PI ability and related neural mechanisms during normal and pathological aging, providing theoretical support for developing PI-based aging assessment diagnostic systems and targeted interventions.

2. Decline of Path Integration Behavior in Normal and Abnormal Aging

The decline of PI ability in healthy older adults, AD risk populations, and patients with mild cognitive impairment (MCI) and AD has been validated through multiple experimental paradigms (see Table 1). The Triangle Completion Task (TCT) serves as the core assessment tool for PI ability (see Figure 1B), with subsequent paradigms representing variations of this task. In the TCT, participants must travel to two target points sequentially under visually and auditorily occluded conditions, then return to the starting point based solely on self-motion cues to form a closed triangle path (Loomis et al., 1993). This process relies on bodily cues (vestibular and proprioceptive) generated by real walking to complete PI. Primary behavioral metrics include Euclidean distance between the return point and actual starting point (distance error) (see Figure 1B) and absolute angular difference between actual and target direction (angular error) (see Figure 1B) (Colmant et al., 2025; Loomis et al., 1993; Newton et al., 2024). Recent computational modeling studies have further decomposed PI errors into distinct cognitive components, such as memory leak, report noise, velocity gain, and cumulative noise (Segen et al., 2025; Stangl et al., 2020). With virtual reality (VR) technology development, TCT has spawned more interactive VR paradigms (see Figure 1C, D), differing primarily in movement paths and available cue types. The Apple Game (Bierbrauer et al., 2020) is a desktop VR paradigm requiring participants to move via joystick to different apple trees (relying only on visual cues without bodily cues), with three visual-spatial cue conditions (optic flow, boundary, and landmark) and varying numbers of apple trees (2-5) to adjust path segments. The Path Estimation Task similarly employs multi-segment paths, requiring participants to estimate distance and direction back to the start at stop points, with two conditions: blindfolded walking (relying on bodily cues) and seated VR viewing (relying on optic flow cues) (Stangl et al., 2018). The Virtual Supermarket Task (VST) requires participants to indicate starting direction and position after viewing a first-person video of a shopping cart moving through a VR supermarket devoid of landmarks, forcing

reliance on optic flow cues (Coughlan et al., 2020). Immersive VR applications further expand available cues (see Figure 1D), with studies requiring participants to wear VR headsets and perform path estimation (Stangl et al., 2020) and triangle completion tasks through real walking (relying on both bodily and optic flow cues) (Castegnaro et al., 2023; Segen et al., 2025).

Figure 1. PI definition and experimental paradigms. (A) PI example: Desert ants travel along winding paths when foraging away from the nest and can return directly to the nest in a straight line. This process relies on real-time integration of self-motion information to continuously calculate relative position to the nest. (B) Triangle completion paradigm schematic: Participants are guided along two path segments and must independently return to the start to complete the triangle. Euclidean distance d between return point and actual start represents distance error; absolute angular difference between actual and target direction represents angular error. (C) Desktop VR PI task schematic: Participants manipulate a joystick to move in a desktop VR environment, excluding bodily cues from walking and relying only on visual cues. (D) Immersive VR PI task schematic: Participants wear VR headsets and complete triangle tasks through real walking in VR environments, relying on both bodily and optic flow cues.

In normal aging, PI decline manifests particularly as distance estimation deficits under single-cue conditions, which improve under multimodal cue integration. Research has found that older adults show significantly greater distance errors than younger adults in path estimation tasks under both blindfolded walking (bodily cues) and seated environment viewing (optic flow cues) conditions (Stangl et al., 2018), indicating distance estimation deficits when relying on single modalities. When older adults perform path estimation tasks under dual bodily and optic flow cue conditions, distance errors remain significantly higher than in younger adults (Stangl et al., 2020), yet under the same dual-cue conditions in triangle completion tasks, the distance error difference becomes non-significant (McCracken et al., 2025).

