Journal of Neuroscience Methods 237 (2014) 16–25

Contents lists available at ScienceDirect

Journal of Neuroscience Methods

journal homepage: www.elsevier.com/locate/jneumeth

Clinical Neuroscience

An object location memory paradigm for older adults with and without mild cognitive impairment

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HIGHLIGHTS

- Development of a simple standardized tool (LOCATO) for object-location memory (OLM).
- The parallel sets are equivalent within the groups of healthy older adults and MCI.
- Only small re-tests effects after 6 month without ceiling were revealed.
- LOCATO detects differences in formation of OLM between healthy older adults and MCI.
- Systematically assessment of OLM formation and its modulation by adjuvant therapies.

ARTICLE INFO

Article history:
Received 18 June 2014
Received in revised form 20 August 2014
Accepted 21 August 2014
Available online 28 August 2014

Keywords:
Cognitive mild impairment
Ageing
Visuospatial memory
Associative learning
Transcranial direct current stimulation
Non-invasive brain stimulation

ABSTRACT

Background: Object-location memory is critical in every-day life and known to deteriorate early in the course of neurodegenerative disease.
New method: We adapted the previously established learning paradigm "LOCATO" for use in healthy older adults and patients with mild cognitive impairment (MCI). Pictures of real-life buildings were associated with positions on a two-dimensional street map by repetitions of "correct" object-location pairings over the course of five training blocks, followed by a recall task. Correct/incorrect associations were indicated by button presses. The original two 45-item sets were reduced to 15 item-sets, and tested in healthy older adults and MCI for learning curve, recall, and re-test effects.
Results: The two 15-item versions showed comparable learning curves and recall scores within each group. While learning curves increased linearly in both groups, MCI patients performed significantly worse on learning and recall compared to healthy controls. Re-testing after 6 month showed small practice effects only.
Comparison with existing methods: LOCATO is a simple standardized task that overcomes several limitation of previously employed visuospatial task by using real-life stimuli, minimizing verbal encoding, avoiding fine motor responses, combining explicit and implicit statistical learning, and allowing to assess learning curve in addition to recall.
Conclusions: Results show that the shortened version of LOCATO meets the requirements for a robust and ecologically meaningful assessment of object-location memory in older adults with and without MCI. It can now be used to systematically assess acquisition of object-location memory and its modulation through adjuvant therapies like pharmacological or non-invasive brain stimulation.

Abbreviations: PC, percent correct; NIBS, non-invasive brain stimulation; FR, free recall; CR, cued recall.

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http://dx.doi.org/10.1016/j.jneumeth.2014.08.020
0165-0270/

1. Introduction

Remembering the place of an object (object location memory) is crucial for adapting to changing environments in everyday life, an ability known to decline during ageing (e.g., Hedden and Gabrieli, 2004; Kessels et al., 2007) and with an acceleration in pathological conditions like mild cognitive impairment (MCI) or Alzheimer's disease (AD) (Bucks and Willison, 1997; Petrella et al., 2007; Troyer et al., 2008; Vacante et al., 2013). Due to the continuous increase of the elderly population world-wide, the incidence of age-associated memory impairment may increase dramatically (Bishop et al., 2010; Plassman et al., 2011). Current research focuses on prodromal AD stages like MCI to allow for early intervention with the ultimate goal to delay progression of the disease (Langbaum et al., 2013).

In the face of lacking effective pharmacological treatments (Bond et al., 2012; Tricco et al., 2013; Yue et al., 2012), non-pharmacological enhancement including cognitive training (Reijnders et al., 2013; Simon et al., 2012), physical activity (Ruscheweyh et al., 2011), dietary modifications or nutrition supplements (Janssen et al., 2010) as well as techniques like non-invasive brain stimulation (NIBS, Floel, 2014) have gained increasing attention in the treatment of MCI and AD. Importantly, cognitive training may be combined with and boosted by any of the other interventions. A well-defined cognitive training paradigm is therefore paramount not only to enhance cognitive function by training per se, but also to assess the impact of training-adjuvant therapies like NIBS. Moreover, this paradigm should be applicable in both older individuals and in MCI patients in order to test effectiveness of interventions under controlled conditions and to study pathological mechanism.

