

Title: The differential effect of normal and pathological aging on recent and remote egocentric and allocentric spatial information

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Acknowledgements

The first author was supported by the project “Epidemiology of Topographical Disorientation and Mild Cognitive Impairment in a South Italian elderly population” - Action Co-funded by Cohesion and Development Fund 2007–2013 - APQ Research Puglia Region “Regional programme supporting smart specialization and social and environmental sustainability – FutureInResearch” (Grant Code CEY4SQ4). The present study is part of the PhD program of the second author, under the supervision of the last author.

Conflict of Interest

The authors declare that they have no conflict of interest.

Introduction

Topographical Disorientation (TD) is defined by the seminal work by Aguirre and D'Esposito [1] as a particular condition which determines the loss of spatial orientation and is characterized by the difficulty in acquiring spatial information in new and unknown environments, and in encompassing familiar environments such as one's neighborhoods or one's house. TD and spatial memory impairments occur relatively early as effect of cognitive decline in aging, and it is possible to observe transient episodes of TD, other than in people suffering from dementia, especially of Alzheimer's type [2], even in prodromal stages of dementia, defined as Mild Cognitive Impairment (MCI) [3]. Following Aguirre and D'Esposito taxonomy, TD is not a unitary concept, but it is possible to split it into four components: Egocentric Disorientation, Heading/Allocentric Disorientation, Landmark Agnosia, and Anterograde Disorientation.

As pointed out by a recent review [4], it is noteworthy that egocentric and heading (allocentric) components refer to previously learned information, that is retrospective spatial memory traces, while anterograde disorientation component refers to all the learning processes in order to acquire new spatial memory traces. Most studies requested elderly people to deal with recently learned information, which has not yet had sufficient time to be consolidated and transferred to brain structures other than the hippocampus [5], and this may in part account for the difficulties in the use of egocentric and even more allocentric spatial information. Thus, there could be an overestimation bias when observing a decreased performance in both egocentric and allocentric tasks in elderly with a normal cognition compared to young or adult people.

Although most studies investigating egocentric and allocentric spatial memory employed tasks based on learning new information, the relevance of remote spatial information is supported by a limited but growing number of research. The seminal works by Evans and Pezdek [6] and Thorndyke and Hayes-Roth [7] introduced the concept of *familiarity* related to spatial information, showing that environments learned through direct and continuous experience and navigation were better represented and remembered than environments learned through indirect experience (i.e., map study). Behavioral and cognitive studies employing familiar information with young and old participants found similar results, reporting no significant age effect [8-14]. Also, neuroscience and neuroimaging studies have provided relevant support for the effect of familiarity in spatial memory [15, 16].

A recent contribution by Lopez and colleagues [10] investigated recent and well-consolidated spatial memory within the egocentric and allocentric frames of reference in young and healthy elderly people. Young and healthy elderly participants were tested on four spatial tasks requiring allocentric and egocentric judgments, based on recent and remote spatial information. Results

showed an age effect on both egocentric and allocentric tasks in recently learned spatial information. The age effect was not present in tasks regarding well consolidated spatial information. A gender effect favoring males was found in performance in allocentric tasks regarding both recent and well-consolidated memory.

All the studies cited so far dealt with familiarity in spatial memory traces in healthy elderly. Several studies investigated egocentric and allocentric spatial memory in people with MCI, using tasks based on new information to be learned, and all of them found a lower performance at least in allocentric spatial memory with respect to healthy elderly [17-25]. Moreover, very few studies included also people with Subjective Memory Complaints (SMC), and found that they showed a performance comparable to healthy elderly in tasks based on new information to be learned [e.g., 18]. The SMC is a condition in which individuals complain to have a memory impairment, but no clear impairment on objective psychometric memory test is detectable [26, 27]. The functional meaning of this condition is still debated, nonetheless it is considered as a subtle marker of a subsequent state of cognitive impairment [28, 29]. No studies, to our knowledge, addressed the topic of familiarity of spatial information in people with SMC and MCI.

