Postprint: The Multilevel Formation Mechanisms of Individual Differences in Spatial Navigation Ability

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Abstract

Spatial navigation activities occur constantly in our daily lives, and navigation ability exhibits significant individual differences across the population. The decline of this ability also represents an important early behavioral manifestation of cognitive impairment brain diseases such as Alzheimer' s disease. Previous studies have investigated the cognitive-behavioral characteristics and associated neural substrates underlying individual differences in spatial navigation ability, yet the origins of these individual differences remain unclear. The present study reviews research advances from the past decade, adopts a two-factor theoretical perspective, summarizes the key genetic and environmental factors contributing to individual differences in spatial navigation and their underlying mechanisms, preliminarily establishes a genetic/environment-brain network-cognition and behavior pathway model for spatial navigation, and proposes future research directions. The refinement of this pathway model will facilitate our understanding of the formation and developmental patterns of spatial navigation, provide a theoretical foundation and comprehensive perspective for investigating related causal mechanisms, and hold significant applied value for further exploring the potential clinical applications of spatial navigation in brain diseases such as cognitive impairment.

Full Text

Preamble

Individual Differences in Spatial Navigation: A Multi-Scale Perspective

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Abstract: Spatial navigation occurs every day in our lives. Decline in spatial navigation is an important early behavioral manifestation of various brain disorders, including Alzheimer' s disease (AD). Existing researches have revealed significant individual differences in spatial navigation. However, the biological and environmental origins of such differences are not well defined. From a multi-scale perspective, we reviewed the latest studies on this important topic, and proposed a gene-brain-behavior model for mapping the links between genetic and environmental factors and individual differences in spatial navigation. Integrative analysis of multi-omics and clinical data would be promising for future studies concerning the complex pathways of spatial navigation. Results will help us understand the development patterns of spatial navigation and further explore the potential clinical application relevant brain diseases.

Keywords: spatial navigation; individual differences; genetic basis; cognitive map; environmental factors

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2. Measurement of Individual Differences in Spatial Navigation

Researchers have developed diverse experimental paradigms to study spatial navigation processes and have revealed significant individual differences in navigation ability. Given the differentiated yet integrated nature of spatial navigation ability, measurement can be approached from different perspectives and using various methods. The measurement perspective primarily concerns different scales, as navigation ability encompasses not only macro-level comprehensive spatial navigation skills and different facets of large-scale environmental abilities (such as path integration and navigation strategy use), but also more fundamental spatial abilities including spatial graphics, mental rotation, and spatial working memory that are associated with small-scale environments. Measurement methods must be selected according to the specific scale of navigation ability being assessed.

2.1 Questionnaire-Based Measures Using Long-Term Experience or Real-World Learning

Self-report questionnaires are widely used in spatial navigation research due to their simplicity and high reliability and validity. These instruments typically require individuals to make judgments based on their long-term navigation expe-

riences across different scenarios, yielding results that serve as accurate indicators of specific components of individual spatial navigation. The Santa Barbara Sense of Direction Scale (Hegarty et al., 2002) is a frequently used comprehensive measure with good psychometric properties (Condon et al., 2015). The Wayfinding Strategy Scale primarily distinguishes between orientation strategies and route strategies to assess individual navigation strategy preferences (Lawton, 1994). The Spatial Anxiety Scale measures individual spatial anxiety traits (Lawton & Kallai, 2002), though this construct focuses narrowly on anxiety during environmental navigation. Lyons et al. (2018) further subdivided spatial anxiety into three subscales—imagination, operation, and navigation—representing internal-static, internal-dynamic, and external-dynamic spatial abilities, respectively. These scales have been applied in numerous studies to reveal sex and age differences in spatial navigation (Boone et al., 2018).

Beyond questionnaire measures based on long-term navigation experience, some studies employ more specific navigation scenarios. After learning routes in real environments, researchers administer various tests of environmental knowledge to quantify different aspects of spatial navigation ability, thereby providing a comprehensive reflection of navigation capacity (Muffato et al., 2016; Stites et al., 2020).

2.2 Virtual Reality-Based Measures

Virtual reality technology offers unique advantages in terms of high testability and controllability, making it widely used for specific testing tasks in spatial navigation research and yielding important findings. Virtual reality enables more diverse participant inclusion (such as individuals with disabilities) while being more cost-effective and safer than real-world testing (Cogné et al., 2017). Combined with fMRI, EEG, and PET technologies, virtual reality also allows exploration of brain activity during spatial navigation, further advancing understanding of the neural mechanisms underlying human navigation (Ekstrom et al., 2003; Tarnanas et al., 2015).

Virtual navigation tasks designed with VR technology can be categorized into several types. Virtual water maze tests, memory island tasks, and wayfinding tasks are typical comprehensive navigation ability paradigms. These tests usually consist of a learning phase and a testing phase: during learning, participants must memorize the spatial location of a target platform while researchers record exploration time and distance; during testing, navigation ability is quantified using metrics such as success rate in reaching the target, time spent, and route distribution (He et al., 2019; Rizk-Jackson et al., 2006; Yasen et al., 2015). Similar learning-testing paradigms can also measure individual spatial learning capacity (Grzeschik et al., 2019).

