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Dissociation of Measures of Topographical and Non-topographical Cognitive Ability in Older Adults

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Abstract

The relationship between topographical and non-topographical cognitive measures was studied for 25 elderly participants. The topographical measures were the Camden Topographical Recognition Memory Test (CTRMT), a Topographical Mental Rotation Test (TMRT), and a Virtual Pond Maze (VPM). The non-topographical tests were the Montreal Cognitive Assessment (MoCA), the Trail-Making Test-B (TMT-B), and a matching-to-sample Visual Short-Term Memory Test (VSMT). Only the correlation (0.48) between the TMT-B and the TMRT attained significance; the bivariate correlations among the three topographical measures were modest, ranging from 29 to 33, although they did correlate highly with a topographic composite score (0.69-0.78). A factor analysis yielded a further distinction between the topographical and non-topographical measures. Loadings for the three topographical measures on a presumed "topographical" factor ranged from 0.62 to 0.71 but only from 0.17 to 0.23 for the second factor. The MoCA and TMT-B loaded on both factors, while the VSMT measure loaded poorly (-0.03) on the topographical factor but highly (0.89) on the second factor. The results suggest that standard measures of cognitive function may not be optimal for specific assessment of topographical abilities, the best predictor of impending Alzheimer's dementia.

Keywords: Topographical, Memory, Hippocampus, Aging, Alzheimer's.

Abbreviations: CTRMT- Camden Topographical Recognition Memory Test, TMRT- Topographical Mental Rotation Test, VPM-Virtual Pond Maze, MoCA- Montreal Cognitive Assessment, TMT-B- Trail-Making Test-B

Introduction

The topographical orientation system, also known as the spatial navigation, topo-kinetic and action-extrapersonal systems, is one of the four major networks in the brain governing our interaction with our 3D environment [1]. It is believed to be composed mainly of subcortical regions such as the caudate nucleus and anterior thalamus and three posterior regions-the medial-temporal lobe/hippocampus, posterior cingulate, and parietal-temporal cortex [1-3]. It is the system responsible for scene and route memory, a sense of presence in the world, and topographical orientation and way finding in the plane of the Earth's surface [1].

It is widely accepted that the topographical memory component of this system is centered in the hippocampus. Activation of the hippocampus occurs during recall of topographical routes [4] whereas damage to it results in amnesia for spatial landmarks and maps and severe topographical disorientation [5]. Although the topographical memory system deteriorates during normal aging [6-8], severe disruption of it is a very early diagnostic sign of Alzheimer's disease [8-15]. Indeed, atrophy and/or metabolic deactivation of key components of the topographical neural network are among the best predictors of impending Alzheimer's disease [16-19].

Despite their neurophysiological basis and good predictive validity, topographical tests are not routinely used in assessment of early Alzheimer's disease.

The purpose of the present study, therefore, was to compare topographical versus more widely used non-topographical measures of cognitive ability in older adults. To test topographical memory, three tests were used in the present study:

1. The Camden Topographical Recognition Memory Test (CTRMT)
2. A computerized Topographical Mental Rotation Test (TMRT) similar to the "four mountains" test used by Bird et al. [9] and Hartley and Harlow [20].
3. A Virtual Pond Maze (VPM) similar to the widely used Morris water maze in rodents and virtual mazes that have been developed for humans [21-23]. While the CTRMT has not been specifically linked to hippocampal function, memory for distinct scenes is dependent on this region [24,25]. Memory for scenes requiring topographical mental rotation is also dependent on the hippocampus and the critical role of the hippocampus in the water maze has been repeatedly shown in both animals and humans [20-22].

The tests of non-topographical function were the Montreal Cognitive Assessment (MoCA), the Trail-Making Test Part B (TMT-B), and a computerized Visual Short-Term Memory Task (VSMT) that had a

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similar appearance to the TMRT except that it involved a matching-to-sample object recognition memory rather than a topographical transformation. Even though it was a basis for screening of the participant population, the MoCA ended up replacing a different non-topographical test-the Camden Short Recognition Memory Test for Words-because scores on the latter severely violated normality due to a ceiling effect.