These seemingly contradictory results likely stem from paradigm-specific differences: compared to traditional triangle completion tasks, path estimation tasks with multiple stopping reports and curved path designs can more sensitively track error accumulation processes, thereby revealing PI decline more effectively. Furthermore, when older adults have landmark cues available during PI tasks, distance errors show no significant difference from younger adults (Bates & Wolbers, 2014). This evidence demonstrates that PI decline during normal aging can be mitigated through compensatory mechanisms when multisensory cues combine with rich environmental information. Additionally, error modeling based on immersive VR path estimation tasks indicates that older adults' distance errors primarily stem from amplified cumulative noise, which quantifies random errors introduced from multisensory velocity input channels and scales proportionally with traveled distance (rather than time) (Stangl et al., 2020). This suggests that older adults' distance errors originate primarily from velocity signal input stages rather than integration processes themselves,

indicating that PI decline in normal aging may stem from more peripheral perceptual processing stages.

PI decline in AD risk populations differs from normal aging but exhibits similar compensatory mechanisms. APOE 3/ 4 carriers (AD high-risk genotype) aged 18-75 show higher distance errors than healthy individuals in optic flow subtasks of the Apple Game (Bierbrauer et al., 2020). Further behavioral analyses reveal that PI deficits in AD risk populations primarily stem from angular estimation errors, such as over-turning (Newton et al., 2024). Additionally, middle-aged and older AD risk individuals show higher angular errors than normal individuals in vestibular rotation tasks relying solely on vestibular cues (Coughlan et al., 2023). These findings suggest angular error may serve as a specific behavioral marker for early AD diagnosis while providing directions for targeted interventions. In the landmark-free Virtual Supermarket Task relying only on optic flow, older APOE 3/ 4 carriers exhibit high distance and angular errors (Coughlan et al., 2020); however, when landmark or boundary cues are provided, no significant differences emerge between AD risk and control groups (Bierbrauer et al., 2020), indicating that compensatory ability using rich environmental information remains effective in AD risk populations. Age further exacerbates the negative impact of genetic AD risk on PI, with older individuals in the high-risk group showing more pronounced deficits in optic flow tasks (Bierbrauer et al., 2020), suggesting that age-related pathological accumulation may intensify PI decline. Subjective cognitive decline is considered an AD risk factor; individuals reporting subjective cognitive decline show higher distance errors in triangle completion tasks relying on both bodily and optic flow cues, with computational modeling revealing that these errors primarily stem from memory leak (Segen et al., 2025)—the decay rate of internal spatial representations that accumulates error with distance, reflecting core deficits in spatial computation itself. Moreover, AD risk populations show no differences from normal individuals on other neuropsychological tests (Coughlan et al., 2020). This evidence suggests that PI performance without landmark or boundary cue compensation, particularly angular error and memory leak, may provide a sensitive indicator for very early AD diagnosis.

As disease progresses to the prodromal AD stage, Aβ+ individuals (amyloid-positive, considered preclinical AD) show significantly higher distance and angular errors than normal older adults in optic flow subtasks of the Apple Game, but no significant differences in landmark cue tasks (Colmant et al., 2025). Further analysis reveals that angular errors under optic flow conditions correlate positively with medial temporal lobe tau levels, while distance errors correlate only with age (Colmant et al., 2025). In MCI and clinical AD stages, PI function further deteriorates, with MCI and AD patients showing significantly larger distance and angular errors than healthy older adults (Mokrisova et al., 2016). Computational modeling further reveals that angular overestimation constitutes the core source of PI deficits in MCI patients during immersive VR triangle completion tasks (Castegnaro et al., 2023). These studies consistently indicate that angular error represents a specific manifestation of PI decline during pathologi-

cal aging. Additionally, MCI patients show higher distance and angular errors than both preclinical AD individuals and normal older adults, with landmark cues failing to improve their performance (Colmant et al., 2025; Howett et al., 2019), suggesting compensatory mechanisms become ineffective in later disease stages. This contrasts sharply with normal older adults, AD risk populations, and preclinical AD individuals, where landmark information can still trigger some compensatory effects.

In summary, PI decline during normal aging manifests primarily as distance estimation deficits based on single sensory modalities—a characteristic also observed in AD risk stages. However, both AD risk and prodromal AD populations show significantly increased angular errors, while retaining the ability to use environmental cues for compensation. In contrast, pathological aging involves comprehensive deterioration of both distance and angular errors, with significantly reduced compensatory effects from environmental cues. Notably, both the Apple Game and Virtual Supermarket Task exclude bodily cues from real walking; given VR environment peculiarities (Hill et al., 2024) and age-related visual decline, this may amplify observed PI deficits (Colmant et al., 2025). AD risk population definitions vary across studies: biomarker-based studies best reveal early neurophysiological changes in preclinical AD (Colmant et al., 2025), while gene-based risk definitions (Bierbrauer et al., 2020; Coughlan et al., 2020) reveal genetic susceptibility rather than definitive pathological states, affecting result interpretation and understanding of pathological progression stages.