Individual differences in spatial navigation also manifest in various facets including navigation strategy use, path integration, and cognitive map formation. Navigation strategy measurement paradigms follow two main approaches. The

first involves virtual maze scenarios such as Y-mazes, eight-arm mazes, and star mazes (Blanchette et al., 2020; Iglói et al., 2015; Rodgers et al., 2012). These paradigms typically separate learning trials from probe trials, with researchers observing participants' choices during probe trials to distinguish whether they use response-based or location-based strategies—that is, egocentric versus allocentric navigation strategies. The second approach creates multiple-choice conditions without artificially manipulating the environment, instead observing natural responses such as in the Dual-Solution Paradigm and virtual corridor tasks (Boone et al., 2018; Vukovic & Shtyrov, 2017).

Path integration involves processing self-motion cues and forming spatial representations through spatial updating (Wolbers & Hegarty, 2010). Most path integration tasks focus on orientation updating, typically presenting position updates from a first-person perspective before asking participants to judge relative positions or directions. Performance is measured using pointing error, pointing latency, and pointing accuracy metrics through tasks such as loop closure, 3D maze pointing, and triangle completion (Chrastil et al., 2017; Kong, Pu, et al., 2017; Xie et al., 2017). Compared to path integration, which relies on self-motion cues for self-referenced navigation, cognitive map formation represents a more flexible, observer-independent representation method (Wolbers & Hegarty, 2010) that shows significant individual differences (Weisberg & Newcombe, 2018). For instance, using the Virtual Silcton paradigm, researchers found that the population can be roughly divided into three types based on cognitive map formation ability: integrators (who can form comprehensive environmental representations), non-integrators (who can only recognize traveled routes), and imprecise navigators (who cannot form spatial representations). Integrators demonstrate good memory for buildings categorized by routes, enabling hierarchical environmental representations and better performance in model-building tasks (Weisberg & Newcombe, 2016, 2018). Other paradigms investigating cognitive maps are similar, requiring participants to recall or construct environmental knowledge after virtual environment exposure (He et al., 2021; Nazareth et al., 2018).

Spatial navigation also involves more fundamental spatial abilities. Spatial orientation/perspective-taking ability requires individuals to imagine themselves at one location and then determine directions to another location or sequence of turns, representing a foundational skill for navigation tasks. Common paradigms include spatial orientation tasks, city walking tasks, three-mountain tests, and relative direction judgments (Münzer et al., 2020; Newcombe, 2019; Tarampi et al., 2016; Vander Heyden et al., 2017). The relative direction judgment task, for example, requires participants to mentally manipulate their imagined position before making directional judgments, unlike simple pointing tasks (Kraemer et al., 2017). The spatial reorientation paradigm can reveal strategies individuals use for spatial orientation, such as simultaneously utilizing geometric and landmark cues versus using only one type of cue (Vieites et al., 2020). Similarly, when studying how environmental cues affect spatial memory, researchers often use object location memory

paradigms in virtual environments, measuring spatial memory ability through the error between remembered and actual positions. fMRI studies using these paradigms have identified brain regions responsive to boundary and landmark cues and parallel hippocampal-striatal processing systems (Doeller et al., 2008). Preferences for navigation strategies using different cues constitute part of the individual differences in navigation ability itself, and researchers can use these classic paradigms to further investigate how different cue properties affect spatial navigation ability (郝鑫 et al., 2022).

While most studies measure spatial navigation ability by having participants follow pre-planned routes, increasing attention has been paid to quantifying behavioral patterns during free exploration (Gagnon et al., 2018). Analyzing free exploration requires recording individual trajectories to extract metrics, which virtual reality environments facilitate. Gagnon et al. (2018) quantified revisit behavior and diffusion patterns during free exploration: the former indicates exploration caution, while the latter represents the rate of dispersion within an area. Results revealed clear sex differences in free exploration patterns, with women more frequently revisiting previously visited locations and showing lower diffusion rates within areas (Gagnon et al., 2018). Brunec et al. (2023) similarly quantified free exploration patterns, proposing roaming entropy and experienced integration metrics: the former describes the dispersion of individual movement over time, while the latter describes the degree to which individuals explore well-connected environmental regions. Individuals spending more time in highly integrated areas show higher experienced integration, and results indicated that higher experienced integration correlates with more accurate cognitive map formation (Brunec et al., 2023).

