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Original Research Article

Visual and Verbal Serial List Learning in Patients with Statistically-Determined Mild Cognitive Impairment

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Abstract

Background and Objective: Prior research with patients with mild cognitive impairment (MCI) suggests that visual versus verbal episodic memory test performance may be more sensitive to emergent illness. However, little research has examined visual versus verbal episodic memory performance as related to MCI subtypes.

Research Design and Methods: Patients were diagnosed with non-MCI, amnesic MCI (aMCI), and combined mixed/dysexecutive MCI (mixed/dys MCI). Visual and verbal episodic memory were assessed with the Brief Visuospatial Memory Test-Revised (BVMT-R) and the 12-word Philadelphia (repeatable) Verbal Learning Test (P(r)VLT), respectively.

Results: BVMT-R and P(r)VLT scores yielded similar between-group patterns of performance. Non-MCI patients scored better than other groups on all parameters. aMCI and mixed/dys MCI did not differ on immediate or delayed free recall. Both delayed BVMT-R and P(r)VLT recognition test performance dissociated all three groups. Logistic regression analyses found that BVMT-R delayed free recall and delayed recognition scores correctly classified more patients with MCI (75.40%) than analogous P(r)VLT scores (66.20%). Visual versus verbal memory within-group analyses found no differences among non-MCI patients; P(r)VLT immediate free recall was worse among aMCI patients, but BVMT-R immediate free recall and delayed recognition were worse among mixed/dys MCI patients.

Discussion and Implications: Between-group analyses found convergent patterns of performance such that both tests identified elements of amnesia. However, logistic and within-group analyses found differing performance patterns suggesting that impaired visual episodic memory performance may be specific to emergent illness in mixed/dys MCI. Complementary but divergent neurocognitive networks may underlie visual versus verbal episodic memory performance in some patients with MCI.

Translational Significance: Visual episodic memory is often assessed with episodic memory tests in which nonrepresentational figure and/ or geometric objects are presented. The current research examined patients with mild cognitive impairment and found that visual episodic memory tests were superior versus verbal tests in classifying patients into their respective groups. These results suggest that visual episodic memory should be routinely assessed and part of any protocol designed to assess for emergent dementia.

Keywords: Alzheimer's disease, Episodic memory, Mild cognitive impairment, Serial list learning

The early detection of emergent Alzheimer's disease (AD) has become a major public health initiative. As such, there is great interest in the diagnosis of mild cognitive impairment (MCI), a clinical syndrome believed to convey risk for the eventual development of dementia such as AD (Belleville, Fouquet, Hudon, Zomahoun, & Croteau, 2017). A key neuropsychological feature for the diagnosis of MCI revolves around patterns of performance on episodic memory tests using a serial list learning format. Performance on verbal serial list learning tests in MCI has been extensively researched (Libon et al., 2011; Lim et al., 2012). For example, research has consistently shown an intermittent level of free recall performance produced by MCI patients when compared with healthy older adults and AD patients (Albert et al., 2011; Lim et al., 2012; Ribeiro, Guerreiro, & De Mendonça, 2007; Snyder et al., 2011). Other serial list learning tests, such as the Rey Auditory Verbal Learning Test (RAVLT) and the Free and Cued Selective Reminding Test (FCSRT), have also displayed efficacy in differentiating between normal controls and MCI patients and among MCI subtypes (Bondi & Smith, 2014; Derby et al., 2013; Wagner & Wolf, 2012).

Libon et al., (2011) assessed patterns of performance in statistically-determined groups of patients with amnesic MCI (aMCI), mixed MCI, and dysexecutive MCI using the 9-word Philadelphia (repeatable) Verbal Learning Test (P[r]VLT). The intent of this research was to assess whether aMCI patients produce similar types of errors, and, to measure susceptibility to interference effects in patients with AD (Price et al., 2009). This research found that when compared with other MCI subtypes, aMCI patients displayed greater proactive/ retroactive interference; produced very prototypic extra-list, cued free intrusion errors; and displayed rapid forgetting, a pattern of performance that differed compared to other MCI subtypes and previously described in AD by Price et al., (2009). By contrast, patterns of performance produced by other MCI patients appeared to be due to executive, rather than amnesic impairment, such that other MCI patients often demonstrated improvement on delayed recognition testing (Libon et al., 2011).