Table 1. PI impairment and neural mechanisms in older adults, AD risk populations, and MCI patients

[The table content appears fragmented in the original text. The translation preserves the structure while clarifying the key findings:]

- **Triangle Completion Task**: Following a triangular path to two target points then returning to start. Using VR headsets with real walking. AD risk populations (middle-aged) show significantly higher distance and angular errors when distal cues are removed, with excessive angular errors causing final position deviation. MCI groups show greater distance errors than healthy controls, with MCI+ (CSF biomarker-positive) patients showing larger errors than MCI- patients and healthy controls. Compared to healthy older adults, MCI and AD patients show significantly higher distance errors; AD groups show significantly higher angular errors than controls, while aMCI groups show no significant angular error differences from healthy older adults. Task conditions include: 1) environment matching practice phase (both distal cues and surface texture); 2) distal cue removal (disrupting environmental geometry); 3) surface texture removal (disrupting visual flow).
- **Apple Game**: Desktop VR paradigm where participants move via joystick from start to target trees. When finding an apple-bearing tree, they must return via shortest path. Includes pure PI (PPI), boundary-

supported PI (BPI), and landmark-supported PI (LPI) conditions. AD risk populations (18-75 years) show significantly worse PPI performance than BPI and LPI, with LPI performing best. APOE4 carriers perform significantly worse in PPI but not in BPI/LPI. APOE4 carriers show more significant error accumulation with longer return distances. In APOE4 carriers, EC volume correlates positively with PI performance at long return distances; EC and hippocampal activation during return phase correlate with PI performance; hippocampal activation correlates with target proximity. Medial EC grid-like representations correlate with PPI performance; retrosplenial cortex activation is significantly higher in LPI tasks.

- **Virtual Supermarket Task**: Participants watch first-person videos of shopping cart movement in VR supermarkets without landmarks, requiring egocentric navigation strategies. Compared to Aβ- groups, Aβ+ groups show higher distance and angular errors in PPI, but landmark cues eliminate group differences in LPI. MCI patients show higher errors in both PPI and LPI, with landmarks failing to improve performance. Medial temporal lobe tau levels correlate positively with angular errors, while distance errors correlate only with age, not tau or amyloid. Hippocampal volume reduction correlates with poor LPI performance, while EC volume shows no significant association.
- **Path Estimation Task**: Participants walk along 8 curved paths with 3 stop points each, verbally reporting distance and angle back to start. Two modalities: 1) bodily cues (blindfolded, real walking); 2) optic flow cues (seated, VR viewing). Older adults show significantly higher PI errors than younger adults under both conditions. Grid representation strength correlates significantly and negatively with PI errors in older adults; grid strength independently predicts PI errors in older adults while other factors (age, cognitive test scores) show no predictive power.

3. Neural Mechanisms of Path Integration Ability

Compared to other navigation functions, PI more heavily relies on self-motion cues for continuous position updating (Sjolund et al., 2018), emphasizing multi-level neural system coordination in processing and integrating self-motion cues. At the cellular level, grid cells collaborate with place cells, head direction cells, speed cells, and other spatial neurons, forming the neural basis for processing self-motion cues into spatial information required for PI. At the brain network level, key regions including the vestibular system, posterior cingulate cortex, retrosplenial cortex, hippocampus, entorhinal cortex, medial septum, and medial prefrontal cortex support precise calculation and spatial localization based on self-motion cues through functional connectivity and dynamic interactions.

3.1. Neuron-Level Path Integration Information Coding

The entorhinal-hippocampal system and adjacent brain regions contain highly specialized spatial information-coding neurons, including grid cells, place cells, head direction cells, and speed cells, which collaboratively support PI function (see Table 2) (Bicanski & Burgess, 2020).

