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Refining memory assessment of elderly people with cognitive impairment

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4 **Refining memory assessment of elderly people with cognitive**
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7 **impairment: insights from the short-term memory binding test**
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11 Mario A Parra¹⁻⁴, Clara Calia⁵, Ana Frank García⁶, Javier Olazarán-Rodríguez⁷, Juan Antonio
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13 Hernandez-Tamames⁸, Juan Alvarez-Linera⁹, Sergio Della Sala⁴, and Sara Fernandez Guinea¹⁰
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19 *¹School of Psychological Sciences and Health, Department of Psychology, University of*
20
21 *Strathclyde, Glasgow, UK.*
22
23

24 *²Universidad Autónoma del Caribe, Barranquilla, Colombia.*
25
26

27 *³Alzheimer Scotland Dementia Research Centre and Neuroprogressive and Dementia Network,*
28
29 *UK.*
30

31 *⁴Human Cognitive Neuroscience and Centre for Cognitive Ageing and Cognitive Epidemiology,*
32
33 *Department of Psychology, University of Edinburgh, UK.*
34
35

36 *⁵School of Health in Social Science, University of Edinburgh. UK*
37
38

39 *⁶Neurology Department, University Hospital la Paz, Madrid, Spain.*
40

41 *⁷Neurology Department, University Hospital Gregorio Marañón, Madrid, Spain.*
42
43

44 *⁸Magnetic Resonance Physics Group. Radiology and Nuclear Medicine Department, Erasmus*
45
46 *MC, Rotterdam, The Netherlands.*
47

48 *⁹Neuroradiology Department. Hospital Ruber Internacional, Madrid, Spain*
49
50

51 *¹⁰ Department of Basic Psychology II (Cognitive Processes), Faculty of Psychology,*
52
53 *Complutense University of Madrid, Spain.*
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4 **Corresponding author:** Dr Mario A Parra, School of Psychological Sciences and Health,
5
6 Department of Psychology, University of Strathclyde, Graham Hills Building, 40 George Street,
7
8 Glasgow, G1 1QE. mario.parra-rodriquez@strath.ac.uk
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11 **Short Title:** Visual Short-Term Memory Binding in Prodromal AD
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14 15 16 **Abstract** 17

18
19 Alzheimer's disease (AD) affects temporary memory for bound features more remarkably than
20
21 for individual features. Such selective impairments manifest from presymptomatic through
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23 dementia stages via titration procedures. A recent study suggested that without titration and with
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25 high memory load the binding selectivity may disappear in people at risk of AD such as those
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27 with Mild Cognitive Impairment (MCI). We compared data from two studies on temporary
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29 binding which assessed people with MCI and controls using different memory loads (2 or 3
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31 items). Selective binding impairments were found in MCI, but relative to controls, such
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33 selectivity was contingent upon memory load (i.e., present with 2 items). Further analysis with
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35 MCI people who tested positive to neuroimaging biomarkers (i.e., hippocampal atrophy)
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37 confirmed that this specific binding impairments are a feature of prodromal AD. The temporary
38
39 binding task has been recently suggested by consensus papers as a potential screening tool for
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41 AD. The results presented here inform on task properties that can maximise the reliability of this
42
43 new assessment tool for the detection of memory impairments in prodromal cases of AD.
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53 **Keywords:** Short-term memory binding; Mild Cognitive Impairment; prodromal Alzheimer's
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55 disease; Neuropsychological assessment; Early detection
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Introduction

Memory assessment in individuals at risk of Alzheimer’s disease (AD), such as those with Mild Cognitive Impairment (MCI), has long focused on episodic memory functions (Fields, Ferman, Boeve, & Smith, 2011; Parra, Abrahams, Logie, Mendez, et al., 2010; Parra et al., 2011). Examples are Paired Associates Learning (PAL) tasks (Sahakian et al., 1988), the Face Name Associative Memory Exam (FNAME) (Amariglio et al., 2012; Rentz et al., 2013), the Free and Cued Selective Reminding test (FCSRT) (E. Barbeau et al., 2004; Buschke, 2014; Grober, Buschke, Crystal, Bang, & Dresner, 1988; Sarazin et al., 2007), and other episodic memory tests (Ivanoiu et al., 2005). These tests are known to assess functions of the hippocampus which are essential to episodic memory formation i.e., associative memory (Tulving, 2002). Tests assessing associative memory functions of the hippocampus are considered markers for AD (Auriacombe et al., 2010; E. J. Barbeau et al., 2008; Dubois et al., 2010; Rentz et al., 2013; Sarazin et al., 2007). To uphold the claim that the associative function is that selectively impaired in AD, it is necessary to demonstrate that such impairments are greater than those found when patients remember the individual items. For instance, memory for faces (Sperling et al., 2003), lists of words (Gallo, Sullivan, Daffner, Schacter, & Budson, 2004), or locations (Stehli, Chubb, & Jacob, 2003), are functions affected by AD. This makes it difficult to ascertain that holding associations between these items in memory (e.g., faces and locations, faces and names) is the hallmark of AD. This is important because item memory and associative memory dissociate (Chalfonte, Verfaellie, Johnson, & Reiss, 1996; Old & Naveh-Benjamin, 2008) and the form of representation claimed to be specifically affected by the hippocampal amnesia of AD is the