2.3 Measures Based on Online Games and Big Data

The rise of big data methods has enabled large-scale data collection and analysis. Sea Hero Quest (SHQ) is a mobile and tablet game that gamifies traditional wayfinding and path integration tasks, analyzing game trajectories to measure individual spatial navigation ability (e.g., route length). Game performance significantly correlates with real-world navigation ability, demonstrating good ecological validity (Coutrot et al., 2019). Researchers have collected over 3 million player datasets worldwide using this mobile game, with large-scale data analysis revealing effects of sex, age, and living environment on spatial navigation ability (Coutrot et al., 2022). Another big data approach involves using GPS data from large numbers of individuals in real environments, analyzing spatial navigation psychological mechanisms through computational modeling (Bongiorno et al., 2021). Additionally, by analyzing trajectory metrics such as road segment similarity, trajectory entropy, and total turning angle from real-world GPS data, researchers have identified significant differences in navigation patterns between healthy individuals and AD patients, and have used machine learning methods to build AD prediction models based on these trajectory features (Ghosh et al., 2022).

3. Genetic Factors in Spatial Navigation

As a complex cognitive ability, spatial navigation is influenced by genetics to a certain degree, similar to other cognitive abilities (Boomsma et al., 2002). Human genetics studies have confirmed this view (Flowers & Rebeck, 2020; Nishiyama et al., 2002). For example, Polk et al. (2007) found that monozygotic twins showed more similar brain activation patterns than dizygotic twins when recalling locations, indicating genetic influence on human spatial navigation. Family, twin, and adoption studies further demonstrate that spatial abilities have moderate heritability (30-50%) (Bratko, 1996; DeFries et al., 1979; Tosto et al., 2014). Rimfeld et al. (2017) measured small-scale spatial abilities using 10 integrated tests and found heritability as high as 69% in large twin samples; Malanchini et al. (2020) measured large-scale spatial orientation using 6 integrated tests and found 64% heritability in large twin studies. These findings provide important support for genetic variation in human spatial navigation ability.

To date, researchers have identified multiple genes that may affect spatial navigation, including BCL-2, S100B, and APOE.

3.1 BCL-2

BCL-2 is an anti-apoptotic gene involved in regulating neuronal death in the central nervous system; overexpression of this gene slows hippocampal cell apoptosis (Kuhn et al., 2005). By overexpressing human BCL-2 in normal mice, researchers found decreased spatial navigation ability in the water maze. Specifically, in random-start training tasks that rely more on environment-referenced navigation strategies, Hu-bcl-2 transgenic mice took significantly longer to find the platform, indicating impaired ability to form correct spatial representations or use them effectively. In fixed-start training tasks (where both egocentric and allocentric reference frames can be used), Hu-bcl-2 transgenic mice showed no navigation impairment. Functionally, these transgenic mice exhibited severely weakened long-term potentiation (LTP) in hippocampal CA1 region, preventing formation of precise place fields and affecting normal spatial representation formation or use. In terms of neuron numbers, Hu-bcl-2 transgenic mice had larger dentate gyrus volume and more neurons (Rondi-Reig et al., 2001). Additionally, impairing learning and memory in normal mice significantly reduced BCL-2 gene expression in the hippocampus (Hu et al., 2011; Wang & Han, 2009), with obvious neuronal loss in CA1 and CA3 regions (Wang et al., 2017), a phenomenon also observed in bats with impaired navigation ability (Hsiao et al., 2016). In rats with existing memory impairment (due to vascular dementia, Alzheimer' s disease, or drug injection), significantly improved water maze performance after various interventions was accompanied by increased BCL-2 protein and mRNA expression in hippocampal CA1, CA3, pyramidal cell layer, and dentate gyrus, reduced apoptosis, and enhanced hippocampal-related memory and spatial navigation (Long et al., 2020; Nakamura et al., 1999; Wang et al., 2009; Wang et al., 2011; Wu et al., 2020; Yuliani et al., 2021). This suggests

that BCL-2 gene expression must be maintained at optimal levels to maximize hippocampal cognitive functions, with either excessive or insufficient expression impairing memory and other cognitive abilities.

3.2 S100B

S100B is another gene that may affect spatial navigation. The S100B protein is primarily found in astrocytes and oligodendrocytes of the central nervous system and serves as a specific nervous system protein. As a calcium-binding protein, nanomolar concentrations of S100B stimulate neurite growth and promote neuronal survival, while higher micromolar concentrations have opposite effects and can even induce neuronal apoptosis and accelerate neuroinflammation. Therefore, S100B concentration in cerebrospinal fluid or serum is considered an important diagnostic or prognostic indicator for neurodegenerative diseases (Steiner et al., 2011). Studies show that transgenic mice carrying large amounts of human S100B perform worse on water maze tests (e.g., longer training times, less time spent at the hidden platform during probe trials). The possible molecular mechanism is that excessive S100B affects calcium-dependent synaptic processes, leading to weakened LTP and impaired hippocampal function (Gerlai & Roder, 1996). Conversely, knocking out this gene improves mouse performance on water maze tasks (Nishiyama et al., 2002). Additionally, intracerebroventricular injection of low-concentration S100B after experimental brain injury can induce neurogenesis in the hippocampus and is associated with enhanced cognitive function after brain injury (Kleindienst et al., 2005).