The aim of the present study is twofold: the first is to show that components linked to familiar spatial knowledge (egocentric and allocentric disorientation) are relatively spared with respect to unfamiliar ones (anterograde amnesia) in normal aging, whilst they are not in prodromal stage of dementia, namely MCI. The second aim is to investigate gender differences for their impact on egocentric and allocentric frames of reference. An advantage of men on allocentric frame of reference is expected [10].

Methods and Materials

Participants

Forty healthy young and one-hundred-and-twenty elderly participants were recruited and took part in the study. All the participants were from the metropolitan area of Bari, Italy. Elderly participants were divided into three groups: forty healthy elderly (HE), forty elderly participants with subjective memory complaints (SMC), forty participants with probable MCI (MCI). Young participants (YC) were university students from introductory courses in psychology. Elderly participants were recruited from senior centers, third-age universities with a support of a proxy informant, generally undergraduate or graduate students, trainees, employers of the centers and also general practitioners. They were blinded to the hypothesis of the study and signed a consent form for participating. The Ethical Committee of the Institution approved the study protocol, and the whole study was performed following Helsinki Declaration and its later amendments.

Materials and Procedure

Neuropsychological tests

All the participants were consecutively enrolled between May 2017 and March 2018. Elderly participants were administered a) a general anamnesis, carried out by supervised trainees in psychogeriatric care assessment, in order to exclude people with a history of suspected uncompensated systemic/traumatic/psychiatric diseases, or with severe vision/hearing loss, which could have affected cognition, and b) a standardized neuropsychological battery, in order to establish a diagnosis of SMC or probable MCI, according to the MCI working group of the European Consortium on AD [30]. Global cognitive function was evaluated by the Montreal Cognitive Assessment (MoCA) [31]. A possible occurrence of functional decline, usually associated with a severe cognitive impairment and with dementia was evaluated by the Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL) [32]. The 15-item version of the Geriatric Depression Scale (GDS) [33] was administered in order to exclude major depressive symptoms. Subjective complaints regarding memory loss were evaluated by the Subjective Memory Complaints questionnaire (SMCq) [27]. Verbal episodic memory was evaluated by the Rey Auditory Verbal Learning Test [34], with both immediate and delayed recall. Executive function was evaluated by the Frontal assessment Battery (FAB) [35] and the Clock Drawing Test (CDT) [36]. Some thresholds of the sample size were reached early, such as healthy elderly females and males with probable MCI. Data of all potential participants, not fulfilling the requirements, were not recorded.

Spatial tests

All the participants were administered three spatial tests, two of them used to assess egocentric (Landmark Positioning along a Route, LPR) and allocentric (Landmark Positioning on a Map, LPM) spatial memory based on remote familiar information. Such tasks were described in details elsewhere [4, 10]. Briefly, in LPR task participants had to identify and pinpoint the correct position of eight well-known landmarks of their hometown on a path orally described by the research assistant (See Figure 1). The score consisted of a single measure over correct position and correct side, ranging from 0 to a maximum of 36 points. In LPM task participants had to identify and pinpoint the correct position of eight well-known landmarks of their hometown, different from those used in LPR task, on a blind map of the city, keeping in mind metric (i.e., relative distances) as well as categorical (“A is above/below and left/right of B”) spatial relationship between landmarks. The total score for the LPM task ranged from 0 to 56 points (See Figure 2).

The third test, namely the Ego-Allo Task (EAT) [37] was composed of two subtasks, and was used to assess egocentric and allocentric spatial memory based on recent and newly learned spatial information, in a table-top format. Participants were instructed to memorize the position and the characteristics of three 3-dimensional solids (shape and color). In the testing phase solids were presented on the table, in order to judge distances between them and the observer (egocentric judgment), or between the solids themselves (allocentric judgment). The maximum total score was 8 points for egocentric and 8 points for allocentric judgment, respectively.

The entire procedure was made clear to the participants beforehand. Participants were assessed individually in a well-lit and quiet room without disturbances. Data were collected in one session. The whole assessment lasted a maximum of 2 h. The order of the tasks was the same mentioned in the text. Breaks were allowed upon request.