To determine relationships within and across the two sets of measures, a biserial correlation matrix and factor analysis were performed on scores from the six measures.

Methods

Participants

A total of 25 active individuals between the ages of 70 and 85 participated in this study. All participants were prescreened for dementia and those scoring less than 19 on the MoCA-the recommended cutoff for the normal designation for a similar age sample-were excluded from the study [26]. All but two of 27 originally recruited participants that met other exclusionary criteria achieved the MoCA criterion. Participants were additionally excluded if they had ever suffered a stroke, seizure, traumatic brain injury, or had a diagnosed neurological condition. Finally, participants were excluded if they were currently taking any psychoactive drugs and engaged in other than moderate caffeine consumption (no more than 300 mg per day, the equivalent of three cups of coffee per day), moderate alcohol consumption, and mild pain medication (used by two participants). Participants signed an informed consent document approved by Biomed IRB (Biomedical Institute of America; San Diego, CA).

Apparatus

All cognitive testing was performed in an outpatient office setting and required approximately 90 min. Two of the three topographical tests (the VPM and TMRT) were programmed for this study and administered using a Compaq NC6400 computer (Hewlett-Packard) under moderately dim illumination in a quiet room while the participant was seated. The third topographical test was the CTRMT, administered from a test booklet using standardized procedures in a well-lit room [27].

The three non-topographical tests were the MoCA (which includes a clock-drawing and a Necker-Cube copying task but no topographical assessment per se), the TMT-B, and a computerized short-term visual memory test. The MoCA and the TMT-B were administered as paper-and-pencil tests, while the VSMT was programmed for this study and also administered on the Compaq NC6400 computer. These tests were carried out as part of a larger study that also analyzed several measures of vestibular function and their relationship to topographical abilities with vestibular testing performed in a separate facility [28].

Tests

Camden Topographical Recognition Memory Test (CTRMT):

This task required participants to view 30 urban scenes during a 3-s interval and report whether the photograph was taken by an amateur or a professional photographer. Immediately after the completion of the presentation sequence, participants were shown the same 30 scenes in a different order along with two never-before-seen versions of each scene taken from different distances and egocentric viewing perspectives. In a three-alternative forced-choice recognition procedure with self-pacing, participants were then required to point to the scene that was originally presented. Each score was based on the total correct out of 30.

Virtual Pond Maze (VPM):

Participants started from one of six locations around the virtual pond, surrounded by six houses and six trees, all evenly spaced such that each starting location provided a unique set of spatial landmarks (see **Figure 1**, right panel). Using only the left and right cursor arrows, participants were required to navigate to a fixed platform slightly offset from the middle of the pond, with the forward speed set by the computer at a simulated 7 m/s. The location and size of the platform was set such that participants had to make at least one cursor correction to reach the platform from each of the starting points. A cutoff value of 60 s was imposed to end the trial, which many participants reached, especially from the more remote starting points.

After approximately 20 min of instructions and practice, participants were tested on 18 trials, consisting of one platform-visible trial followed by two platform-nonvisible trials, in which spatial memory was required to reach the platform. The performance measures were the time taken to reach the platform, the virtual distance travelled, and the number of corrections made. Only the time to reach the platform was included in the final analysis, since the number of corrections partly involved strategy and the virtual distance almost perfectly correlated with, and was therefore redundant to, the time to reach the platform. Also, participants reached the platform rapidly and with little variation in the visible trials (a "ceiling effect"), presumably because forward speed was set by the computer; thus, only data from the nonvisible trials were used to assess navigational memory.