S100B is also potentially linked to human spatial navigation. Spatial navigation impairment is an early symptom of AD patients, and brain regions showing abnormalities in AD significantly overlap with the spatial navigation brain network (Fu et al., 2017). Postmortem studies of AD patients found increased S100B mRNA and protein concentrations in the hippocampus and temporal lobe (Marshak et al., 1992), higher density of S100B-positive astrocytes (Simpson et al., 2010), and elevated S100B concentration in cerebrospinal fluid compared to normal individuals (Peskind et al., 2001), with concentrations gradually increasing from mild to moderate AD stages. Whether serum S100B concentration is higher in AD patients remains controversial (Steiner et al., 2011). Mechanistically, excessively high S100B concentration can cause brain inflammation characterized by astrogliosis and microgliosis (Mori et al., 2010), leading to Aβ generation, deposition, and plaque formation—pathological phenomena considered primary diagnostic criteria for AD (Zhang et al., 2022). Furthermore, postmortem studies of normal human brains revealed that the spatial expression pattern of S100B correlates with brain activation patterns during spatial navigation, particularly scene processing activation patterns (Kong, Song, et al., 2017).

Beyond evidence from protein concentration and gene expression, studies have preliminarily established associations between S100B-related single nucleotide polymorphisms (SNPs) and human spatial navigation. Lambert et al. (2007)

found that the rs2300403 locus is associated with lower cognitive performance and increased AD risk; Wang et al. (2021) found that the rs9722 polymorphism may increase AD risk by altering miRNA binding capacity and upregulating S100B expression. Kong, Song, et al. (2017) integrated genotype, gene expression, brain imaging, and behavioral data to discover associations between S100B polymorphisms and scene processing brain activity in the retrosplenial cortex (RSC) and parahippocampal place area (PPA). Specifically, individuals with different rs11542311 genotypes showed significant differences in functional activation of the posterior right RSC, while rs3788266 was significantly associated with both right RSC and left PPA. Moreover, serum S100B levels significantly mediated the association between rs3788266 and right RSC functional activation (Kong, Song, et al., 2017).

3.3 APOE

The APOE gene is considered the most important risk gene for AD (Belloy et al., 2019; Genin et al., 2011). Decline in navigation ability is an important early behavioral manifestation of cognitive disorders like AD, and neurodegeneration in medial temporal, parietal, and frontal regions associated with early AD is also closely related to decreased spatial navigation ability (Coughlan, Coutrot, et al., 2018). This suggests that the APOE gene may affect cognitive abilities including spatial navigation. The APOE gene is located on chromosome 19q13.2 and has four possible alleles. APOE1 has only been found in 4 cases worldwide; APOE3 is most common in human populations; while APOE2 and APOE4 have distinct functions. APOE2 is considered protective against AD, with more copies reducing AD risk and delaying potential onset age; APOE4 is an AD risk gene, with risk and earlier onset age increasing with the number of APOE4 alleles. Specifically, compared to non-carriers, APOE3/4 heterozygotes have 2-4 times higher AD risk, while APOE4/4 homozygotes have 8-12 times higher risk (Belloy et al., 2019). This may be related to APOE lipoprotein concentration, the gene' s expression product. Animal models and human studies have found that APOE2 promotes protein concentration while APOE4 shows lower protein concentration in prefrontal cortex, hippocampus, and cerebrospinal fluid (Castellano et al., 2011; Cruchaga et al., 2012; Riddell et al., 2008). APOE protein concentration affects amyloid protein clearance, so the APOE4 gene leads to increased Aβ production and deposition (Wang et al., 2018), considered a major pathological cause of AD.

Not all APOE4 carriers develop AD, but the gene' s effects on cognition may persist throughout life (Flowers & Rebeck, 2020; Weissberger et al., 2018). Spatial navigation impairments can be observed in mild cognitive impairment and preclinical stages, also showing sensitivity to APOE4 allele dosage. For example, in computer-simulated virtual water maze tests, individuals with amnestic mild cognitive impairment (aMCI) show worse spatial navigation accuracy than healthy individuals, particularly on self-referenced tasks, with APOE4 homozygotes performing worse than heterozygotes. The possible neural mechanism is

right hippocampal atrophy (Laczó et al., 2014), an effect that also appears in real-world water maze tasks (Laczó et al., 2011). In memory island tasks with healthy older adults, APOE4 carriers spent significantly less time in the target quadrant during probe trials, showing spatial memory impairment (Berteau-Pavy et al., 2007). In SHQ game wayfinding tasks, they also required longer paths (Coughlan et al., 2019). Similarly, healthy adult APOE4 carriers already show reduced basic cognitive abilities related to spatial navigation, such as visual-spatial attention reorientation, location memory retention, and target location memory modulation. Specifically, in spatial cue discrimination tasks, more APOE4 alleles correlate with slower spatial attention reorientation to invalid cues; in spatial working memory tasks, the APOE4 dosage effect becomes more pronounced with higher memory load, with APOE4 homozygotes showing significantly impaired location memory retention; and in tasks requiring both abilities, APOE4 homozygotes show lower accuracy and higher reaction times (Greenwood et al., 2005). Notably, APOE4 effects on cognition may show different characteristics across age stages. For example, in adolescence, APOE4 effects on episodic memory and executive function are inconsistent, with some studies showing better performance (Mondadori et al., 2007; Rusted et al., 2013), but in spatial navigation, APOE4 carriers do not show target quadrant preference in memory island tasks (Acevedo et al., 2010).