Statistical analyses

Data were analyzed using R 3.5.1 statistical software. We obtained demographic data (gender, age and years of education) and scores on neuropsychological and spatial tests. A one-tailed value of $p < .05$ was determined to be statistically significant. Pearson's chi-squared analysis was performed to assess for differences in the distribution of gender among the four groups. A series of univariate analysis of variance (ANOVAs) were carried out to compare means from the three diagnostic groups for demographic continuous data, and scores on neuropsychological tests used to establish a diagnosis of SMC and probable MCI. A series of multivariate General Linear Models (GLMs) were performed in order to compare means on the spatial tests depending on group, gender and education scores. GLMs were replicated excluding the group of young participants in order to compare means on the spatial tests depending on three diagnostic groups of elderly participants, gender, age, education and depression scores. Pairwise comparisons were carried out on univariate results of each GLM for each outcome with Tukey's Honestly Significant Difference (HSD) post hoc tests. Effect size estimates were reported by calculating partial eta squared for each effect on continuous outcome and W for each effect regarding association between categorical variables.

Results

Table 1 reports socio-demographic characteristics of the participants, mean scores and standard deviations on the neuropsychological screening tests for the elderly groups, and statistical tests for their differences. The three elderly groups differed by age: HE were on average younger than MCI, while no differences were found among SMC and the two other groups. The four groups did not

show any difference by gender distribution, but differed by schooling years, with YC being on average more educated than HE, which in turn were more educated than SMC and MCI. The three groups of elderly participants showed significant differences on the neuropsychological screening tests. HE showed to be less depressed than SMC, but both groups did not show significant differences in level of depression with respect to MCI. The latter group had a MoCA score significantly lower than HE and SMC. No differences were found among the three groups on ADL and IADL. SMC showed a significant difference in SMCq score with respect to the other groups. MCI obtained significant lower scores in the RAVLT Immediate and Delayed recall, FAB, and CDT scores.

A multivariate general linear model (GLM) was performed in order to test for the hypothesis that group, gender and education years could have a significant impact on total score of the LPR task and on total score of the LPM task as outcome variables. Results showed a main effect of group (Wilks' Lambda=0.624, $p < .001$). Education years, gender and the interaction term gender x group were not significant. Follow-up univariate analyses were conducted, as appropriate, to test for main and interactions effects on univariate measures. No main nor interaction effects emerged for group, gender and education years on total score the LPR task. A main effect of group was found on total score of the LPM task ($F(3,151)=28.57$, $p < .001$, $\eta^2_p=0.36$). Tukey's HSD post hoc analysis revealed that MCI had a lower performance in LPM task with respect to the other three groups, which did not show significant differences among them (see Figure 3).

A second multivariate GLM was performed with the same predictors on total score of the egocentric task and on total score of the allocentric task of the EAT as outcome variables. Results showed again a main effect of group (Wilks' Lambda=0.495, $p < .001$). Education years, gender and the interaction term gender x group were not significant. Regarding univariate analyses, a main effect of group emerged for egocentric task ($F(3,151)=34.71$, $p < .001$, $\eta^2_p=0.41$). Tukey's HSD post hoc revealed that MCI had a significant lower performance compared with that of HE and SMC, which in turn had a lower performance with respect to YC on the egocentric task (see Figure 5). For the allocentric task, a main effect of group ($F(3,151)=23.61$, $p < .001$, $\eta^2_p=0.32$), a main effect of gender ($F(1,151)=4.40$, $p < .05$, $\eta^2_p=0.03$) and an interaction effect group x gender ($F(3,151)=3.41$, $p < .05$, $\eta^2_p=0.06$) were found to be significant. Tukey's HSD post hoc revealed a similar pattern of results for the four groups on allocentric score, and a slight advantage for man with respect to women. Regarding the interaction effect group x gender, the extent of differences in allocentric score for men with respect to women with MCI was significantly larger than in the other three groups (see Figure 4).

The two previous GLMs were re-run without the group of YC, in order to include age and GDS scores as additional predictors, for which significant differences among the three elderly groups were found. Analyses yielded the same pattern of results for LPR (no significant effects of any predictor) and LPM (main effect of group $F(2,111)=28.07$, $p<.001$, $\eta^2_p=0.34$) tasks. Tukey's HSD post hoc found a significant lower performance for MCI with respect to both HE and SMC for LPM task. Regarding egocentric score of Ego-Allo task, again a main effect of group was significant ($F(2,111)=26.18$, $p<.001$, $\eta^2_p=0.32$), with MCI having a lower performance with respect to the other two groups of elderly. Regarding allocentric score of Ego-Allo task, a main effect of group ($F(2,111)=14.86$, $p<.001$, $\eta^2_p=0.21$) and a main effect of gender ($F(1,111)=7.21$, $p<.01$, $\eta^2_p=0.06$) were found to be significant. Again, MCI had a lower performance with respect to the other two groups of elderly, and men obtained higher scores than women. No interaction effects emerged.