Topographical Mental Rotation Test (TMRT):

Participants viewed a scene containing a set of three objects (e.g., red cylinder, blue sphere, green cube) and were then shown a figure instructing them to rotate their viewpoint 90° left, 90° right, or 180° opposite (see Figure 1, left panel). They were then shown three scenes from each of the rotated viewpoints and asked to click on the image that depicted the correct viewpoint shift. A yellow box indicated the participant's choice while a green box (appearing only during practice trials) showed the correct viewpoint. Participants had 12 s to view each scene and 14 s to make their response, with a timer appearing during the last 5 s of the forced-choice interval. After being presented with instructions, which included demonstrations of the task using actual objects, participants viewed a set of 12 practice trials (they could view a second set if they chose to) and then were presented with 15 test trials. Each score was based on the total number of correct responses out of 15.

Montreal Cognitive Assessment (MoCA):

The MoCA consists of 30 points derived from a set of 12 tasks, including a miniature version of the trail-making task (1 pt), a Necker cube copy (1 pt), clock drawing (3 pts), naming (3 pts), delayed recall (5 pts), forward and reverse digit span (2 pts), go/no-go attention (1 pt), serial-seven subtraction (3 pts), sentence repetition (2), verbal fluency (1 pt), verbal analogous reasoning (2 pts), and general orientation (6 pts) (see www.mocatest.org) Testing on the MoCA required about 10 min [29].

Trail-Making Test Part B (TMT-B):

The TMT consists of two tasks: Part A, which presents a connect-the-dots sequencing and visual scanning task for numbers only; and Part B, which requires alternate sequencing of numbers and letters. Each task is preceded by a sample that provides for training and practice. The dependent variable was time to completion, with timing beginning immediately after the participant began to move the pencil. Errors were corrected immediately by returning the participant to the last correct point in the sequence, in accordance with standardized administration procedures. Only time to completion for Part B was included in the final analysis.

Visual Short-Term Memory Test (VSMT):

This task was designed as a non-topographical comparison to the TMRT. The stimuli and grid were identical to the TMRT task shown in Figure 1, except that four objects were presented rather than three. However, the task differed in that the viewing perspective and spatial locations of the objects never changed during the testing phase; rather, the three test stimuli consisted of the original scene and two scenes in which one of the four objects in the original scene changed its shape or color (but not both). In the two discrepant scenes, the same object could change in different ways (e.g., a red sphere could become a red cube in one scene or a blue sphere in
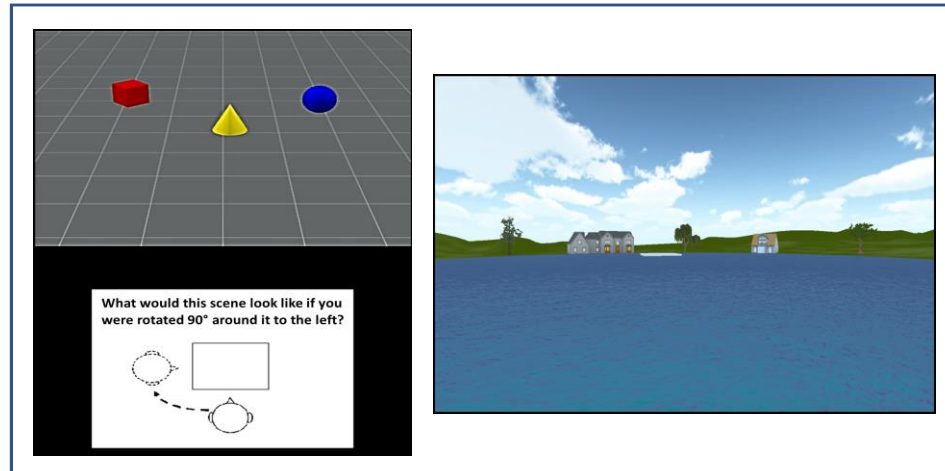
Figure 1: An illustration of the stimuli used in the TMRT task (left) and pond maze (right).

the other) or different objects could change in the same (both color changes) or different ways (e.g., a blue sphere could change to a green sphere in one scene while a yellow cone could turn into a yellow cube in the other). Participants had 9 s to view each scene and 12 s to make their response, with a timer appearing during the last five seconds of the forced-choice interval. As in the TMRT, participants were required to click on the original image during the recognition period, which caused a yellow box to appear over their selection while a green box surrounded the correct response (green box appeared only during practice trials). After being presented with instructions, participants viewed a set of 12 practice trials (they could view a second set if they chose to) and then were presented with 15 test trials. Each score was based on the total number of correct responses out of 15.