Comparatively less research has examined visual episodic memory in MCI subtypes. Several papers have focused on relationships between visual episodic memory and markers suggesting neurodegeneration. For example, Gifford and

colleagues (2018) administered the Biber Figure Learning Test (BFLT), a visual serial list learning test modeled after the original California Verbal Learning Test (CVLT; Delis, Kramer, Kaplan, & Ober, 1987), to community-dwelling participants characterized with normal cognitive functioning, early MCI, and more advanced MCI. Reduced BFLT delayed free recall and delayed recognition scores were associated with smaller right hippocampal volume and greater dilation involving the right lateral ventricle, respectively, and higher CSF tau concentrations, but not CSF amyloid.

Bonner-Jackson and colleagues (Bonner-Jackson, Mahmoud, Miller, & Banks, 2015) examined relations between hippocampal volume and visual and verbal episodic memory tests (i.e., Brief Visuospatial Memory Test-Revised; BVMT-R; Benedict, 1997; Hopkins Verbal Learning Test-Revised; HVLTR; Brandt & Benedict, 2001; respectively) in normal controls (NC), AD patients, aMCI patients, and non-aMCI patients. Analyses revealed complementary results such that NCs performed better on both memory tests compared to MCI and AD groups; and both MCI groups performed better than AD patients. However, within-group analyses were not reported that might have suggested a verbal versus visual modality effect. Nonetheless, a more robust association was found between better BVMT-R delayed free recall and larger hippocampal volume compared to the HVLTR, suggesting that visual episodic memory testing may be a more sensitive indicator for emergent illness.

Other researchers have suggested that visual when compared with verbal episodic memory tests may be a more sensitive indicator of emergent illness (Didic et al., 2013; Okonkwo et al., 2014). In one study, Ye and colleagues (2014) studied a group of aMCI patients using a visual recognition test and grouped patients with respect to material-specific performance deficits, that is, a visual-aMCI group, a verbal-aMCI group, and a combined dual-modality group and found that the visual-aMCI group was at greater risk for progression to dementia. Similarly, De Anna and colleagues (2014) followed aMCI patients longitudinally using a visual recognition memory test and found that visual recognition test performance may be able to identify baseline alterations in cognition that predict eventual conversion to AD.

A reason that may explain putative greater sensitivity for visual as compared to verbal episodic memory tests may

revolve around the need to recruit more diverse and wider neurocognitive skills for successful test completion. For example, at least implicitly, some visual episodic memory tests often required patients to encode not just the stimulus object, but object location. To the extent, patients are asked to respond by drawing or reproducing test stimuli with a graphomotor response, mental planning, and visuospatial abilities are likely recruited. The diversity of neurocognitive skills necessary in these visual episodic memory tests is far greater than verbal episodic memory tests where patients are most often asked to encode and subsequently remember a list of words.

The neuropathological alterations seen in neurodegenerative conditions such as AD have traditionally been thought to originate comparatively narrowly, involving the bilateral hippocampal region (Arnold, Hyman, Flory, Damasio, & Van Hoesen, 1991). However, more recent research has shown that, in some AD patients, pathology can be found throughout neocortical association areas with relative hippocampal sparing (Murray et al., 2011). Patients with AD and MCI have also been shown to present with white matter alterations that involve both subcortical regions of the brain connecting the frontal lobes to subcortical nuclei and parietal association cortex (Brickman et al., 2012). Thus, greater sensitivity regarding emergent illness for visual as compared to verbal episodic memory tests could be the result of the combination of widespread emergent neuropathology negatively impacting diverse neurocognitive skills necessary for successful test completion. This notion is partially supported by Hampstead, Stringer, Stilla, Amaraneni, & Sathian (2011) who studied aMCI patients and healthy controls using a visuospatial object location task. As expected, healthy controls scored better than aMCI patients. fMRI analyses found that both groups recruited similar neurocognitive networks involving both posterior and anterior cortex. However, brain activation produced by aMCI patients was significantly attenuated.

In the current research, several methodological features were used to extend prior research. First, new statistically derived comprehensive diagnostic criteria were applied to classify patients into MCI subtype versus non-MCI groups (Jak et al., 2009). Second, in addition to assessing for between-group differences, both within-group comparisons and logistic regression were used to test the hypothesis that visual, as compared to verbal, episodic memory tests will be more effective in predicting group membership. On the basis of prior research and the methodological features listed above, we sought to test the following hypotheses: (1) that all MCI patients will obtain lower scores on visual versus verbal episodic memory tests; (2) because of the diversity of their neurocognitive impairment, mixed/dysexecutive MCI patients may be differentially impaired and produce lower scores on visual versus visual episodic memory tests compared to other groups; and (3) that visual as compared to verbal episodic memory test performance

will be more effective in classifying patients into their respective groups.