Discussion

The present study aimed to give a further contribution to the investigation of recent and remote spatial memory in healthy young participants and elderly people with and without cognitive impairments.

The increase of age seemed to affect allocentric spatial representation of remote and familiar information only in presence of MCI. Egocentric spatial representation of familiar information seems to be spared, even in presence of MCI. This differential vulnerability across egocentric and allocentric representations of familiar environments was shown in previous studies and supported by neuropsychological evidences regarding the preserved egocentric component of spatial memory from neurodegenerative processes [38-40]. Thus, information consolidated across a huge number of retrieval episodes seems more solidly preserved in elderly people, and it is likely that the consolidation is preserved in areas other than the hippocampus [41-43]. Our results are consistent with aforementioned investigations on the effect of familiarity on spatial memory [4, 8-11], and substantiate the usefulness of familiar spatial tasks also in case of an initial cognitive impairment.

A progressive decrease in performance on both egocentric and allocentric tasks based on recent and unfamiliar spatial information emerged. It is worthwhile to note that in pathological aging, especially in the MCI condition, participants showed impairments in several spatial tasks, such as map drawing, landmark location, direction pointing, navigation in both real and virtual environments [e.g., 17, 40]. What is common among these studies is the manipulation of recent information. Our results are in line with those findings, indeed MCI participants showed a decline in the performance on both egocentric and allocentric tasks based on recent information.

To the best of our knowledge, this is the first study that uses ecological tasks in both normal and pathological aging. As shown in a previous research [10], the Multiple Trace Theory (MTT) [5] framework supports the idea that in normal aging old memories are less prone to disruption than recent memories because of their frequent reinstatement of traces. When information is well-established in memory, egocentric representation seems to be fairly accessible for the elderly, even with a probable cognitive impairment. Allocentric ones are compromised only in people with MCI. It is reasonable to support the idea that the magnitude of difference between egocentric and allocentric judgments in normal aging is somewhat attributable to the characteristic of spatial tasks, showing a continuum for tasks based on well-consolidated information. Overall, well-consolidated information seemed to be better preserved in memory and less prone to the impairment with respect to newly learned ones in healthy elderly and in elderly with SMC with respect to elderly with MCI. Regarding SMC participants, we supposed that they are aware of their memory failures, although not recognizable by objective neuropsychological tests. This condition does not require objective sign of cognitive impairment [28], so the results shall be considered plausible also in the light of the MTT Theory

A more recent theoretical framework, the Default – Executive Coupling Hypothesis of Aging (DECHA) [44] suggest that autobiographical memory becomes increasingly semanticized over the adult lifespan, and the engagement of such representations is associated with preserved cortical thickness in lateral and anterior temporal lobe regions. Elderly people may then still rely to crystalized cognition in order to efficiently solve goal-directed thoughts or actions.

An overall gender difference was found for elderly participants, favoring men on allocentric unfamiliar task. The extent of such difference was greater for MCI than for the other two elderly groups. This result partially confirmed those of previous studies, which found an advantage of elderly men on allocentric familiar and unfamiliar tasks [10]. Nori and colleagues [45] reported similar results on young participants, showing that gender differences disappeared when women had the necessary time to acquire spatial information, and that retrieving environmental information through the use of allocentric coordinates was more difficult than the use of egocentric ones. Also another previous study reported a greater accuracy and speed of men than women in a buildings' location task [46], and this difference was particularly evident in participants unfamiliar with the environment. It seems that familiarity may be relevant to dissolve gender differences in both young and elderly people, although more research is needed on this topic.

Familiarity of spatial memory traces can thus represent a protective factor for retrospective components of TD in normal aging. Conversely, using newly learned information for assessment

may lead to overestimating TD severity as it combines two contributing factors, namely heading (allocentric) disorientation and anterograde agnosia.