Analysis

A total of six variables were analyzed in this study: CTRMT (# correct), TMRT (# correct), VPM (time to completion), MoCA (# correct), TMT-B (time to completion), and VSTMT (# correct). SPSS (IBM, Chicago, IL) was used to perform an exploratory factor analysis on the data using a varimax rotation and Kaiser Normalization. Because higher scores (times) on the VPM and TMT-B reflected poorer performance whereas higher scores on the other four tests reflected better performance, time to completion scores on the VPM were subtracted from the cutoff time of 60 s whereas times on the TMT-B were subtracted from the maximum time in the study (164 s). Longer times on the VPM and TMT-B now reflected better performance, without otherwise transforming the data; hence, the correlation between the actual and inverted times was -1.0 for both measures.

A "composite" topographic measure was created by turning the three raw topographic scores for each participant into percentiles, based on established norms (in the case of the CTRMT) or the present study's means and standard deviations (for the VPM and TMRT scores), and then averaging all three together.

Results

The sample consisted of 16 females and nine males, with an average age of 76.4 years. Nine of the 25 participants were Hispanic, 12 were non-Hispanic Caucasians, three were Asian-Americans, and one self-described as "other". In terms of education level, seven had high-school degrees, six had college degrees, and 12 had graduate degrees.

The means and standard deviations for the six cognitive measures are shown in (**Table 1**). The complete correlation matrix containing all 21 bivariate correlations is shown in (**Table 2**), while the results of the exploratory factor analysis are shown in (**Table 3**).

Variable	M	SD
CTRMT	24.04	4.23
TMRT	9.52	3.74
VPM	34.2	11
MoCA	24.88	2.42
TMT-B	86.44	28.99
VSMT	9.08	2.18

Table 1: Means and Standard Deviations for the Topographical and Non-topographical Measures.

	CTRMT	VPM	TMRT	MoCA	TMT-B	VSMT	Topo COMP
CTRMT	-	0.33	0.32	0.22	0.32	0.05	0.73
VPM		-	0.29	0.22	0.22	-0.06	0.78
TMRT			-	0.19	.48*	-0.08	0.69
MoCA				-	0.26	0.08	0.29
TMT-B						0.17	0.41
VSMT						-	-0.04
Topo COMP							-

Table 2: The Correlational Matrix for the Topographical and Non-topographical Measures.

On the tests in which number of correct was measured, mean performance ranged from slightly over 60% (TMRT and VSMT) to slightly over 80% (MoCA and CTRMT). The average score on the CTRMT, MoCA and TMT-B tests were similar to age-adjusted norms from previous studies [26, 30-31].

Many participants had trouble with the VPM, TMRT, and VSMT, either exceeding the cutoff time in the case of the VPM or scoring at chance levels or below on the TMRT and VSMT. The largest variability (as a percentage of the mean) occurred in the TMRT test, partly because of a large (>50%) gender difference, with males

averaging 12.44 correct and females averaging 7.8 correct. No other measure yielded a gender difference of more than 15%.

The bivariate correlation matrix is shown in Table 2. Because scores on all but one of the six measures violated normality according to the Shapiro-Wilk statistic, Spearman's rho was used to determine all correlations.

	Factor 1	Factor2
CTMRT	0.69	0.17
TMRT	0.71	-0.23
VPM	0.62	0.03
MoCA	0.55	0.35
TMT-B	0.7	-0.34
VSMT	-0.03	0.89

Table 3: Factor Loadings on Principal Components.