Table 2. Spatial coding cells related to path integration

Cell Type	Primary Location	Core Function	Features and Roles
Grid cells	Medial EC	Generate spatial coordinates	1) Spatial metric foundation: periodic hexagonal firing patterns (Fyhn et al., 2004); 2) Context-dependency: stability influenced by environmental cue types (Lv et al., 2024)
Place cells	Hippocampus	Encode specific locations	1) Core positioning: selective firing marks animal' s location (Hafting et al., 2005); 2) Error correction: dynamically regulated by external cues to compensate and reduce accumulated PI errors (Sheffield & Dombeck, 2019)
Head direction cells	Hippocampal subiculum, thalamus, dorsal tegmental nucleus	Encode spatial orientation	1) Direction coding: maximal firing rate at specific head directions (Taube, 2007); 2) Stable grid coding: head direction information modulates grid cell firing patterns (Winter et al., 2015)

Cell Type	Primary Location	Core Function	Features and Roles
Speed cells	Medial EC	Encode instantaneous speed	1) Speed coding: encode animal' s instantaneous movement speed (Góis & Tort, 2018); 2) Collaborative with grid cells: provide velocity input for distance calculation (Dannenberg et al., 2019)

Grid cells, primarily located in medial entorhinal cortex (EC), are most relevant to PI function (Moser et al., 2005). These cells fire near specific periodic triangular grid vertices and have been identified across multiple animal models and humans (D. Chen et al., 2024; Jacobs et al., 2013), showing cross-species consistency. The evenly spaced firing pattern provides a uniform, metric coordinate system for PI (Dong & Fiete, 2024). Moreover, grid firing remains stable under darkness or landmark occlusion, indicating updates primarily depend on self-motion cues (velocity, head direction, acceleration) rather than visual landmarks, consistent with PI' s dynamic position updating using self-motion information (Poucet et al., 2014). Grid representations show context-dependency, remaining stable with only distal cues or environmental boundaries while proximal cues (e.g., local landmarks) disrupt stability (Lv et al., 2024), potentially related to cue compensation mechanisms in PI.

Grid cell inactivation impairs PI function in mice, manifesting as global vector direction confusion and shortened PI length (Gil et al., 2018). In early AD mouse models, grid cell dysfunction leads to impaired self-motion cue integration, potentially causing PI ability decline (Ying et al., 2023). Grid cells play equally important roles in human PI (Banino et al., 2018). fMRI studies reveal that grid-like representations in human medial entorhinal cortex correlate closely with performance in VR triangle completion tasks (Bierbrauer et al., 2020). When human self-motion cues are disrupted, grid-like representations significantly weaken (Moon et al., 2022). These findings demonstrate that grid cells constitute a crucial neural mechanism supporting PI function.

Unlike grid cells with multiple firing fields, hippocampal place cells typically fire only when the organism occupies specific locations (Hafting et al., 2005). Before grid cell maturation, place cells can form rough spatial representations through PI relying on self-motion information (Bjerknes et al., 2018). In mature nervous systems, place cells achieve precise self-localization by integrating self-motion information from grid cells (Hafting et al., 2005) and environmental information from boundary cells (Solstad et al., 2008). However, hierarchical

relationships and information flow between these systems in mature brains remain debated (Morris & Derdikman, 2023). Additionally, place cell activity is modulated by external cues (Sheffield & Dombeck, 2019), enabling correction of position deviations accumulated from movement errors and internal noise through recalibration mechanisms when animals traverse familiar environments (G. Chen et al., 2013; Fyhn et al., 2007), potentially representing the neural mechanism for cue compensation in PI (Muessig et al., 2015).

Head direction cells, located in hippocampal subiculum, thalamus, and dorsal tegmental nucleus, fire when the animal' s head points in specific directions, encoding spatial orientation (Taube, 2007). These cells depend on vestibular and proprioceptive inputs, maintaining discharge even without visual cues (Shine et al., 2016), providing directional information for PI (Page et al., 2018). Head direction cells modulate grid cells, with signal disruption causing grid cell periodic firing pattern disturbances (Winter et al., 2015). Speed cells in medial EC encode instantaneous movement speed, providing crucial velocity information for PI (Góis & Tort, 2018). Grid cell firing frequency shows linear relationships with movement speed, suggesting rate-coding mechanisms may constitute the mathematical basis for distance estimation in PI (Dannenberg et al., 2019; 赵辰豪, 吴德伟, 2021). These findings indicate that coordinated action among head direction cells, place cells, speed cells, and grid cells constitutes the key neural mechanism for maintaining PI stability and precision.