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4 latter. This caveat i.e., limited underlying constructs, has been recently highlighted by a recent
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6 consensus paper (Costa et al., 2017).
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10 The Visual Short-Term Memory Binding Test (VSTMBT) was developed to investigate if the
11 function responsible for binding features within object representations is affected by AD above
12 and beyond that supporting single feature processing (Parra, Abrahams, Logie, & Della Sala,
13 2010). The test assesses participants' memory for single features such as shapes and for
14 combination of features such as shape-colour bindings. When memory load is controlled for (i.e.,
15 via titration to keep patients' and controls' memory performance for individual features at the
16 same level), patients with AD show memory binding deficits which are far greater than those
17 found when memory for single features is assessed (S. Della Sala, Parra, Fabi, Luzzi, &
18 Abrahams, 2012; Parra et al., 2009; Parra, Abrahams, Logie, & Della Sala, 2010; Parra,
19 Abrahams, Logie, Mendez, et al., 2010; Parra et al., 2011). Such specific increase of the cost of
20 binding has been observed since the preclinical stages of AD. This fits well current trends in the
21 assessment of AD which have shifted towards a new lexicon (Costa et al., 2017; Dubois et al.,
22 2010; Dubois et al., 2016) that encourages the detection of subtle cognitive impairments in stages
23 prior to dementia. The VSTMBT detects such early impairments, even when other novel and
24 traditional tests have failed (Parra, Abrahams, Logie, Mendez, et al., 2010; Parra et al., 2011).
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46 The results from a recent study (Koppara et al., 2015) suggest that memory load may be a factor
47 precluding the specificity of the VSTMBT (i.e., greater cost of binding in patients than in
48 controls). Previous studies have manipulated memory load by presenting patients and controls
49 with a different number of to-be-remembered items (Sergio Della Sala, Data, Stamate, & Parra,
50 2017; S. Della Sala et al., 2012; Parra et al., 2009; Parra, Abrahams, Logie, & Della Sala, 2010;
51 Parra, Abrahams, Logie, Mendez, et al., 2010; Parra et al., 2011). Such manipulation rested on
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4 the assumption that VSTM stores a limited number of items (Luck & Vogel, 1997; Vogel,
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6 Woodman, & Luck, 2001) and that increasing the number of items above such a limit (i.e., 4)
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8 would overload memory, rendering the task more challenging and performance poorer. Titration
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10 aimed at reducing differences at baseline (i.e., memory for single features). This led to
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12 suggesting that patients with AD present with a selective deficit of VSTMB. (Koppara et al.,
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14 2015) showed that without titration (i.e., patients and controls tested with the same visual arrays
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16 of 3 items), the selectivity of the VSTMBT holds for people with Subjective Cognitive Deficits
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18 (SCD) but not for people with MCI. Considering that memory binding is maintained to be
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20 selectively impaired in AD and that MCI is an uncertain clinical category which holds limited
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22 value to predict future risk of dementia, it is important to demonstrate the precise testing
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24 conditions with which selective impairments of VSTMB can be found. Is the specific impaired
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26 ability to binding features in VSTM that has been considered a hallmark of AD. Hence,
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28 identifying such a hallmark in MCI people might provide more reliable evidence of AD
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30 pathology as the likely underlying mechanism. To address these outstanding issues, in the
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32 present paper we present data from groups of healthy older adults and people with MCI who
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34 were assessed with the VSTMBT using arrays of 2 and 3 items and without titration. If the
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36 above-mentioned selectivity is contingent upon memory load, it would be observed only under
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38 the low memory load condition (i.e., 2 items).
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51 **Methods**