The methodological quality of interventional cognitive training studies differed widely (see also, Papp et al., 2009; Reijnders et al., 2013; Simon et al., 2012). Participation-orientated interventions (generally including not only memory training but additional cognitive domains like attention and executive functions, or acquisition of memory strategies) and their outcome parameters were heterogeneous, rendering critical comparisons between interventions difficult and impeding assessment of training effects within a specific cognitive domain (Lovden et al., 2012). Furthermore, despite its obvious validity for activities of daily living, object location memory has rarely been used in larger training studies in MCI patients.

In the current study, our main goal was therefore to develop an ecologically valid paradigm for assessing object-location learning and recall without floor or ceiling effects, which can be applied over several learning sessions in older adults with and without MCI. To achieve this goal, we adapted a previously established object-location learning paradigm (LOCATO) developed for healthy older adults (Floel et al., 2012). A shorter (15 instead of 45 items) and thus cognitively less demanding version of LOCATO was designed in two parallel versions. These versions were tested for equivalence in each group, as well as practice effect after 6 months. Moreover, we assessed if the short LOCATO version would be sufficiently sensitive to detect memory differences between healthy older adults and patients with MCI.

2. Materials and methods

2.1. Overview

In an earlier study, we used a standardized computer-based object-location learning task called "LOCATO" (learning of 45 correct positions of buildings (objects) on a street map (locations)) in healthy older adults in a study that assessed learning with and without non-invasive brain stimulation. Here we will provide only a short overview about the development of long LOCATO (stage I, for more details, see the original publication by Floel et al., 2012) and will then focus on describing specific modifications for a shorter and thus simpler version of the task and its validation in healthy older adults (stage II) and MCI patients (stage III).

Data reported here were taken from three interventional studies conducted in our laboratory (two with healthy older adults, one with MCI patients). From these studies, baseline assessments as well as follow-up assessments in the respective "placebo conditions" were employed. All subjects were native German speakers and underwent a medical examination prior to baseline testing. The latter included structural magnetic resonance imaging (MRI) of the brain, several serum-based parameters, and a comprehensive neuropsychological test battery (comprising general intellectual functioning, attention, executive functions, and verbal memory; see e.g., Witte et al., 2013) for a complete description; and see below for details on memory testing). Memory impaired subjects were additionally tested with the cognitive subscale of the Alzheimer's Disease Assessment Scale (Rosen et al., 1984). Depression was monitored using the Beck's Depression Inventory (BDI; Hautzinger et al., 2001). The affective state at the time of the testing was assessed with the Positive and Negative Affect Schedule (PANAS, Watson et al., 1988), and handedness was determined by the Edinburgh Handedness Inventory (Oldfield, 1971).

Healthy older adults were recruited via advertisements in the internet, local newspapers and the Charité University Hospital intranet in Berlin, Germany. They had to fulfil the following inclusion criteria: (1) no current intake of medication that affects the central nervous system (e.g., antipsychotics or antidepressants); (2) normal routine medical and neurological examinations; (3) no recreational drug use; and (4) no signs of dementia (Mini Mental State Examination of minimal 26 points (Folstein et al., 1975)); (5) no subjective memory complaints; (6) all neuropsychological test results within 1 SD of age/education norms.

MCI patients were referred to the study from the local memory clinic of the Charité University Hospital. They fulfilled core clinical criteria for the diagnosis of MCI outlined by Petersen and others (Petersen, 2004; Petersen et al., 2001; Winblad et al., 2004) which did not comprise novel biomarkers as suggested in more recent MCI criteria (Albert et al., 2011). Patients reported subjective memory complaints, which were confirmed by standardized neuropsychological testing using the Consortium to Establish a Registry for Alzheimer's Disease test battery (CERAD; Memory Clinic Basel, www.memoryclinic.ch) and the Verbal Learning and Memory Test (VLMT, Helmstaedter et al., 2001). All MCI patients had maintained independence and reported minimal if any impairment of function in daily life. A clinical interview, neurological examination, and structural MRI revealed no systemic or brain diseases accounting for declined cognition. Patients diagnosed with amnestic or amnestic plus MCI (in the following referred to as MCI) were included.

All subjects received a small reimbursement and gave written informed consent prior to the study. Each part of the study was approved by the Ethics Committee of the Charité University Hospital Berlin, Germany, and was conducted in accordance with the declaration of Helsinki.

2.2. Stages of development

2.2.1. Stage I

The original version of the LOCATO task comprised the consecutive presentation of a series of 45 buildings (objects) on a street map (location). Associations between an object and a certain location had to be acquired based on the frequency of associations, that is, correct object-location pairings were shown more often than