In summary, grid cells continuously track displacement vectors by receiving and integrating information from speed and head direction cells, generating and updating spatial position representations, while place cells serve localization and error correction functions. These spatial coding-related cells collaboratively provide essential support for PI (see Figure 2 [Figure 2: see original paper]).

Figure 2. Schematic of grid cell collaboration with spatial coding-related cells. During PI, speed cells and head direction cells preliminarily process self-motion information, transmitting velocity and direction outputs to grid cells. Place cells integrate external environmental cues with self-motion information: when reliable external cues are absent, place cells primarily depend on self-motion information to maintain position coding; when external cues are available, they help correct accumulated errors in PI. Grid cells continuously update and track self-position through coordinated interactions with these spatial coding cells, thereby completing PI.

3.2. Brain Network-Level Path Integration Mechanisms

3.2.1. Information Input and Integration Regions for Path Integration PI depends on dynamic tracking of self-motion information. Though not a brain parenchymal structure, the vestibular system serves as a crucial input source for self-motion information, forming an important sensory foundation for PI (Donaldson et al., 2019). The vestibular system supports PI through semicircular canals and otolith organs: canals provide spatial rotation information

while otoliths encode linear displacement (Semenov et al., 2016). Neuromodulation studies show that vestibular interference significantly reduces triangle completion task accuracy (Karn & Cinelli, 2019). Clinical evidence further demonstrates that vestibular damage impairs direction control and distance estimation in PI (Péruch et al., 2005).

Vestibular self-motion information transmits through parietal-temporal association cortex to posterior medial cortex, where posterior cingulate cortex (PCC) and retrosplenial cortex (RSC) play critical information integration roles in PI (Liu et al., 2021). PCC integrates vestibular information (Schindler & Bartels, 2018), transforming dynamic velocity signals into static position parameters to support hippocampal spatial updating (Liu et al., 2021). PCC also participates in coordinating eye, head, and body movements during PI through projections to brainstem vestibular nuclei (Shinder & Taube, 2010). RSC constructs dynamic spatial representations by integrating sensory, motor, and memory multimodal information (Sugar et al., 2011) and can track Euclidean distance between individual and starting point, providing distance coding for PI (Chrastil et al., 2015). Studies have also identified grid-like representations in RSC (D. Chen et al., 2021), though whether their role in PI matches entorhinal grid representations requires further investigation (Alexander & Nitz, 2017).

3.2.2. Core Computational Regions for Path Integration Medial EC, closely connected to multiple brain regions representing spatial information (McNaughton et al., 2006), undertakes core computational functions in PI. Medial EC lesion rats exhibit PI deficits (Van Cauter et al., 2013). Human medial EC grid representation strength correlates with PI performance (Newton et al., 2024). EC theta oscillations closely associate with grid cell activity; human intracranial electrophysiological studies reveal hexadirectional modulation of EC theta oscillations during rapid movement, consistent with grid cell spatial coding features (D. Chen et al., 2018, 2021; Lv et al., 2024). However, relationships between human EC theta oscillation grid-like representations and PI require further validation.

The hippocampus, as the core structure for spatial memory encoding and storage, has an uncertain specific role in PI (Jin et al., 2020). Some propose that the hippocampus corrects accumulated grid cell errors through feedback mechanisms to maintain PI stability (Burgess et al., 2007). Human PI pointing errors correlate negatively with right hippocampal activation (Wolbers et al., 2007), while bilateral anterior hippocampal activation correlates positively with accurately encoded translation and rotation magnitudes (Chrastil et al., 2016), suggesting hippocampal involvement in integrating distance and direction information between self-position and starting points. However, evidence also shows that hippocampal lesion patients can accurately estimate distance and direction back to the start under blindfolded conditions (Shrager et al., 2008). Arnold et al. (2014) observed no hippocampal activation when requiring participants to estimate return distance in triangle completion tasks. Researchers propose

that the hippocampus may primarily participate in short-term maintenance and updating of spatial information like target locations during PI (Fukawa et al., 2020), while path computation itself may depend more on EC. Future research requires more refined behavioral paradigms and decoding techniques to clarify specific cognitive processes involving the hippocampus in PI.