52 **Participants**

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54 Participants came from two separate samples of people with MCI and matched controls assessed
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56 with different versions of the VSTMBT. One sample was tested with a version of the task
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4 presenting 2 items, the other sample was assessed with a version presenting 3 items. Table 1
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6 shows the demographic, clinical and neuropsychological variables of the participants tested with
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8 the two set sizes. All participants underwent neuropsychological assessment. People with MCI
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10 met criteria proposed by (Petersen, 2004). Participants were fully informed about the study and
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12 they signed an Informed Consent Form prior to participation. The study was approved by Ethics
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14 Committees from the Psychology Faculty, Complutense University of Madrid, Clinical
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16 University Hospital San Carlos from Madrid, and the University Hospital Gregorio Marañón also
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18
19 from Madrid.
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26 **The Visual Short-Term Memory Binding Test (VSTMBT)**

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28 The VSTMBT required participants to remember visual arrays in which two or three black
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30 shapes (Shape Only condition) or coloured shapes (Shape-Colour Binding Condition) were
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32 presented for 2 seconds (Figure 1A). After a brief delay (1 second), a test display appeared
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34 showing the same or different items all presented in new random locations. The task was to
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36 indicate verbally whether the study and test display showed the same (50% of the trials) or
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38 different items. Different trials in the Shape Only condition presented two new shapes at test.
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40 Different trials in the Shape-Colour Binding condition presented two re-arranged combinations
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42 of shape and colour (i.e., two shapes swapped their colours at test). Normal perception of shape-
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44 colour bindings was ensued prior to the VSTMBT. Each condition presented 32 trials in random
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46 order. Conditions were counterbalanced across participants. We calculated proportion of correct
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48 recognition (see (Parra, Abrahams, Logie, & Della Sala, 2010), for a detailed description of the
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50 task). The above described VSTMBT has been used extensively in experimental studies
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52 involving different populations with AD dementia or at risk of such dementia. More clinically
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4 friendly versions of the task (i.e., shorter version on PC or flashcard versions; see (Della Sala, et
5 al., 2017)) have been recently developed and validated. Using these clinical versions of the test,
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7 patients with AD dementia and controls were discriminated via ROC analyses with 100%
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9 sensitivity and specificity. These versions of the test are available for use on request (contact
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11 corresponding author).
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19 **Analysis**

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22 A mixed ANOVA model was used with Group (Controls Set Size 2 vs. people with MCI Set
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24 Size 2 vs. Controls Set Size 3 vs. people with MCI Set Size 3) as the between-subjects factor and
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26 Condition (Shape Only vs. Shape-Colour Binding) as the within-subjects factor. We calculated
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28 effect size and power for main effects and interactions.
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35 **Results**

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38 The groups were matched on age, education, and depression scores. People with MCI showed a
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40 profile compatible with the multi-domain amnesic stage. The two groups of people with MCI
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42 showed a very similar profile of cognitive impairments. Control groups from the two samples did
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44 not differ in any of the neuropsychological scores (see Table 1).
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55 Insert Table 1 about here
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8 The ANOVA model revealed a main effect of Group [$F(3,100)=24.9$, $p<0.001$, $\eta^2=0.43$; $\beta=1.0$],
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10 main effect of Condition [$F(1,100)=187.14$, $p<0.001$, $\eta^2=0.65$; $\beta=1.0$], and a significant Group x
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12 Condition Interaction [$F(3,100)=6.93$, $p<0.001$, $\eta^2=0.17$; $\beta=0.97$] (Figure 2). To unfold this
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14 interaction we ran two separate Group x Condition ANOVAs for each Set Size. For Set Size 3
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16 the interaction was non-significant [$F(1,50)=2.91$, $p=0.094$, $\eta^2=0.05$; $\beta=0.39$], because of a large
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18 drop in binding performance in controls. For Set Size 2 it was significant [$F(1,50)=14.86$,
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20 $p<0.001$, $\eta^2=0.23$; $\beta=0.79$]. Post-hoc analysis (Table 1) revealed that MCI people's performance
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22 on the Shape-Colour Binding condition was disproportionally lower than that on the Shape Only
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24 condition, a discrepancy not observed in controls. Although these results are appealing, they may
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26 still face limitations for diagnosis purposes as having MCI and VSTMB deficits may not
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28 unequivocally inform about the presence of prodromal AD. We ran further analyses using
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30 neuroimaging data to investigate if such a pattern of selective impairment holds for those who
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32 are considered biomarker positive (Dubois et al., 2010; Dubois et al., 2016).
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44 **Additional Analysis**