Limitations

The present study has some limitations, due to different features of familiar and unfamiliar tasks employed. The first one is due to a different modality in the acquisition of spatial information: in the case of remote information related to the hometown, it is possible to suppose that an unintentional learning process has happened throughout the entire life of the individual, while in the case of recent information, a form of intentional learning based on direct instruction has happened. This feature is difficult to be overcome, since we do not have control on spatial learning processes occurred during lifetime, and constitutes a somewhat insuperable limitation, due to the intrinsic nature of the concept of familiarity [4]. The second one is related to the format of the information: familiar tasks gather spatial information based on a direct navigation of the environment, whilst unfamiliar tasks rely on spatial information acquired through a table-top format. The third one is related to the format of response: hometown tasks rely on a non-verbal response, while unfamiliar tasks require a verbal response. Those weaknesses limit the possibility to draw a direct comparison between familiar and unfamiliar tasks. In order to remediate to the latter two limitations, it would be appropriate to build equivalent tasks for familiar and unfamiliar environments, in order to compare them directly.

Conclusion

The advantage of supplementing neuropsychological evaluation of spatial cognition with tasks based on familiar information is to avoid a penalty for healthy elderly, which may have an initial, but not pathological, decline in working memory as well as in learning abilities. Proposing tools which rely on remote spatial knowledge may help the clinician to conduct a fair evaluation of spatial abilities closely linked to a functional activity of daily living, i.e., the ability to navigate the environment and to travel from one place to another in one's own hometown or neighborhood. Further research should investigate the role of familiarity with spatial information in elderly people with different types of cognitive impairment, i.e., elderly with amnesic and non-amnesic as well as with single and multiple domain MCI, and persons suffering from Alzheimer Disease.

Compliance with Ethical Standards

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

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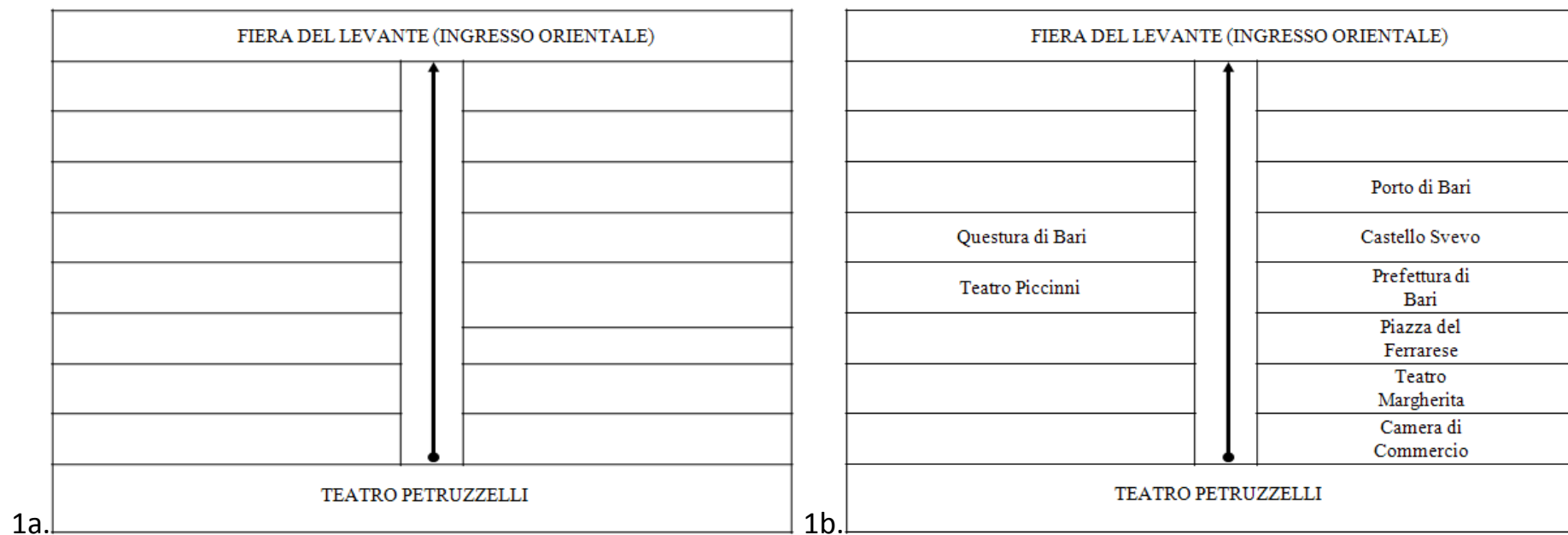