Medial septum (MS) primarily influences PI through theta oscillation modulation. As the pacemaker for limbic system theta rhythms, MS directly projects to medial temporal lobe, regulating rhythmic theta oscillations and maintaining phase consistency in this region' s interneurons (Király et al., 2023). This theta activity is crucial for grid cell function (D. Chen et al., 2021) and directly supports PI and spatial memory (Maidenbaum et al., 2018). Medial septum inactivation disrupts grid cell firing, impairs hippocampal self-motion cue integration, and affects PI distance coding (Nordlund et al., 2025).

3.2.3. Auxiliary Regions for Path Integration Medial prefrontal cortex (mPFC) maintains working memory and goal-related representations for goal-directed behavior. Effective PI execution depends on mPFC regulation of working memory and goal representations, enhancing representation and updating of critical target points while resisting internal and external interference (Arnold et al., 2014). Functional connectivity between mPFC and other high-level cortices plays important roles in maintaining goal spatial information encoding (Sapiurka et al., 2016). In rodent models, hippocampal-mPFC neural synchrony increases during PI (Jones & Wilson, 2005). In human studies, individual differences in mPFC gray matter volume predict position tracking ability in PI, with greater activation when approaching targets (Chrastil et al., 2017). PI tasks significantly enhance mPFC BOLD signals (Izen et al., 2018), and mPFC, together with hippocampus and retrosplenial cortex, constitutes a core activation network during successful task execution (Chrastil et al., 2015). Additionally, grid-like representations in mPFC and EC work cooperatively through theta oscillations, forming a cross-regional grid network (D. Chen et al., 2021). This evidence confirms the importance of mPFC-medial temporal lobe coordination for PI.

4. Specific Neural Features of Path Integration Aging

PI ability decline universally exists in both normal and pathological aging processes, closely related to vulnerability of its core brain regions to aging (see Figure 3 [Figure 3: see original paper]). Building on the previous review of PI neural mechanisms, this section further explores specific neural representations of PI aging.

Figure 3. Schematic of key brain regions involved in PI and their functions. Gray areas show major brain regions vulnerable to AD pathology.

Given grid cells'core role in PI and their functional dependence on the entorhinal-hippocampal circuit, structural and functional integrity of this circuit consti-

tutes the primary factor affecting PI performance. The entorhinal-hippocampal circuit is affected early in aging, making its abnormalities likely the main cause of PI decline during normal aging. Research shows that older adults' grid representation strength correlates significantly and negatively with PI errors—stronger grid representations correspond to smaller PI errors and better PI ability (Stangl et al., 2018). After controlling for age, sex, and multiple neuropsychological test scores, grid representation strength remains the strongest predictor of PI performance in older adults, a relationship not found in younger adults (Stangl et al., 2018). This indicates that weakened EC grid representations constitute a key mechanism for PI decline in normal aging. Meanwhile, age-related hippocampal volume atrophy, neuronal loss, and functional network disruption lead to decreased firing stability of place and head direction cells (Iglói et al., 2015; Schimanski et al., 2013), potentially causing grid cell spatial instability, reduced activity, and decreased firing rates (Stangl et al., 2018), ultimately impairing PI function (Fu et al., 2017; Ying et al., 2022). In summary, grid representation impairment resulting from entorhinal-hippocampal circuit aging represents the key neural signature of PI decline in normal aging.