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47 A subsample of 17 people with MCI who were assessed with set size 2 underwent MRI scans.
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49 The volume of their hippocampus was measured and corrected for their intracranial volume.
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51 Individual hippocampal atrophy was assessed using voxel-based morphometry, as described in
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53 (Olazaran et al., 2013). Hippocampal volume measurements were calculated using the freely
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55 available software FreeSurfer (<http://surfer.nmr.mgh.harvard.edu/>). We used automatic
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57 subcortical segmentation based upon the existence of an atlas containing probabilistic
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4 information on the location of structures. We followed the procedures described by (Fischl et al.,
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7 2002). The accuracy of FreeSurfer results was then assessed visually for the different
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9 participants. The extracted volumes were corrected for the total Intra-cranial Volume (ICV). The
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11 cut-off to identify pathological atrophy was set at -1SD from controls (see Supplementary Figure
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13 1; see also (Jack et al., 1997)). According to these data, 10 participants with MCI show
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15 hippocampal atrophy (MTA) (see Supplementary Figure 1). We ran additional analyses with the
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17 VSTMB data collected from this subsample of MCI+MTA using the model described above.
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19 These analyses revealed that 12 people with MCI showed binding deficits that did not overlap
20
21 with healthy controls' score, (Figure 1C). Among these MCI patients were those considered
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23 MCI+MTA (n=10). When the ANOVA model was rerun entering solely the data from
24
25 MCI+MTA, the interaction described above was replicated (Figure 1D). The pattern shows the
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27 selectivity of binding deficits previously reported in AD samples (Group x Condition Interaction:
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29 $F(1,33)=13.07, p=0.001, \eta^2=0.28; \beta=0.94$).
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Insert Figure 1 about here

Discussion

The present study was carried out to investigate whether and under what condition people with MCI present with the typical pattern of VSTMB impairments consistently found in patients with AD dementia. We were driven by the need of providing evidence of the task's psychometric

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4 features that can be clinically friendly as within these setting, procedures such as titration of task
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6 difficulty are unfeasible. We also sought evidence of whether VSTMB deficits in MCI are
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8 observed in those people who meet criteria for prodromal AD (i.e., significant atrophy of the
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10 hippocampus as documented by imaging biomarkers). Below we discuss the main implications
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12 of our findings.
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15 16 17 ***Why dissecting memory binding impairments is important?*** 18