Neurally, healthy APOE4 carriers show impaired function in some brain regions while potentially enhanced function in others. APOE4 risk gene carriers have affected small hippocampal regions (Flowers & Rebeck, 2020), with grid cell impairment in the entorhinal cortex of healthy individuals preventing stable grid-like representations and leading to poorer spatial memory performance. However, a compensatory mechanism appears, including enhanced hippocampal activity and boundary cells' error angle correction (Hardcastle et al., 2015; Kunz et al., 2015). This enhanced hippocampal activation can also be observed in young carriers during resting state and memory encoding tasks (Filippini et al., 2009), with APOE4 associated with enhanced medial temporal lobe activity (Flowers & Rebeck, 2020). Similarly, healthy middle-aged APOE4 carriers perform worse on pure path integration tasks but show stronger dependence on spatial cues when landmarks or boundaries are present; younger individuals can better use landmarks and boundaries for path integration, reflecting compensatory effects of RSC and boundary cells on path integration ability (Bierbrauer et al., 2020). This also explains why APOE4 carriers' wayfinding trajectories in SHQ stay closer to boundaries (Coughlan et al., 2019).

3.4 Other Candidate Genes

In addition to the main genes discussed above (summarized in), recent studies have identified other candidate genes potentially related to spatial navigation. The hippocampus is considered the core structure of the spatial navigation brain network, and hippocampal volume shows high heritability (approximately 70%) (den Braber et al., 2013; Rentería et al., 2014). Multiple genes affecting hip-

pocampal volume have been identified. The MYT1L gene (Myelin Transcription Factor 1 Like) is expressed in mammalian neurons and controls central nervous system formation and development, with its product being a brain-specific transcription factor (Vierbuchen et al., 2010). Kepa et al. (2017) found that reduced MYT1L expression in the hippocampus leads to decreased expression of LTP and synaptic transmission-related genes, with neuroimaging evidence showing positive correlation between MYT1L expression and hippocampal volume, suggesting its potential role in spatial navigation through memory-related neurophysiological mechanisms (Kepa et al., 2017). Another gene affecting hippocampal volume is ANKRD37 (ankyrin repeat domain 37), whose rs1053218 mutation causes overactivation of ANKRD37 expression, leading to reduced hippocampal volume—a relationship more pronounced in AD patients (Xu et al., 2022). Genetic variations reducing hippocampal volume are often associated with increased AD risk (Hibar et al., 2017), making this gene variant a potentially important genetic basis for individual differences in spatial navigation. Recently, the SHARPIN gene (SHANK associated RH domain interactor) was found to have important associations with AD. In Japanese populations, ultra-rare variants with a minor allele frequency of approximately 0.0002 increase AD risk nearly 6-fold (Asanomi et al., 2019), while the rs34173062 mutation was found to increase AD risk and brain degeneration in Western populations (Soheili Nezhad et al., 2020). Additionally, a genome-wide association study identified loci and genes significantly associated with hippocampal volume (such as ASTN2, DPP4, MAST4), though their genetic mechanisms and pathways require further investigation (Hibar et al., 2017). These genes provide important candidate genes for basic genetic research on spatial navigation.

In summary, spatial navigation genetic research has employed increasingly rich technical methods and yielded growing results, but remains preliminary. Only a few genes have been linked to spatial navigation, and their replicability requires further verification, with specific mechanisms needing deeper exploration. Particularly lacking are integrated studies of genes, brain imaging, and behavioral data. Moreover, environmental and learning exposure factors may play key roles in these pathways. Therefore, to better understand the genetic-brain-behavior pathway of spatial navigation, it is necessary to clarify environmental exposure factors from an exposomics perspective (Maitre et al., 2022).

4. Sex, Age, and Environmental Exposure Factors

4.1 Sex Differences

Sex differences in spatial navigation have been extensively validated in both behavioral performance and neural mechanisms. Behaviorally, an overall male advantage in navigation ability has been demonstrated, confirmed in a mobile game-based assessment covering 57 countries and regions worldwide (Coutrot et al., 2018). Large-sample data from Chinese populations also show that males exhibit stronger spatial cognition overall between ages 11-40 (Xu et al., 2023). Studies find that male spatial navigation ability is superior to females' in both

landmark-rich and landmark-limited environments (Astur et al., 1998). In strategy use, males tend to simultaneously use both landmark and geometric cues, while females primarily rely on landmark cues (Sandstrom et al., 1998). In navigation-related scene processing, males show stronger bilateral PPA activation (Kong, Huang, et al., 2017). During spatial representation in navigation, males typically depend on survey strategies that form spatial layout information in an observer-independent reference frame, enabling more flexible navigation and shortcutting when necessary; females more often depend on route strategies, remembering when and where to make specific turns, but with less flexibility in some situations (Boone et al., 2018; Lawton, 1994). These differences may relate to differential brain region activation during navigation: males show significant activation in the left hippocampus, while females consistently use the right parietal and right prefrontal cortex (Grön et al., 2000).