Only one correlation-that between the TMRT and TMT-B scores-proved significant, with the correlations among the three topographical measures ranging from 0.29 to 0.33. The correlations between each of the three topographic measures and the topographical composite score ranged from 0.69 to 0.78; these high correlations would be expected in that each of the topographic scores contributed a third to the composite score. The correlations between the topographical composite and the non-topographic scores were much more modest, the highest (0.41) being the TMT-B-composite one.

The results of the factor analysis revealed two principal components with eigenvalues greater than 1.0 that accounted for 54.6% of the variance (Factor 1=36.1%; Factor 2=18.5%). The loadings for each of the six variables on each factor are shown in Table 3. The three topographical variables loaded very highly on Factor 1 (0.69, 0.62. and 0.71, for the CTMRT, VPM, and TMRT measures, respectively) but loaded poorly on Factor 2 (0.17, 0.03, and -0.23, for those same variables). Hence, it may be concluded that Factor 1 is related to topographical abilities. The TMT-B also loaded highly on Factor 1 (0.70) and the MoCA moderately no ("0.55), while the VSMT loaded poorly (-0.03). Conversely, the three non-topographic measures loaded better than the topographic ones on Factor 2.

To illustrate further the dissociation between the topographical and non-topographical measures, MoCA scores for the four participants with the highest topographical composites (range=23-27, M=25.5) overlapped the MoCA scores for the four participants with the lowest topographical composites (range=19-27, M=23.25). In fact, the participants with the two lowest topographical composites (6th and 16th percentile) scored near- and above-average on the MoCA (23 and 27, respectively, relative to the sample mean of 24.88).

Discussion

The results of this preliminary study show dissociation between topographical and non-topographical measures of cognitive function. Despite some limitations of this study that will be addressed, this result could hold potentially important implications for future screening for mild cognitive impairment and early Alzheimer's dementia.

The two principal components derived from the factor analysis distinguished the topographical measures from the non-topographical measures. The topographical memory measures all loaded highly on the first factor (>.6) but poorly on the "non-topographical" factor (<.25). The reverse was true for the visual memory test, which loaded highly on the second factor (.89) but poorly on the "topographical" factor (-.03). The TMT-B also loaded very well on the "topographical" factor (.70) and the MoCA somewhat (.55), but they also loaded more strongly than the topographical measures on the second factor, which presumably involved non-topographical memory ability. The results of the factor analysis must be viewed with caution, however, given that the sample size was relatively small and none of the bivariate

correlations between the topographical measures proved statistically significant.

It is unclear why the bivariate correlations among the topographical memory measures were so modest, given their loadings on the "topographical" factor. Although the three topographical memory measures have been shown to tap into hippocampal function [9, 20-22, 24-25], it is likely that they represent slightly different cognitive processes. It has previously been shown that topographical memory and active navigation are not always well correlated [10]. Moreover, the gender bias only in the TMRT suggests that it additionally reflects some of the same spatial rotational processes previously shown to be superior in males [32], possibly involving the parietal-temporal portion of the topographical memory system. It may very well be the case that poor performance on a single topographical test is of less clinical significance than a global topographical impairment, as assessed by a composite topographical score.

The partial dissociation between the topographical and non-topographical measures in this study has potentially important implications for screening for Alzheimer's disease. Although widely used measures of dementia such as the MoCA and TMT-B may tap into topographical abilities and even hippocampal function in the latter case, they are also dependent on other brain areas such as the frontal lobes, which fail later in the time-course of Alzheimer's disease. [33,34]. The TMT-B requires cognitive shifting and other executive functions, while the MoCA is mostly composed of verbal and working-memory items. While the TMT-B can discriminate the mildly cognitively impaired from healthy controls [11,35], it may not be as sensitive as pure topographical measures in diagnosing the initial topographical deficit in Alzheimer's [11,15].

Of the topographical tests, the CTRMT may be the most advantageous in that it is standardized, normed, easy to administer, and achievable by all participants, in addition to loading highly on composite "topographical" factor measures. More studies with larger sample sizes are required to determine if current widely used cognitive measures are as effective as specific topographical ones in the earliest prediction of Alzheimer's.

Acknowledgements

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