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20 There are memory functions the decline of which could be detected prior to the dementia stage of
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22 AD (e.g., temporary binding abilities). These memory functions have proved both sensitive and
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24 specific to AD (Cecchini et al., 2017; S. Della Sala et al., 2012; Parra, Abrahams, Logie, & Della
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26 Sala, 2010). To ascertain whether they are selectively impaired, we need to refine the assessment
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28 procedures (R. H. Logie, Parra, & Della Sala, 2015). Such developments may enable us to map
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30 cognitively the continuum of AD. For instance, asymptomatic carriers of the mutation E280A-
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32 PSEN1 leading to familial AD (Parra, Abrahams, Logie, Mendez, et al., 2010) and patients with
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34 SCD (Koppara et al., 2015) tested under high memory load (3 items) showed selective memory
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36 binding impairments contrasting with a normal neuropsychological background. Without
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38 titration and with high memory load, (Koppara et al., 2015) reported that such selectivity
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40 disappeared in MCI samples. However, when memory load is low, the selectivity of binding is
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42 restored in these MCI people and mirrors that found in patients with AD dementia (Sergio Della
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44 Sala et al., 2017). Here we show, for the first time, that MCI people with evidence of
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46 hippocampal atrophy (MCI+MTA) show significant binding deficits when tested under low
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48 memory load condition. Interestingly, a subgroup of controls (n=7) showed performance below a
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50 recently reported cut-off (Sergio Della Sala et al., 2017) despite an intact neuropsychological
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52 background.
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4 A potential account for these findings could be that under high working memory load (n=3) the
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6 reliance on Medial Temporal Lobe structures such as the hippocampus increases (Doherty &
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8 Logie, 2016; Unsworth, Brewer, & Spillers, 2013), thus rendering the paradigm less specific
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10 (i.e., performance on both conditions will drop). Recent single case studies of neurological
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12 patients with hippocampal damage (Baddeley, Allen, & Vargha-Khadem, 2010; Jonin et al.,
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14 2018; Parra et al., 2015) confirmed that these patients present with preserved STMB even when
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16 memory load was higher (3 and 4) than that used with the MCI sample that underwent MRI
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18 scans (n=2). However, in all cases memory load was below or within the reported capacity of
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20 working/short-term memory (n=4; (Cowan, 2010)). Future studies with larger samples should
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22 investigate if supraspan stimulation engages hippocampal functions and if so, whether such
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24 involvement reduces the specificity of the STMBT to dissect binding deficits in samples at risk
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26 of AD.
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37 Our results suggest that titration might not be necessary if the task demands are adjusted to and
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39 interpreted in line with the different stages of the disease. For example, strategies aimed at