Notably, female disadvantage in spatial ability is not universal. Women show greater advantages when memorizing object locations (Voyer et al., 2007), and spatial ability is influenced by physiological factors—women perform as well as men on navigation tasks when estrogen levels are low (Chabanne et al., 2004), while male advantage is associated with higher testosterone levels (Driscoll et al., 2005). From an evolutionary perspective, the range size hypothesis suggests that to reproduce successfully, males must cover larger activity areas, leading to stronger spatial abilities through evolution (Jones et al., 2003), a hypothesis validated in free exploration spatial tasks (Gagnon et al., 2018). Coutrot et al. (2018) found through SHQ that countries differ in spatial navigation ability and sex-specific patterns, with national GDP positively correlating with navigation ability. The Gender Gap Index (GGI), indicating gender equality, significantly explains sex differences in navigation ability, suggesting that sex effects in cognition may relate to women' s social status across countries (Coutrot et al., 2018).

4.2 Development and Aging

Different age stages show different spatial navigation abilities. Developmentally, small-scale spatial cognition increases rapidly from childhood through adolescence and early adulthood, peaking at ages 21-35 before declining steadily (Xu et al., 2023). Using spatial reorientation paradigms, researchers found that children under 5.5 years primarily rely on environmental geometric properties for object location representation, while adults use both geometric and non-geometric cues (Hermer, 1997). Older adults perform worse than young adults on route learning, landmark sequencing, location learning, and path integration (Stangl et al., 2020), indicating age-related spatial memory impairment. Age-related navigation memory deficits may result from less efficient path encoding in posterior fusiform gyrus, parahippocampal gyrus, and parietal cortex, as well as hippocampal atrophy (Jack et al., 1997; Moffat, 2009). In terms of strategies, older adults perform worse on both egocentric navigation tasks (fixed start-end wayfinding) and allocentric navigation tasks (virtual Morris water maze), indi-

cating both strategies decline with age (Driscoll et al., 2005; Moffat & Resnick, 2002). Electrophysiological results show that aging impairs LTP induction and maintenance in the hippocampus and lowers LTP/LTD thresholds, weakening spatial memory (Han et al., 2006). Allocentric navigation deficits correlate with weaker hippocampal and parahippocampal activation (Antonova et al., 2009), while egocentric navigation decline relates to reduced parietal cortex and precuneus function (Coughlan, Laczo, et al., 2018). Additionally, navigation strategy preferences shift with age: older adults self-report more egocentric strategy use compared to younger adults (Driscoll et al., 2005), preventing good external environment representation. In cue use, younger adults prefer boundary cues while older adults prefer landmark cues (Schuck et al., 2015), with boundary use associated with smaller response errors in navigation tasks (Bullens et al., 2010), partially explaining older adults'poorer navigation. However, not all older adults show poor navigation—significant individual differences exist within the group. High-performing older adults can show good path integration ability in environments with multisensory information or multiple available cues due to information integration (Bates & Wolbers, 2014; Ramkhalawansingh et al., 2017). With age, hippocampal function decreases, but enhanced functional connectivity between PPA and occipital lobe (Ramanoël et al., 2019) and strengthened prefrontal activation (Reynolds et al., 2019) partially preserve navigation ability in some older adults, which has important survival significance.

4.3 Environment and Plasticity

Beyond sex and age differences, environmental differences individuals encounter throughout life can create broader individual differences (Vermeulen et al., 2020), including macro-level dimensions such as cultural background, language habits, and living environment, as well as individual-level specific dimensions like training and health habits (Liu et al., 2023).

Cultural Background. Cultural background forms the foundation of one' s life and influences spatial navigation ability. For example, hunting cultures have open spatial environments and require hunting and returning in similar, uniform environments, leading to stronger navigation ability (Berry, 1971). Influenced by tribal culture, the Spanish Barcelona people use the sea and mountains to determine cardinal directions, creating unique direction sense systems that directly cause group differences in spatial navigation (许琴 et al., 2010). Different cultures often involve different language systems, and language differences constitute thinking and cognitive differences (Vygotsky, 2012). Cross-cultural studies show that language systems shape spatial cognition—individuals' languages align with the reference frames that optimize spatial memory and reasoning. Egocentric reference system languages (e.g., "the cat is to the left of the dog" from self-perspective) tend to form egocentric spatial representations, while geocentric cognitive system languages (using cardinal directions) more easily form allocentric spatial representations (Goeke et al., 2015; Hao et al., 2017). Individuals with better spatial abilities show better performance (Haun et al., 2011)

due to different encoding strategies caused by language (Lovett & Forbus, 2011). Neuroimaging studies show that language understanding and spatial representation tasks involve covarying brain network activity, proving language' s shaping effect on spatial cognition (Vukovic & Shtyrov, 2017).

