



Cognitive & Behavioral Assessment

Continuous measurement of object location memory is sensitive to effects of age and mild cognitive impairment and related to medial temporal lobe volume

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Abstract

Introduction: We present findings of a novel and ecologically relevant associative memory test, the Object Location Touchscreen Test (OLTT), which was posited as sensitive to early medial temporal lobe compromise associated with mild cognitive impairment (MCI).

Methods: A total of 114 participants, including healthy young and older controls and patients with MCI, completed the OLTT and standard neuropsychological testing. The OLTT required participants to recall the location of objects under free and cued recall conditions, with accuracy evaluated using distance measures (i.e., a continuous error score), and a standard recognition format. Correlations between performance and volumetric data were evaluated from a subset of 77 participants.

Results: Significant age effects were dwarfed by MCI effects across all test conditions. OLTT Cued Recall was strongly and specifically related to the volume of disease-relevant medial temporal lobe regions, generally more than traditional memory tests.

Discussion: The OLTT may be sensitive to early structural compromise in regions affected by Alzheimer's disease.

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Keywords:

MCI; Alzheimer's disease; Dementia; Ecological validity; Hippocampus; Entorhinal cortex; MRI; Volumetrics; Brain volume; Memory; Cognitive

1. Introduction

A substantial body of evidence indicates that Alzheimer's disease (AD) begins years before the onset of clinical symptoms [1], with neurofibrillary tau deposition in the transentorhinal region of the medial temporal lobes being

among the earliest pathological changes [2,3] and particularly associated with cognitive decline [4]. This anatomic location is significant because the entorhinal cortex serves as (1) the convergence zone for multimodal input from the amygdala, perirhinal, parahippocampal, auditory, and olfactory cortices and (2) the "gateway" to the hippocampus via the perforant and alvear pathways that directly innervate the subiculum, CA1, CA3, and dentate gyrus [5,6]. Not surprisingly then, memory deficits are typically the first cognitive symptom of AD and form the basis for the diagnosis of (amnestic) mild cognitive impairment

The authors have declared that no conflict of interest exists.

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<https://doi.org/10.1016/j.dadm.2017.10.007>

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(MCI) [7,8], generally considered a precursor to the dementia associated with AD. Such memory deficits are typically quantified using accepted neuropsychological measures such as memory for word lists, prose, and visuospatial designs, yet older adults [9] and early-stage patients frequently report trouble with associative tasks such as recalling the locations of objects [10,11]. Thus, there may be particular merit in using paradigms that emulate such real-world complaints when evaluating memory in older adults.

A few previous studies have examined object location (OL) memory in patients with MCI, and all have reported significant impairment relative to cognitively intact older adults [12–15]. Such findings are intriguing in light of the cognitive processes and associated neuroanatomic correlates of OL memories (see [15–17]). Specifically, to successfully form a new OL memory, an individual must engage ventral visual stream areas, including the perirhinal cortex [18,19], to identify the object. Processing the object's location is known to engage the parahippocampal gyrus [20]. These different aspects of information about the object must be held in mind via the lateral frontoparietal working memory network until they are bound into a long-term memory, with associative binding generally believed to occur in the hippocampus [21]. The transfer of information from working- to long-term memory is consonant with Baddeley's [22] construct of an episodic buffer, which may be mediated by the entorhinal cortex in the case of OL memories based on the above noted projections into and out of this region as well as neurophysiological evidence of persistent neuronal activation during time delays (see [23]). Thus, early AD-related pathology in the entorhinal region may result in an incomplete integration of objects and their locations, thereby compromising the hippocampal binding process.

The present study extends our earlier work with OL memory [15,17,24,25] and had two primary goals. First, we examined the effects of age and the cognitive phenotype of amnesic MCI on OL memory. While earlier studies required participants to remember an object's location within a standard [12,14] or modified grid (street map) [13] using the traditional dichotomous view of memory (i.e., each item scored as correct vs. incorrect), our paradigm presents common objects within realistic environments [15,17,26] and quantifies the magnitude of impairment using a distance measurement. We posit that this continuous memory measure is especially sensitive to neuroanatomical compromise. Thus, our second goal was to evaluate the relationship between OL memory and the volume of the medial temporal lobes, as measured via magnetic resonance imaging (MRI) data. We predicted that performance would be related to the volume of the entorhinal and parahippocampal cortices and the hippocampus.

2. Methods

2.1. Participants

A total of 114 participants completed the Object Location Touchscreen Test (OLTT) and a brief neuropsychological

protocol (see Table 1). Of these, 36 were healthy young controls (HYCs) and 31 were healthy older controls (HOCs). These participants were free of subjective complaints or objective evidence of memory impairment (i.e., they performed within 1 SD of the mean on the Immediate and Delayed Memory Indices of the Repeatable Battery for the Assessment of Neuropsychological Status [RBANS]) and were independent in all instrumental activities of daily living. The remaining 47 participants had been diagnosed with amnesic MCI according to Petersen's criteria [7] during a consensus conference before study referral. Specifically, there was a subjective decline in memory (reported by the patient or an informant) and objective evidence of memory impairment within the context of relatively preserved everyday functioning. The measures in Table 1 were independent of those used to determine the clinical diagnosis of MCI, thereby reinforcing the stability of the observed memory deficits.

General exclusion criteria included history of neurologic diseases other than MCI (e.g., stroke, moderate–severe traumatic brain injury), psychiatric disorders (e.g., severe depression, bipolar disorder), current or past substance dependence, and learning or attentional disorders.

Participants were recruited from the Atlanta, GA, area between December 2011 and January 2014. All testing was performed in a quiet office setting. The Emory University Institutional Review Board and Atlanta VAMC R&D committee approved the study methods. All participants provided written informed consent.

2.2. Object Location Touchscreen Test

We recently detailed the development and structure of the OLTT and, therefore, provide only a summary below (see [26]). It arose from our previous functional MRI research [15] and was designed as an ecologically relevant memory task that emulates everyday memory demands. In each of three versions of the OLTT, participants were instructed to learn the locations of 15 objects within 5 rooms (3 objects per room) that were presented on a computer screen. Memory was tested following a 15-minute delay (see below).

The OLTT was run using a Dell laptop computer and a 19" ELO touchscreen monitor (model 1915L) using a locally developed software program. The program automatically randomized the order of stimuli for each administration and phase, thereby eliminating any potential order effects.

2.2.1. Stimuli

Following our earlier procedures [15], 45 common household objects were selected (15 stimuli per version), and we created 15 rooms using a computerized design program (www.Plan3d.com) that were used to create three OLTT versions. Within each room, we selected three locations and pseudorandomly assigned objects to each location. These OL pairs were inspected to ensure if there were no inherent (or implicit) relationships and to ensure that each object

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