Figure 1. Landmark positioning on a route (LPR) for the City of Bari: a) sheet for participants, using two landmarks as starting and end points; b) sheet for scoring showing the route with the expected landmark positions and sides.

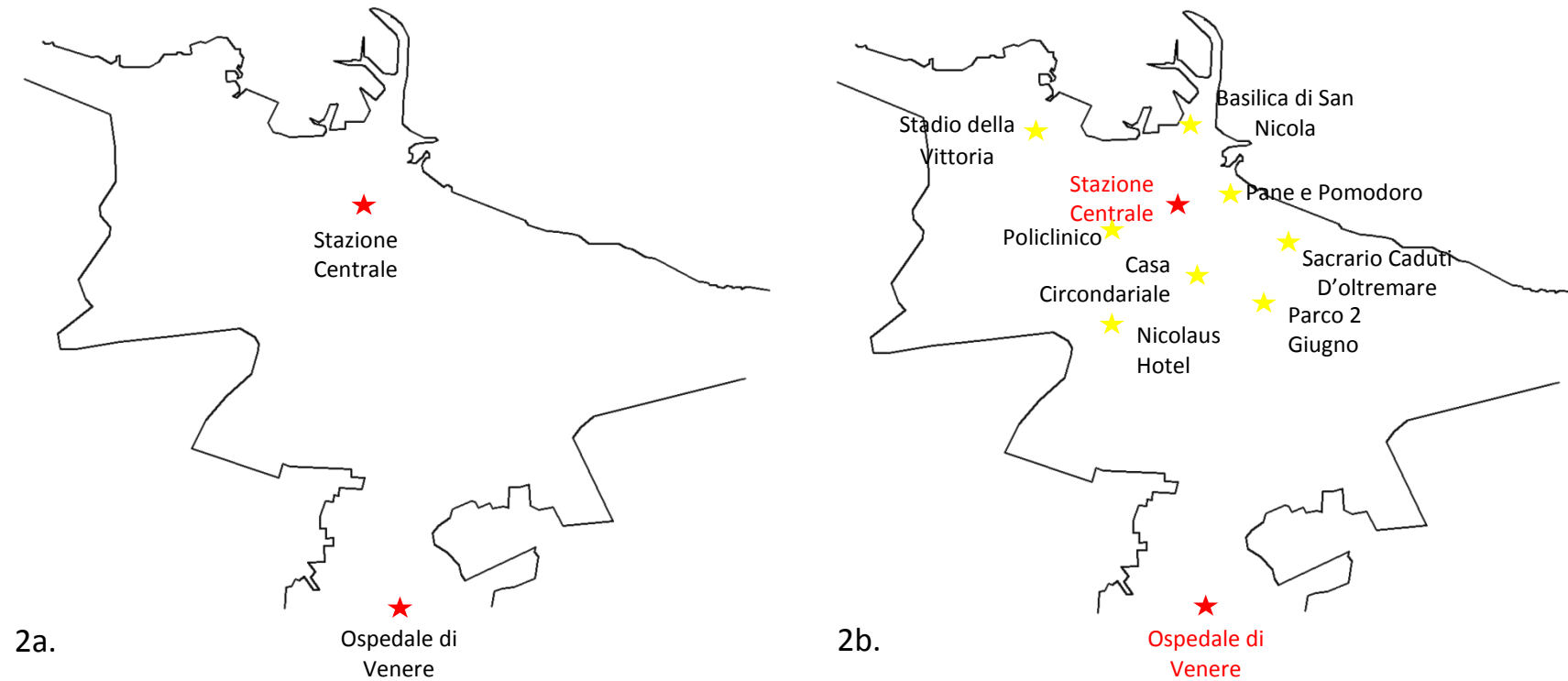


Figure 2. Landmark positioning on a map (LPM) for the City of Bari: a) sheet for participants, using two landmarks as fixed reference points, b) sheet for scoring showing the map with the expected landmark positions.