In AD risk populations, grid cell dysfunction precedes structural atrophy, with this decline triggering compensatory activation in other regions. Although EC and hippocampal volumes show no significant differences between AD risk and healthy populations, posterior medial EC grid representation strength significantly weakens and correlates negatively with immersive VR triangle completion task performance. This association is further moderated by cardiovascular risk factors, CAIDE (Cardiovascular Risk Factors, Aging and Dementia) scores, APOE genotype, and sex: particularly significant in individuals with CAIDE scores >7 (high AD physiological risk) and APOE 4-carrying males (Newton et al., 2024). This suggests that AD genetic and physiological risk factors modulate EC grid system functional degeneration, with males potentially more sensitive to grid cell dysfunction caused by AD risk factors. Notably, AD risk populations show negative grid representation signals; further analysis reveals that unidirectional signal strength correlates positively with PI deficits (Newton et al., 2024), suggesting this group may over-rely on less efficient head direction coding strategies rather than precise grid cell coding mechanisms. AD risk populations recover normal PI performance with landmark or boundary cue assistance, accompanied by strong retrosplenial cortex activation (Bierbrauer et al., 2020), indicating RSC as a key compensatory region for utilizing rich environmental information. Additionally, AD risk populations show preference for environmental boundary-based navigation during PI, differing from healthy individuals' efficient use of environmental centers—a phenomenon associated with significantly reduced functional connectivity between right entorhinal cortex and posterior cingulate cortex (Coughlan et al., 2020), suggesting brain functional connectivity strength may also serve as an important neural indicator for PI decline in AD risk populations.

AD pathological changes closely associate with severe PI impairment. AD neuropathology features a triple cascade: abnormal β-amyloid (Aβ) deposition,

hyperphosphorylated tau-mediated neurofibrillary tangles (NFTs), and progressive brain atrophy (Aisen et al., 2022)—changes also observable in normal brain aging. EC structural and functional abnormalities constitute core mechanisms in AD pathological progression (Igarashi, 2023), with phosphorylated tau tangles appearing earliest in this region. Progressive NFT accumulation eventually causes entorhinal cortex neuronal decline and death, affecting PI function (Koike et al., 2024). Significantly increased distance errors in MCI and AD patients correlate highly with hippocampal volume reduction and EC thinning, indicating structural atrophy corresponding to PI deficits in pathologically aged individuals. Medial temporal lobe tau levels in pathologically aged individuals correlate positively with angular errors, while distance errors correlate with age but not tau or amyloid (Colmant et al., 2025), suggesting AD pathology selectively destroys direction coding in medial temporal lobe structures, causing PI decline. Retrosplenial and posterior cingulate cortices, important for PI function, are also deeply affected by pathological aging. Retrosplenial hypometabolism precedes conversion from MCI to AD (Terstege et al., 2024). MCI and AD patients also show significant posterior cingulate cortex atrophy and decreased metabolic activity (Choo et al., 2010; Lee et al., 2020). However, associations between functional/structural degeneration in these regions and PI decline in pathologically aged individuals remain to be validated.

PI decline in normal older adults and AD risk populations stems from grid representation impairment, while brain functional connectivity strength plays a unique role in PI decline in AD populations. Pathologically aged individuals already show structural atrophy and lesions corresponding to comprehensive PI decline. Current research has not clearly quantified differences between AD pathology-induced grid cell damage and naturally declining grid representations in normal aging, confounding neural features of normal versus abnormal PI decline. Additionally, causal relationships between activation and compensation mechanisms in posterior cortical regions like retrosplenial and posterior cingulate cortices remain to be validated. These limitations constrain interpretation of PI aging mechanisms and pose major challenges for clinical translation.

5. Summary and Future Directions

During both healthy and pathological aging, spatial navigation decline significantly impacts daily life and independence in older adults (Allison et al., 2016). As a fundamental navigation component, PI decline directly affects environmental adaptation. Against public health challenges of population aging and rising AD prevalence, deeply understanding how behavioral performance differences and neural mechanism features of PI are affected by normal and abnormal aging holds important theoretical value and practical significance for determining whether PI can predict early MCI and AD. Through literature review, this article' s main conclusions are: First, normal aging PI decline manifests primarily as distance estimation deficits based on single sensory modalities, while angular error serves as a sensitive indicator for AD risk and prodromal stages. These

populations retain compensatory ability using environmental cues. Pathological aging PI decline involves comprehensive deterioration of both distance and angular errors, with significantly impaired compensatory mechanisms. Second, PI spatial information processing depends on multi-level neural coding networks composed of grid cells, place cells, etc., and coordinated functions of EC, hippocampus, retrosplenial cortex, posterior cingulate cortex, medial septum, and mPFC. Third, the key neural feature of normal aging PI decline is grid representation impairment caused by entorhinal-hippocampal circuit aging. In AD risk populations, grid cell dysfunction precedes structural atrophy, and brain functional connectivity strength may serve as an important neural indicator. Pathologically aged individuals already show structural atrophy and lesions corresponding to comprehensive PI decline.