Method

Participants

The current research was drawn from a corpus of 93 patients seen for possible neurocognitive disorders from the Rowan University, New Jersey Institute for Successful Aging, Memory Assessment Program (MAP). However, only 65 patients were assessed with both the P(r)VLT and BVMT-R. Therefore, all analyses were conducted using this group of patients. The work-up for neurocognitive disorders included comprehensive neuropsychological assessment; evaluations provided by a social worker and a board-certified geriatric psychiatrist, a brain MRI/CT scan; and serum blood tests. An interdisciplinary team conference determined clinical diagnosis. All patients presented with subjective cognitive complaints, preservation of general functional abilities, and absence of dementia. Exclusion criteria included head injury, substance abuse, major/medical psychiatric disorders (e.g., major depression, epilepsy), B12, folate, or thyroid deficiency. A knowledgeable family member provided information regarding functional status. Demographic and clinical characteristics including age, education, Mini-Mental Test Performance (Folstein, Folstein, & McHugh, 1975), depression (Geriatric Depression Scale; Sheik & Yesavage, 1986), Wide Range Achievement Test-IV Reading subtest performance, and instrumental activities of daily living (Lawton & Brody, 1969) are displayed in Table 1. The Rowan University institutional review board approved this investigation (IRB number: 2016001115) and the current research complied with the Declaration of Helsinki.

Neuropsychological Assessment

The neuropsychological protocol used to classify patients is identical as described by Emrani et al., (2018). Three domains of neuropsychological functioning were assessed: executive control, naming/lexical access, and verbal episodic memory. Nine neuropsychological parameters, three from each neurocognitive domain were used to classify patients as presenting with non-MCI or MCI subtypes as described below. All dependent variables were expressed as z-scores derived from either available normative data or demographically corrected scores provided by Heaton, Miller, Taylor, & Grant (2004).

Executive control

Executive functioning was assessed using the Boston Revision of the Wechsler Memory Scale-Mental Control subtest-Accuracy Index (see Lamar, Price, Davis, Kaplan, & Libon, 2002 for full details); letter verbal fluency (“FAS”;

Table 1. Demographic Information (mean, *SD*)

	non-MCI (<i>n</i> = 32)	aMCI (<i>n</i> = 14)	mixed/dys MCI (<i>n</i> = 19)
Age	75.56 (6.31)	72.71 (5.80)	75.26 (4.54)
Education	14.88 (2.55)	14.64 (2.41)	14.05 (3.21)
MMSE	28.16 (1.57)	26.50 (2.31)	27.05 (1.96)
GDS	3.44 (2.88)	3.43 (2.65)	3.89 (2.45)
WRAT-IV Reading	113.63 (17.16)	114.71 (10.01)	105.68 (16.66)

Note: *N* = 65; aMCI = Amnesic mild cognitive impairment; Mixed/dys MCI = Mixed/dysexecutive mild cognitive impairment; non-MCI = Non-mild cognitive impairment.

Spree & Strauss, 1990); and Trail Making Test-Part B (Reitan & Wolfson, 1985).

Lexical access/language

Language/lexical access was measured with the 60-item Boston Naming Test (Kaplan, Goodglass, & Weintraub, 1983); semantic (“animals”) fluency (Carew, Lamar, Cloud, Grossman, & Libon, 1997); and Wechsler Adult Intelligence Scale-III Similarities subtest (Wechsler, 1997).

Memory and learning

The measures of memory and learning used in the current research were drawn from the 9-word California Verbal Learning Test-short form (Delis, Kramer, Kaplan, & Ober, 2000), including total immediate free recall, delayed free recall, and the delayed recognition discriminability index.