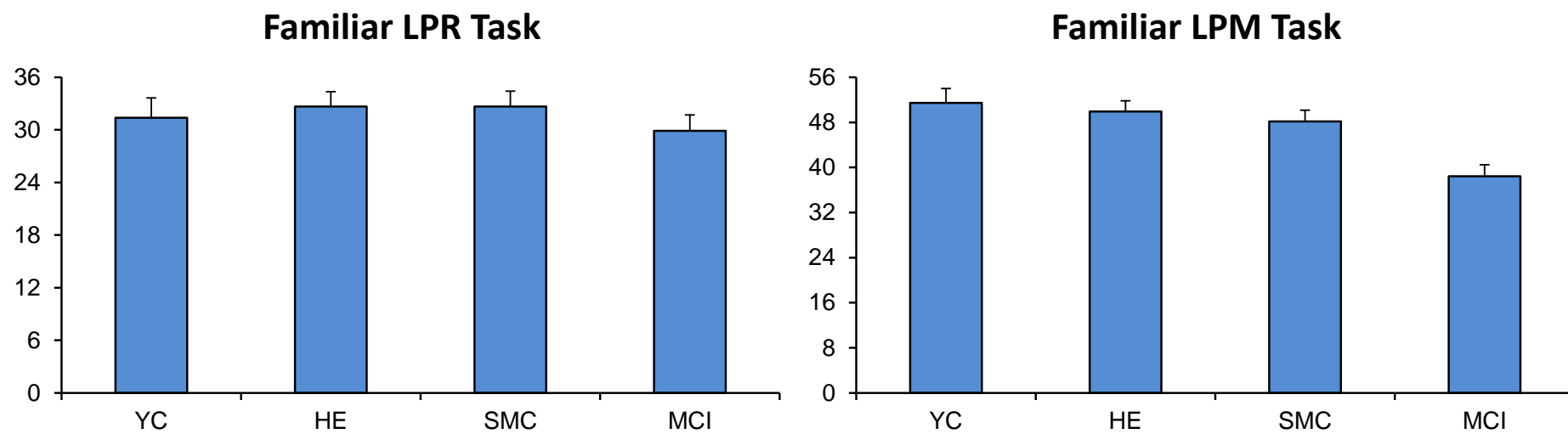


Figure 3. Means and standard errors in bars for the total score of LPR task (left panel) and of LPM task (right panel) for each group.

