

Spatial navigation in preclinical Alzheimer’s disease : A review

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This review aims to synthesize evidence on spatial navigation as an early marker for preclinical Alzheimer’s disease (AD), focusing on its neurobiological rationale, assessment tools, and links to AD biomarkers in cognitively unimpaired individuals. Studies were included if they assessed spatial navigation in cognitively healthy individuals with AD biomarkers (CSF, PET, or plasma).

Preclinical Detection of Alzheimer's Disease: The Potential of Spatial Navigation

Alzheimer’s disease (AD) develops over a prolonged preclinical phase, during which neuropathological changes accumulate long before any symptoms emerge.

Why Spatial Navigation?

- Spatial navigation circuits anatomically overlap with early tau pathology sites (Braak stages I–II) (Braak I–II)
- Less influenced by education level than memory tests
- Scalable digital assessment (tablet, VR, mobile)
- Ecological validity: correlates with real-world GPS data
- Applicable outside specialized memory clinics

Evidence Linking Spatial Navigation Deficits to Preclinical AD

11 studies where included, below is a snapshot of 3 results:

Table 1 | Spatial navigation assessments in cognitively healthy individuals with Alzheimer's diseases biomarkers.

Task	Biomarker	AUC	Sensitivity	Specificity	p-value
Path Integration	p-tau181 (plasma)	0.86	92%	78%	*** (p < 0.001)
Floor Maze Test	Conversion AD (2 year)	0.75	70%	70%	* (p = 0.06)
Cognitive Mapping	Aβ42 (CSF)	0.77	80%	67%	*** (p = 0.003)

Spatial Navigation Computation and Early AD Pathology

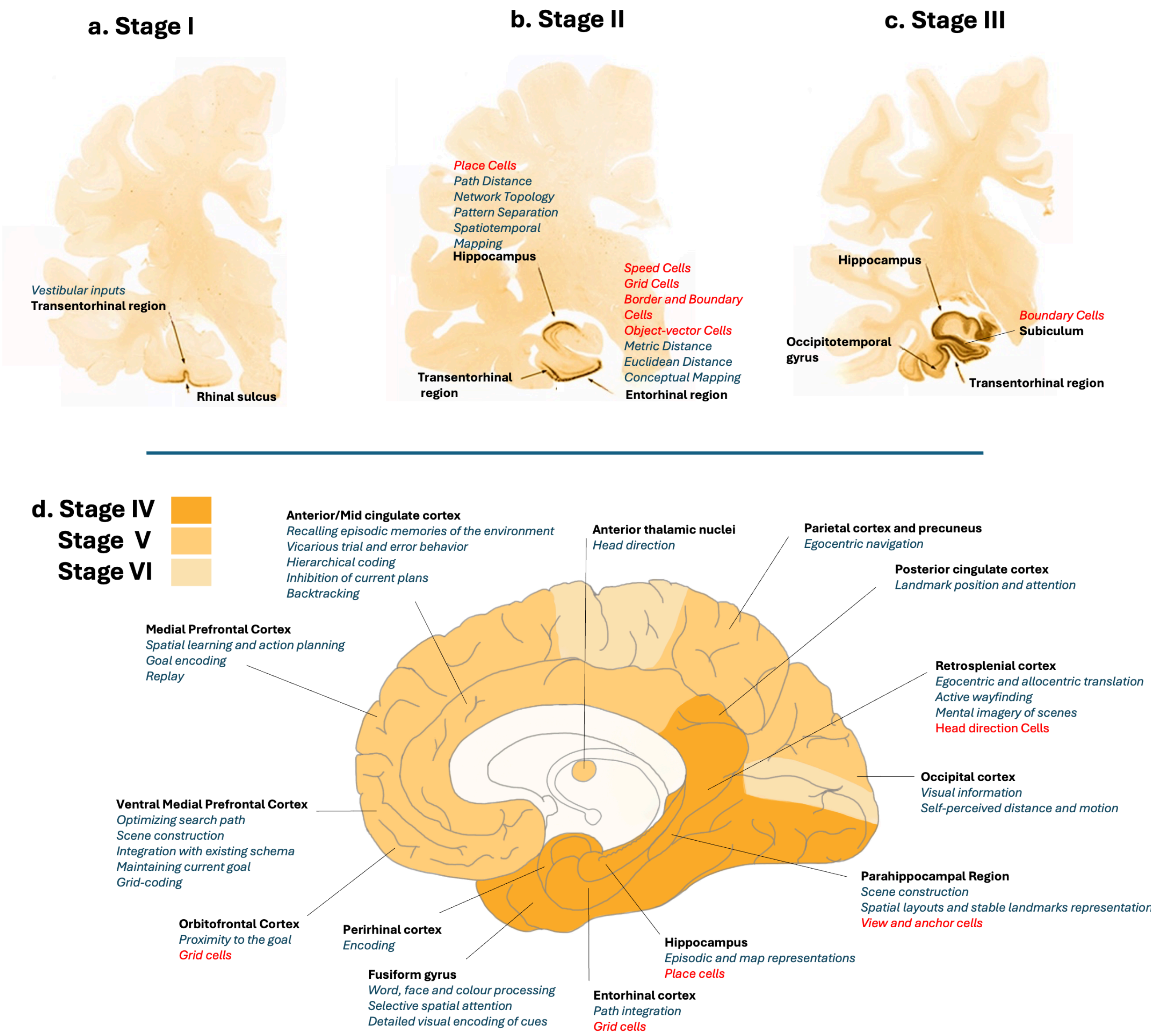


Figure 1 | Anatomical representation of Braak stages in Alzheimer’s disease and spatial navigation computations.

From Research to Clinical Potential

Spatial navigation assessment is a low-cost, scalable, digital tool for detecting preclinical AD. While promising, current evidence is limited by small cohorts and moderate accuracy. Challenges include cognitive complexity, individual variability, and cross-cultural differences. Spatial navigation could serve as a multimodal cognitive and biological framework, it represents a promising and practically deployable component of future preclinical AD detection strategies.

Next Steps:

- Large longitudinal studies linking navigation to biomarkers.
- Harmonized protocols and normative databases.
- Integration into multimodal diagnostic frameworks.