This study also identifies current research limitations. Future research directions should focus on:

First, paradigms for studying spatial cognitive aging have gradually shifted from paper-pencil tests, real-space navigation, and computer visual stimuli to VR spatial navigation (张家鑫 et al., 2019). Different PI paradigms provide different processing cues, potentially making results difficult to compare (Hill et al., 2024). Most older adults are not proficient with keyboards or joysticks, and mismatches between visual and proprioceptive cues easily cause dizziness, potentially leading to imprecise PI ability assessment in older groups and weakening diagnostic efficacy in distinguishing MCI from AD. Therefore, future research urgently needs to develop dynamic PI paradigms integrating multisensory self-motion cues with higher ecological validity, and establish standardized tasks based on refined characterization of older adult and clinical patient populations to optimize screening accuracy for MCI and AD.

Second, research on factors influencing PI ability aging remains incomplete. Although gender, environmental characteristics (e.g., residential density), and lifestyle factors have been confirmed to importantly regulate navigation ability in adults (Coluccia & Louse, 2004; Coutrot et al., 2022; Dobric et al., 2022; Schug, 2016), their specific influence mechanisms in older populations remain unclear. 张凤翔 et al. (2023) summarized genetic and environmental factors'roles in spatial navigation individual differences, and some psychological factors also relate to PI performance (Guo et al., 2019). Both acute and chronic stress impair PI performance (Akan, Bierbrauer, Axmacher, & Wolf, 2023; Akan, Bierbrauer, Kunz, et al., 2023). Therefore, future research should further parse factors behind PI aging differences, constructing physiological-psychological-environmental assessment models to provide theoretical foundations for developing targeted diagnostic methods and intervention strategies.

Third, although PI function involves coordinated participation of multiple brain regions, specific cooperation and connectivity mechanisms among these regions remain unclear (Baumann & Mattingley, 2021; Weisberg & Ekstrom, 2021). Future research urgently needs to shift toward in-depth exploration at neural circuit or network levels to construct neural mechanism models for understand-

ing PI aging processes.

Fourth, both navigation training and neuromodulation can intervene in spatial navigation ability. Existing behavioral training protocols, such as alternative navigation strategy acquisition and route-landmark association learning, have shown significant intervention effects (McGilton et al., 2003; Provencher et al., 2008; Sejunaite et al., 2017), but their effects on PI require validation. In neuromodulation, non-invasive electrical stimulation techniques such as transcranial direct current stimulation have been applied to spatial navigation intervention research (Neuhaus et al., 2012). Temporal Interference (TI) stimulation, which applies high-frequency currents with frequency differences to form modulation envelopes affecting neuronal activity, has proven effective in improving spatial navigation performance (Beanato et al., 2024). However, PI neuromodulation research remains significantly lacking.

With deep AI technology penetration, this study further proposes urgent future directions: 1) Apply AI technology to develop MCI/AD prediction systems. Deep learning models can predict conversion risk to MCI/AD in older adults based on multimodal data (including demographic information, neuropsychological tests, and brain imaging data) (Yue et al., 2025; Qiu et al., 2022). Introducing PI behavioral and neural indicators may further enhance clinical applicability. 2) Utilize AI to support combined neuromodulation and psychological training interventions. AI can construct personalized head models and stimulation parameters to assist TI and other techniques in targeted EC modulation (Newman et al., 2014). Simultaneously, AI models can assess individual PI deficits and related factors to generate personalized intervention protocols. For example, VR technology can create realistic, controllable navigation environments where AI algorithms can analyze participants' navigation performance in real-time, dynamically adjusting task difficulty. For individuals with high navigation anxiety, environmental modifications can regulate anxiety levels. 3) Pay high attention to related ethical issues: when curative treatments are lacking, risk prediction alone may induce anxiety, requiring careful benefit-risk weighing; strict privacy and security protection are essential during genetic and brain data collection. Finally, older populations may feel unfamiliarity and fear toward new technologies and devices, which will affect intervention effectiveness and widespread application.

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[The remaining references are preserved exactly as listed in the original text, maintaining all formatting, DOIs, and citation details.]

Note: Figure translations are in progress. See original paper for figures.