Living Environment. Among primate species, spatial skill differences relate to different evolutionary pressures in nutrient-rich versus nutrient-poor environments (Newcombe, 2018). Human populations similarly show effects of living environment "richness"on spatial navigation. Coutrot et al. (2020) collected SHQ data from 38 countries and found that individuals raised in cities showed poorer navigation than those raised outside cities, though this difference varied by country (e.g., environmental differences in the US were over 6 times larger than in Romania). The irregularity of surrounding street networks largely explains these differences—complex, irregular street networks may pose higher navigation demands, exercising individuals' spatial navigation abilities (Coutrot et al., 2022). Beyond environmental differences themselves, different exploration patterns of surroundings also cause navigation behavior differences. For example, boys are often allowed to explore larger, more complex external environments in childhood, which may contribute to male advantages in wayfinding tasks and help understand sex differences in strategy preferences (Lawton & Kallai, 2002).

Training and Plasticity. Spatial skills are highly plastic—spatial thinking training is effective, durable, and transferable (Uttal et al., 2013). Xu et al. (2023) found through gamified mental rotation tests that small-scale spatial cognition plasticity increases rapidly from childhood to early adulthood, peaking at ages 16-20 and remaining high until age 35. Regarding specific abilities, parental education on spatial graphics in childhood helps children understand and form spatial graphic representations (Szechter & Liben, 2004), while parental spatial language input affects children' s spatial language development, with children receiving more spatial language showing better performance on later spatial problem-solving tasks (Pruden et al., 2011). Early map training also promotes children' s spatial cognition and cognitive map formation (Uttal, 2000). The generally superior spatial navigation performance in Nordic countries may relate to unique map training ("orienteering") (Coutrot et al., 2018). Beyond early training, adult map training can also promote navigation ability—professional London taxi drivers undergo deep hierarchical learning of London' s points, routes, landmarks, road names, and street networks based on maps (Griesbauer et al., 2022), showing exceptional navigation ability and better new route learning than non-taxi drivers (Woollett & Maguire, 2009). Brain imaging shows taxi drivers have increased posterior hippocampal gray matter density and decreased anterior density compared to bus drivers and ordinary people, with posterior hippocampal volume increasing with experience during learning (Maguire et al., 2006; Woollett & Maguire, 2011). Additionally, active driving experience itself shapes navigation ability more than passive spatial knowledge reception (Sandamas & Foreman, 2015). General education level also positively correlates with navigation ability (Coutrot et al., 2018).

Navigation Aid Use. With technological development, GPS navigation devices are widely used, but dependence on external aids seems to hinder active navigation thinking and training (McKinlay, 2016). Studies show excessive GPS reliance impairs spatial knowledge learning and acquisition (Hejtmánek et al., 2018; Ruginski et al., 2019), spatial memory (Gardony et al., 2013), and is associated with habitual route learning (Dahmani & Bohbot, 2020). This navigation ability degradation may further affect independence, autonomy, and quality of life. However, some studies explore how to improve navigation systems to mitigate negative effects. For example, Wunderlich and Gramann (2019) found that adding landmark knowledge to auditory navigation instructions can overcome spatial ability reduction and improve spatial knowledge acquisition (Wunderlich et al., 2020), with personally relevant landmark knowledge also enhancing spatial learning and memory (Gramann et al., 2017).

Lifestyle and Health Status. Diet (Jacka et al., 2015), sleep (Marshall & Born, 2007), exercise (Firth et al., 2018), smoking, and alcohol use (Dobric et al., 2022; Gomez et al., 2015) all affect hippocampal volume. As the hippocampus is crucial for spatial memory and cognitive map formation, poor health status may weaken spatial navigation ability. Functionally, active voluntary movement increases the amount of information the hippocampus encodes about spatial locations, improving encoding quality and stability (Rechavi et al., 2022). Additionally, mental or physical illnesses such as pathological anxiety, depression, autism, and PTSD may affect navigation ability, related to altered hippocampal function and reduced volume (Bremner et al., 2007; Herrero et al., 2006; Sheline et al., 2002; Smith, 2015).

In summary, existing research has examined macro-level environmental factors related to spatial navigation from diverse perspectives, revealing to some extent how environmental exposures varying across time and space influence and shape individual navigation ability (see). Beyond sex and age effects, research on environment and plasticity has mostly revealed surface-level correlations with spatial navigation, lacking in-depth investigation of mechanisms within the genetic-brain-behavior pathway.

5. Summary and Outlook

In conclusion, spatial navigation involves multiple cognitive processes, with different components showing significant individual differences across various facets. This review summarizes recent research on factors influencing spatial navigation individual differences and proposes a multi-level formation mechanism.

