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阿尔茨海默病(Alzheimer's disease, AD)是最常见的痴呆类型,其特征性病理改变可在临床症状出现前15~20年即已发生。轻度认知障碍(mild cognitive impairment, MCI)作为AD的前驱阶段,是早期识别与干预的关键窗口。目前,脑脊液检测与淀粉样蛋白、tau蛋白正电子发射断层显像虽可用于AD病理评估,但因侵入性强、成本高、可及性差等局限,难以在人群中广泛开展,临床亟需无创、便捷、敏感的早期评估手段。

空间导航障碍已被证实是AD最早出现的认知症状之一,其神经环路基础高度依赖内嗅皮层-海马环路。虚拟空间导航任务兼具生态有效度和可控性,能客观检测空间导航功能,成为评估AD早期空间认知损伤的重要手段。内嗅皮层-海马区域是tau病理最早累及的脑区。血浆磷酸化 tau217 (phosphorylated tau 217, p-tau217)作为微创外周血标志物,可反映tau病理负荷,为AD早期病理评估提供重要参考,鉴于海马各亚区在结构、功能及病理易感性上存在显著异质性,其体积变化特征可为揭示AD早期空间认知损伤的影像机制提供潜在线索。

基于上述背景,本研究纳入认知正常者与MCI患者,采用虚拟空间导航任务评估空间导航功能,采集3D T1WI图像后利用FreeSurfer分割海马亚区和内嗅皮层体积,并检测血浆p-tau217水平。通过一般线性模型与偏相关分析,明确各指标的组间差异及相关性;进一步采用logistic回归和ROC曲线评估单一指标及联合模型分类效能。结果显示,MCI患者存在显著的虚拟空间导航功能下降、特征性内侧颞叶结构萎缩及血浆p-tau217水平升高;虚拟空间导航障碍与血浆p-tau217水平及特定海马亚区萎缩密切相关;联合三者构建的多模态模型分类效能优于单一指标。本研究提示,虚拟空间导航是AD早期识别的无创、敏感的行为学生物标志物,联合血浆p-tau217与内侧颞叶精细结构,可为AD高风险人群的早期诊断提供多模态联合新策略。详见内文第19页。

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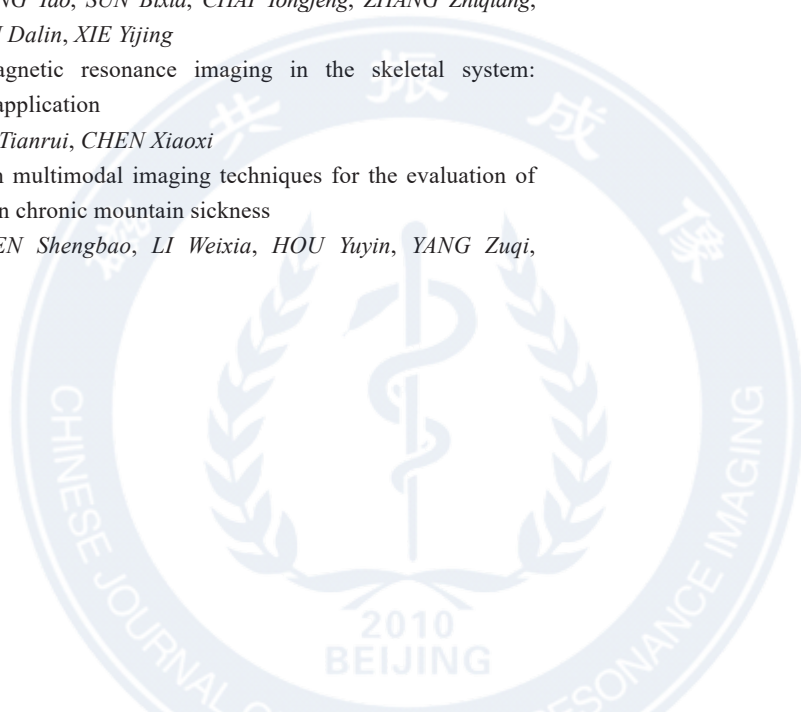
About the cover

Alzheimer's disease (AD) is the most common dementia, with pathological changes beginning 15 to 20 years before clinical symptoms emerge. Mild cognitive impairment (MCI), as a prodromal stage of AD, represents a critical window for early detection and intervention. Conventional cerebrospinal fluid tests and amyloid/tau PET are invasive, expensive, and poorly accessible, underscoring the need for noninvasive, sensitive, and practical early assessment tools.

Spatial navigation impairment is one of the earliest cognitive symptoms of AD and is highly dependent on the entorhinal cortex/hippocampal circuit. Virtual spatial navigation tasks, which combine ecological validity with controllability, offer an objective means to assess navigation function in early AD. The entorhinal/hippocampal region is also among the earliest sites affected by tau pathology. Plasma phosphorylated tau217 (p-tau217), a minimally invasive blood biomarker, reflects tau burden and provides valuable information for early AD assessment. Hippocampal subfields show marked heterogeneity in structure, function, and pathological vulnerability, and their volume changes may yield clues to the imaging mechanisms underlying early spatial cognitive decline.





In this study, we enrolled cognitively normal older adults and MCI patients. Virtual spatial navigation tasks were used to assess navigation function; 3D T1WI images were acquired and processed with FreeSurfer to segment hippocampal subfields and entorhinal cortex; and plasma p-tau217 levels were measured. General linear models and partial correlation analyses were performed to examine group differences and intercorrelations, followed by logistic regression and ROC curves to evaluate the classification performance of individual and combined models. Our results showed that MCI patients exhibited significant navigation deficits, characteristic medial temporal lobe atrophy, and elevated plasma p-tau217 levels. Navigation deficits were closely correlated with p-tau217 levels and atrophy of specific hippocampal subfields. A multimodal model combining all three indicators outperformed any single indicator. These findings suggest that virtual spatial navigation is a noninvasive and sensitive behavioral biomarker for early AD detection, and that combining it with plasma p-tau217 and medial temporal lobe fine structure offers a novel multimodal strategy for early diagnosis in individuals at high risk for AD. Please see text page 19.

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