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41 screening individuals at risk of AD (e.g., asymptomatic mutation carriers of APOE4 genotype or
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43 other mutations) in whom traditional memory tasks fail (Koppara et al., 2015; Parra, Abrahams,
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45 Logie, Mendez, et al., 2010), might capitalise on high memory load while those aimed at
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47 screening in more advanced prodromal stages (i.e., MCI) or at ascertaining the presence of AD,
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49 might focus on lower memory load (Sergio Della Sala et al., 2017; S. Della Sala et al., 2012;
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51 Parra, Abrahams, Logie, & Della Sala, 2010). It is worth noting that reducing memory load to 2
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53 items does not undermine the need of binding (Parra, Della Sala, Logie, & Morcom, 2014).
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55 Hence, use of memory strategies, or lack thereof, should not be the factor explaining the
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4 selective binding deficits reported with this paradigm. There are other psychometric properties of
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6 the STMBT that grants reliability to this tool for the assessment of AD (R. H. Logie et al., 2015).
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9 STMB, as assessed by change detection paradigms, has proved to hold internal consistency (R.
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11 Logie, Brockmole, & Vandembroucke, 2009). This seems to be a feature of tasks relying on these
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13 paradigms (Pailian & Halberda, 2015; Xu, Adam, Fang, & Vogel, 2018). Moreover, the
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15 possibility to adjust the task's demands to the severity of the disease to avoid floor and ceiling
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17 effects while retaining construct validity, is another appealing psychometric property of this novel
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19 tool. This latter feature makes the task suitable for follow up assessments. However, future
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21 studies are still needed to confirm its test-retest and inter-rater reliability.
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27 There might be factors other than age and education (see (Koppara et al., 2015; Parra, Abrahams,
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29 Logie, & Della Sala, 2010)) which can lead to poor performance in healthy ageing populations.
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32 For instance, in this study, healthy older adults assessed with set size 3 showed a
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34 disproportionately large cost of binding compared to that reported in earlier studies (Fernández et
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36 al., 2018; Koppara et al., 2015; Parra, Abrahams, Logie, & Della Sala, 2010). To address this
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38 potential limitation a task that combines the two set sizes may be a more feasible approach.
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41 Alternatively, as recently suggested by (Sergio Della Sala et al., 2017), a version presenting
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43 binding as the only measure drawn from two set sizes could be administered easily and reliably
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45 in clinical settings. Older adults with poor VSTMB performance might be those in the very early
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47 preclinical stages of AD (see (Parra, Gazes, & Stern, 2017)).
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56 ***The construct of memory binding in the assessment of AD***
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4 A recent review paper summarises developments of neuropsychological approaches for the