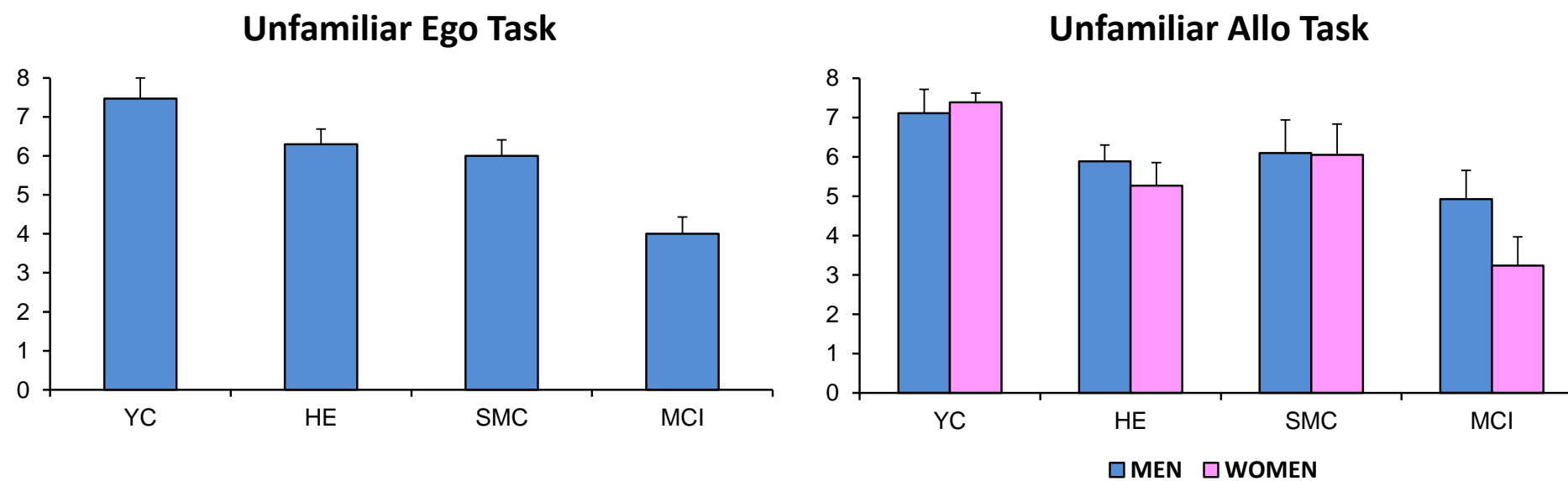


Figure 4. Means and standard errors in bars for the egocentric score of Ego-Allo Task (left panel) for each group, and for the allocentric score of Ego-Allo Task (right panel) for each group and for men and women.

Table 1. Socio-demographic characteristics of the participants, mean scores and standard deviations on the neuropsychological screening tests for the elderly groups, and statistical tests for their differences.

	YC (N=40)	HE (N=40)	SMC (N=40)	MCI (N=40)	F or χ^2	df	p	ηp^2 or W	Post hoc (Tukey HSD)
Age	21.45 ± 2.11	71.30 ± 5.95	73.53 ± 6.55	75.88 ± 6.66	859.24	3, 156	<.001	.94	YC < HE = SMC; YC < MCI; HE < MCI; SMC = MCI
Gender (F/M)	31/9	22/18	20/20	25/15	7.27	3	.06	.21	YC = HE = SMC = MCI
Education years	15.45 ± 1.47	11.33 ± 4.96	8.48 ± 4.75	8.20 ± 3.26	30.28	3, 156	<.001	.37	YC > HE > SMC = MCI
GDS	-	2.08 ± 2.36	3.83 ± 3.15	3.55 ± 3.08	4.26	2, 117	<.05	.07	HE < SMC; SMC = MCI; HE = MCI
MoCA	-	24.40 ± 2.85	23.83 ± 3.17	15.90 ± 0.84	143.29	2, 117	<.001	.71	HE = SMC > MCI
ADL	-	5.98 ± 0.16	5.80 ± 0.56	5.78 ± 0.62	2.27	2, 117	.11	.04	HE = SMC = MCI
IADL	-	7.60 ± 0.71	7.40 ± 0.90	7.33 ± 1.02	1.03	2, 117	.36	.02	HE = SMC = MCI
SMCq	-	2.10 ± 1.63	8.13 ± 1.24	2.30 ± 2.02	170.02	2, 117	<.001	.74	SMC > HE = MCI
RAVLT Immediate Recall	-	39.17 ± 10.48	36.66 ± 10.43	31.70 ± 7.86	6.20	2, 117	<.01	.10	HE = SMC > MCI
RAVLT Delayed Recall	-	8.71 ± 2.76	8.16 ± 3.67	6.08 ± 2.69	8.18	2, 117	<.001	.12	HE = SMC > MCI
FAB	-	15.76 ± 1.75	14.95 ± 1.91	11.32 ± 2.70	48.06	2, 117	<.001	.45	HE = SMC > MCI
CDT	-	9.05 ± 0.99	8.60 ± 1.11	7.03 ± 1.14	38.77	2, 117	<.001	.40	HE = SMC > MCI

Abbreviations: YC, Young Controls; HE, Healthy Elderly; SMC, participants with Subjective Memory Complaints; MCI, participants with probable Mild Cognitive Impairment; GDS, Geriatric Depression Scale; MoCA, Montreal Cognitive Assessment; ADL, Activities of Daily Living; IADL, Instrumental Activities of Daily Living; SMCq, Subjective Memory Complaints questionnaire; RAVLT, Rey Auditory Verbal Learning Test; FAB, Frontal Assessment Battery; CDT, Clock Drawing Test.