Early stages of neurodegenerative diseases and their diagnosis using experimental cognitive tests with a specific focus on spatial navigation

Abstract

This dissertation thesis is focused on early and differential diagnosis of Alzheimer's disease (AD) using experimental cognitive tests. AD starts as a preclinical stage, progresses to the mild cognitive impairment (MCI) and eventually to the dementia stage. It is crucial to diagnose AD very early to slow down its progression. However, the use of specific AD biomarkers, such as amyloid and tau positron emission tomography and cerebrospinal fluid (CSF) biomarkers, is very limited. Experimental spatial navigation and spatial pattern separation tests, unlike conventional cognitive tests, may have a strong diagnostic potential as they depend on brain regions affected early in AD. The first study in a virtual environment showed preference for word-centered navigation in cognitively normal older adults, while participants with early AD preferred body-centered strategy to compensate for neurodegeneration. Using a virtual navigation test, the second study showed different profiles of navigation impairment in MCI participants with AD and other (i.e., non-AD) etiologies and demonstrated that navigation assessment differentiated AD from non-AD participants. Various navigation strategies were associated with atrophy in different brain regions and CSF AD biomarkers. The third study showed that a spatial pattern separation test reliably detected early AD. The fourth study demonstrated that this assessment differentiates MCI participants with AD from those with non-AD etiology and showed that spatial pattern separation is supported by posterior medial temporal lobe regions and basal forebrain. In conclusion, spatial navigation and spatial pattern separation tests may be useful for early diagnosis of AD.

Key words

Alzheimer's disease, basal forebrain, body-centered spatial navigation, cerebrospinal fluid biomarkers, entorhinal cortex, hippocampus, mild cognitive impairment, parietal cortex, spatial pattern separation, world-centered spatial navigation