We find that existing studies have identified key genetic and environmental factors affecting spatial navigation from multiple levels, but several urgent issues remain. First, the few genes currently discovered cannot support and maintain the complex spatial navigation brain network; future research needs to further explore additional genes. Second, while researchers have begun exploring im-

portant associations among genes, brain, and spatial navigation, current studies remain preliminary, and a clear gene-brain-behavior pathway has not been established. Third, spatial navigation ability is highly susceptible to geographic and cultural environmental influences and shows substantial plasticity, but research on environmental factor mechanisms remains thin, particularly regarding environmental roles in the genetic-brain-behavior pathway.

Based on molecular psychology research approaches and methods (Canli, 2015), we propose a genetic/environmental-brain network-behavior pathway framework for spatial navigation individual differences ([Figure 1: see original paper]). This framework integrates genetic, early life experience, environmental, brain structural/functional, and cognitive-behavioral data to examine how key genetic and environmental factors affect the development of spatial navigation brain functional networks and how the integrity of navigation brain networks influences behavioral performance across different navigation activities. For example: How does the S100B gene regulate neural activity in the retrosplenial cortex—a core node of the spatial navigation brain network—to cause individual differences in navigation behavior? How does the APOE gene alter hippocampal structure and function to affect performance on cognitive map-related tasks? How does street complexity around one' s residence modulate hippocampal development, leading to differences in navigation strategies and abilities? Through multi-level analysis, we can further validate these key factors and clarify their mechanisms, while more importantly identifying additional influences to comprehensively map the multi-level formation mechanisms of navigation individual differences.

Based on this framework, we propose three future directions:

First, Genome-Wide Association Studies (GWAS) to comprehensively reveal key genetic variations affecting spatial navigation. Current genetic factors influencing spatial navigation have mostly been discovered in animal models and then validated in humans, with only a few genes showing stable associations. Without numerous other genes, these cannot create and maintain the complex spatial navigation brain network. With advances in genetics and psychological measurement, future research can build large-scale spatial navigation genetic databases and use GWAS to identify significant genetic variants associated with spatial navigation phenotypes across the human genome. Based on this, methods such as polygenic scores, genetic correlation, and enrichment analysis (Wray et al., 2021) can further explore key pathways through which genetic factors regulate spatial navigation and genetic overlap with brain diseases like AD.

Second, Gene-environment interaction studies reveal complex pathways among genetics, environment, cognition, and behavior. Genetics and environment jointly shape individuals, making it crucial to explore their interactions after identifying individual influences. Recent APOE research reflects this integrated approach, showing that APOE4 effects on AD risk differ across race, sex, age, diet, and geography (Coughlan, Coutrot, et al., 2018; Neu et al., 2017; Zhang et al., 2022). For spatial navigation, future research can simulta-

neously obtain genetic, environmental, and navigation data from large samples to analyze gene effects across environments. Although large-scale navigation data acquisition is challenging and lacks unified measurement, SHQ and GPS trajectories provide new solutions. SHQ' s availability in app stores enables worldwide data collection, with game performance reflecting real navigation ability (Coutrot et al., 2019). GPS trajectories reflect real-world behavior and cognition, and trajectory metric analysis can reveal psychological models during navigation, reflecting individual differences across navigation facets (Bongiorno et al., 2021). This approach can also help identify key characteristics of navigation ability in early AD and how environmental factors affect spatial ability, contributing to new cognitive improvement strategies and early AD diagnosis and prevention.

Third, Brain Imaging Genetics (BIG) explores the neurogenetic mechanisms of spatial navigation individual differences. Current genetic-brain-behavior pathway research is limited. BIG links genetics, brain imaging, cognition, and behavior to deepen understanding of formation mechanisms. Spatial navigation is a complex cognitive process, with neuroscience establishing close associations between navigation and hippocampus, entorhinal cortex, parahippocampal gyrus, retrosplenial cortex, medial prefrontal cortex, and other regions (Baumann & Mattingley, 2021; Peer et al., 2021), and attempting to establish brain network foundations from multi-region interactions (Kong, Wang, et al., 2017; Kong et al., 2023; Weisberg & Ekstrom, 2021). Future research should establish stable associations between multi-modal brain imaging metrics and spatial navigation ability to provide an indicator foundation for large-scale imaging genetics studies (Ekstrom et al., 2017; Kong, Wang, et al., 2017). Through international multi-center collaboration (e.g., ENIGMA) and cohort databases (e.g., UK Biobank), spatial navigation-related imaging metrics can be associated with whole-genome and gene expression data (Kong et al., 2020) to comprehensively reveal key genes and genetic mechanisms affecting spatial navigation brain networks. Further determining gene, environment, and interaction effects on navigation brain networks and behavior will help understand navigation development biology and contribute to new cognitive improvement strategies and neurodegenerative disease prevention and treatment.

References

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