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6 detection of preclinical AD (Rentz et al., 2013). For example, the FCSRT (Grober, Sanders, Hall,
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8 & Lipton, 2010), has shown promising results (E. Barbeau et al., 2004; E. J. Barbeau et al., 2008;
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10 Ivanoiu et al., 2005; Lemos et al., 2016; Sarazin et al., 2007). The Mnemonic Similarity Task
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12 (MST), which assesses recognition of common items whose similarity to lures is manipulated,
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14 (MST), which assesses recognition of common items whose similarity to lures is manipulated,
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16 has also revealed promising findings (Stark, Yassa, Lacy, & Stark, 2013). Mnemonic
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18 discrimination relies on pattern separation and such a construct also seems to hold marker
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20 properties for AD (E. Barbeau et al., 2004; E. J. Barbeau et al., 2008). Performance on such tasks
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22 holds the key to understanding memory decline along the continuum of AD (Costa et al., 2017;
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24 Sperling et al., 2011). The FCSRT and the MST tax memory functions carried out in LTM. Such
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26 functions seem to rely on the hippocampus (Bennett, Huffman, & Stark, 2015; Sarazin et al.,
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28 2010) which for long has been thought of as the earliest target of AD pathology. This view has
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30 been recently challenged (Didic et al., 2011). (Papp et al., 2015) used the FCSRT and the
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32 Memory Capacity Test (MCT, recently relabelled as the Memory Binding Test – MBT– by
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34 (Buschke, 2014)) to assess cognitively normal older adults who show evidence of brain
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36 amyloidosis (A β) and neurodegeneration. Z-scores computed over the whole sample revealed
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38 that the MCT, but not the FCSRT, detected impairment only in advanced stages. Hence, a
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40 substantial amount of brain damage needs to accumulate before deficits of LTM binding
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42 functions become apparent. However, (Mowrey et al., 2016) recently investigated the predictive
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44 validity of the MBT for incident aMCI. They reported that in a longitudinal community-based
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46 study of 246 cognitively normal elderly adults aged 70+ the MBT significantly predicted
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48 incident aMCI within a time window ranging from 4 to 7 years. As suggested by (Rentz et al.,
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50 2013), more work needs to be done to investigate the added value of these promising test for the
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4 preclinical detection of AD. Combining in single assessment protocols memory tests that assess
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6 the sub-hippocampal stages of AD ((Didic et al., 2011), e.g., VSTMBT, see also (Wolk, Signoff,
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8 & DeKosky, 2008)) and those sensitive to the hippocampal stages (MBT/MCT/FCSRT, MST,
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10 CANTAB-PAL) to map decline of these functions along the AD continuum in larger
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12 longitudinal cohorts (see (Costa et al., 2017)), will confirm their value for screening and
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14 diagnostic purposes.
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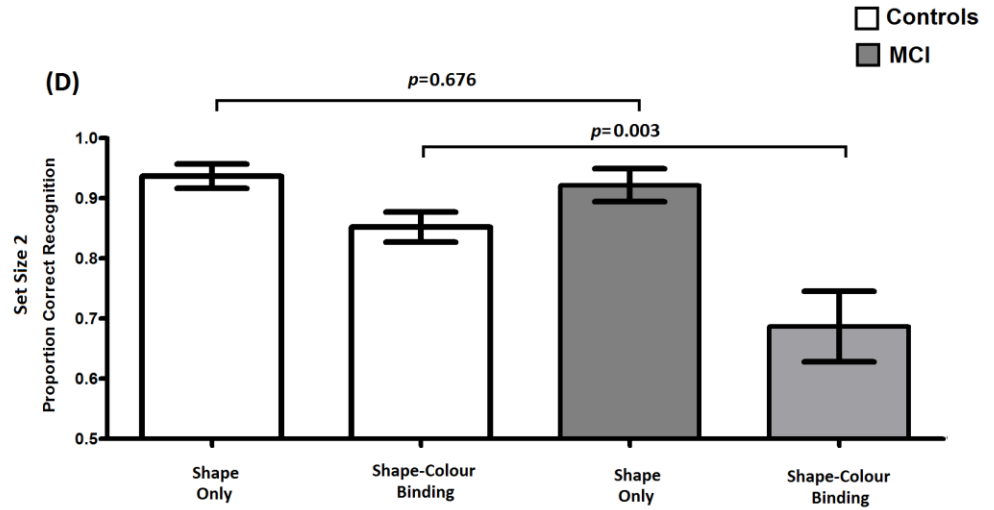
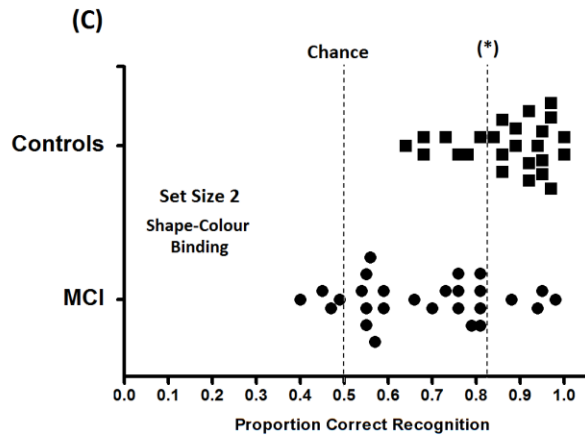
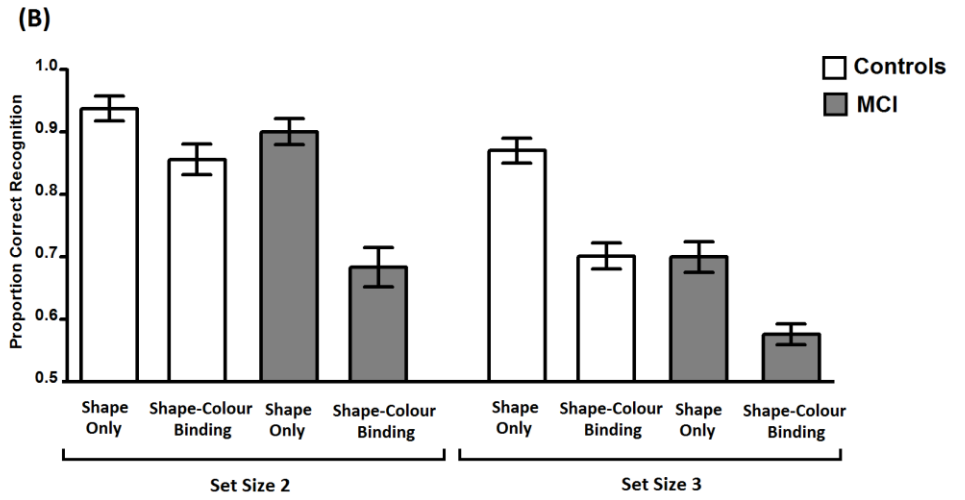
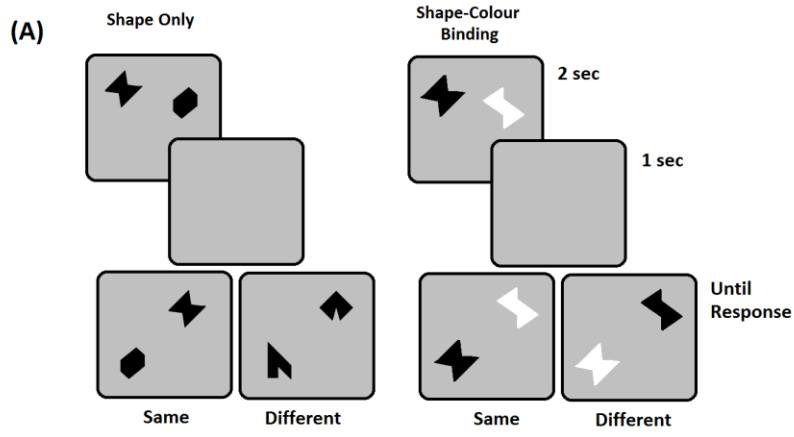


Figure 1. (A) An example trial for each condition of the Short-Term Memory Binding Test using Set Size 2. (B) Mean data from the Short-Term Memory Binding Test (error bars = SEM). (C) Overlap between people with Mild Cognitive Impairment (MCI) and Controls in the Shape-

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Colour Binding condition of the Short-Term Memory Binding Test using Set Size 2. Twelve MCI people did not overlap with controls and fell below the cut-off (*) recently reported by (Sergio Della Sala et al., 2017) There were 7 controls whose score were also below such a cut-off. Their neuropsychological background and that from controls above cut-off did not significantly differ (see Supplementary Table 1). **(D)** Mean data from the Short-Term Memory Binding Test from Controls and the 10 MCI people who had MRI evidence of hippocampal atrophy.

Table 1. Demographic, clinical and neuropsychological variables of subjects tested with the two set sizes.

	Set Size 2				Set Size 3				ANOVA		Post-Hoc			
	Controls (n=25)		MCI (n=27)		Controls (n=29)		MCI (n=23)				SS2	SS3	Ctr	MCI
	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range	F	p	Ctr vs MCI	Ctr vs MCI	SS2 vs SS3	SS2 vs SS3
Age	74.73 (4.74)	(66.00-83.00)	75.07 (5.30)	(65.00-87.00)	72.34 (3.76)	(68.00-80.00)	75.43 (5.77)	(67.00-86.00)	2.25	0.087	1.000	0.157	0.449	1.000
Education	10.84 (5.02)	(4.00-16.00)	10.86 (5.80)	(4.00-20.00)	11.00 (5.11)	(0.00-20.00)	9.43 (2.90)	(6.00-15.00)	0.54	0.655	1.000	1.000	1.000	1.000
GDS	1.12 (1.96)	(0.00-7.00)	2.00 (2.21)	(0.00-7.00)	1.28 (2.02)	(0.00-9.00)	2.39 (1.90)	(0.00-7.00)	2.19	0.094	0.684	0.316	1.000	1.000
MMSE	27.52 (1.98)	(24.00-30.00)	23.90 (2.88)	(20.00-29.00)	28.90 (1.23)	(26.00-30.00)	25.22 (1.73)	(20.00-27.00)	33.42	*	0.001	*	0.101	0.144
Blessed Scale	0.40 (0.76)	(0.00-2.50)	3.05 (2.62)	(0.00-10.00)	1.23 (1.54)	(0.00-7.00)	3.41 (3.02)	(0.00-12.00)	11.31	*	*	0.004	0.979	1.000
TAVEC Imm Free Recall	9.61 (3.34)	(0.00-14.00)	4.50 (3.70)	(0.00-13.00)	10.52 (2.37)	(7.00-16.00)	4.52 (4.04)	(0.00-14.00)	24.25	*	*	*	1.000	1.000
TAVEC Imm Cued Recall	11.21 (2.11)	(7.00-15.00)	6.17 (3.36)	(0.00-13.00)	11.97 (2.28)	(5.00-16.00)	6.74 (3.54)	(1.00-14.00)	29.17	*	*	*	1.000	1.000
TAVEC Delayed Free Recall	10.13 (2.97)	(0.00-14.00)	4.37 (3.64)	(0.00-13.00)	11.31 (1.97)	(9.00-16.00)	4.70 (3.73)	(0.00-14.00)	35.93	*	*	*	1.000	1.000
TAVEC Delayed Cued Recall	11.00 (1.96)	(7.00-16.00)	6.73 (3.68)	(0.00-15.00)	12.17 (2.24)	(7.00-16.00)	6.13 (3.17)	(1.00-12.00)	29.57	*	*	*	0.852	1.000
TAVEC Recognition	14.58 (1.59)	(11.00-16.0)	14.07 (1.89)	(9.00-16.00)	14.76 (1.41)	(12.00-16.00)	13.74 (2.09)	(9.00-16.00)	1.83	0.146	1.000	0.239	1.000	1.000
TMT-A	58.76 (21.58)	(23.00-116.0)	95.80 (56.19)	(31.00-260.00)	55.59 (16.06)	(26.00-97.00)	116.48 (79.33)	(32.00-357.0)	9.21	*	0.038	*	1.000	0.791
TMT-B	167.64 (93.0)	(49.00-360.0)	298.93 (150.86)	(117.00-673.0)	156.34 (76.51)	(74.00-443.0)	381.23 (231.44)	(80.00-929.0)	13.69	*	0.008	*	1.000	0.297
ROF Copy	28.56 (7.39)	(8.00-36.00)	22.92 (9.20)	(6.50-36.00)	33.69 (2.88)	(25.00-36.00)	28.54 (8.10)	(2.50-36.00)	10.83	*	0.033	0.076	0.072	0.037
ROF Imm Recall	12.48 (6.72)	(2.00-29.00)	7.79 (7.06)	(0.00-30.00)	16.50 (6.00)	(6.00-28.00)	7.22 (4.97)	(0.00-17.00)	13.14	*	0.053	*	0.143	1.000
ROF Delayed Recall	11.23 (6.27)	(2.05-26.50)	7.02 (7.04)	(0.00-28.00)	16.60 (6.15)	(3.00-28.00)	6.80 (4.74)	(0.00-18.00)	15.39	*	0.105	*	0.016	1.000
Letter Fluency (FAS)	34.92 (12.12)	(13.00-61.00)	24.03 (8.47)	(11.00-42.00)	35.24 (9.53)	(14.00-54.00)	27.82 (10.01)	(11.00-51.00)	8.43	*	0.001	0.060	1.000	1.000
Semantic Fluency	61.82 (11.30)	(37.00-81.00)	48.87 (11.53)	(24.00-80.00)	59.79 (9.44)	(45.00-76.00)	43.45 (10.95)	(22.00-60.00)	15.82	*	*	*	1.000	0.463
VSTM Shape Only	0.94 (0.10)	(0.57-1.00)	0.90 (0.11)	(0.52-1.00)	0.87 (0.11)	(0.53-1.00)	0.70 (0.12)	(0.53-0.94)	22.37	*	1.000	*	0.150	*
VSTM Shape-Colour Binding	0.86 (0.12)	(0.51-1.00)	0.68 (0.16)	(0.40-0.98)	0.70 (0.11)	(0.53-0.97)	0.58 (0.08)	(0.41-0.75)	21.01	*	*	0.003	*	0.018

* $p < 0.001$; Blessed Scale (Blessed, Tomlinson, & Roth, 1968); GDS: Geriatric Depression Scale (Yesavage et al., 1982); Imm: Immediate Recall;

MMSE: Mini Mental State Examination (Folstein, Folstein, & McHugh, 1975); SS2 & 3: Set Sizes 2 and 3; TAVEC: Spanish version of the California

Verbal Learning Test (Delis, Kramer, Kaplan, & Ober, 1987).

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