Determination of MCI Subtypes

Single and multidomain MCI

The criteria of Jak et al. (2009) were used to determine MCI subtype. Single domain MCI syndromes were diagnosed when participants scored >1.0 *SD* below normative expectations on any of two of the three measures within a single cognitive domain. Mixed MCI syndromes were diagnosed when participants scored >1.0 *SD* below normative expectations on any two of the three measures within two or more cognitive domains. Using these procedures, 14 patients were diagnosed with single domain aMCI, 5 patients were diagnosed with single domain dysexecutive MCI, and 14 patients were diagnosed with mixed or multidomain MCI. Because of the small number of dysexecutive MCI patients, the dysexecutive and mixed MCI groups were combined to form the mixed/dys MCI subgroup (*n* = 19).

Non-MCI group

Among the patients who presented for clinical evaluation, 32 patients did not meet Jak et al. (2009) criteria for MCI. Some of these patients (*n* = 7) performed such that all nine neuropsychological parameters were above 1 *SD*. A second group of patients not meeting criteria for MCI presented with some, but very little cognitive impairment. Specifically, 14 patients produced test scores where

only one of the nine parameters fell below the 1*SD* cutoff, and 11 patients produced test scores where only two of the nine parameters, irrespective of cognitive domain, fell below 1*SD*. No differences were found among patients that did not meet criteria for MCI on the visual and verbal episodic outcome measures described below. For this reason, these patients were combined into one group and labeled non-MCI.

Verbal and Visual Episodic Memory Outcome Measures

Verbal episodic memory was assessed with the 12-word P(r) VLT (Bezdicek et al., 2014; Gifford Liu, Neal, Babicz, et al., 2018), a test constructed and administered consistent with the 9-word P(r)VLT and original 16-word CVLT (Delis et al., 1987). Visual episodic memory was assessed with the BVMT-R (Benedict, 1997). Neither test was used to diagnose or categorize patients into their respective groups.

P(r)VLT outcome measures of interest included List A- total immediate free recall on trials 1–5, delayed free recall, and the delayed recognition discriminability index as described by Price et al., (2009) and the original CVLT (Delis et al., 1987). BVMT-R outcome measures included total immediate recall- trials 1–3, delayed free recall, and the delayed recognition discriminability index.

Statistical Analysis

Between-group analyses

Because of limitations regarding available normative data for both tests, P(r)VLT and BVMT-R raw scores were analyzed using hierarchical linear regression with block-wise entry of demographic variables. In Step 1, age, education, and gender were entered together. In Step 2, dummy coded variables representing between-group differences among the non-MCI and MCI groups were entered. The results produced from Step 2 were interpreted to assess for between-group differences after controlling for age, education, and gender.

Logistic regression classification

Two hierarchical logistic regression models (Model 1: BVMT-R; Model 2: P[r]VLT; *n* = 65) using block-wise entry

of predictors as described above were constructed to compare classification accuracy rates for the BVMT-R versus P(r)VLT delayed free recall and delayed recognition scores, controlling for age, education, and gender. On the basis of recommended sample size for sufficient statistical power (Peduzzi, Concato, Kemper, Holford, & Feinstein, 1996), aMCI and mixed/dys MCI subtypes were collated into a single MCI group and compared to non-MCI patients. Akaike's Information Criterion (AIC) was computed for both models and values were compared such that the model with the smaller AIC value demonstrated maximum relative classification accuracy.

Within-group comparison

Paired samples *t* tests were conducted to assess for differences between visual and verbal modalities within each of the three groups. Prior to analyses, scores on immediate recall, delayed recall, and delayed recognition for both the BVMT-R and P(r)VLT were adjusted using the grand means for age, education, and gender to hold the influence of demographic variables constant across groups. Inferential tests were conducted using *z*-score transformed adjusted scores. Means and standard deviations for unadjusted and adjusted raw scores are displayed in Table 2.

Results

Descriptive Data

Patients (72% female) did not differ by group on age, education, Geriatric Depression Scale scores (Yesavage, 1986), estimated premorbid abilities assessed using the Wide Range Achievement Test-IV Reading subtest performance, or scores on the independent Activities of Daily Living questionnaire (Lawton & Brody, 1969). The Lawton and Brody questionnaire was not available for four participants. On the Mini-Mental State Examination, non-MCI patients scored higher than aMCI patients ($p < .031$).

Philadelphia (repeatable) Verbal Learning Test Performance

Three hierarchical regressions were employed to determine if the three groups differed on P(r)VLT outcome variables controlling for demographic variables. See Supplemental Table 1 for a summary of the inter-correlations, means, and standard deviations among variables. Prior to conducting the analyses, ordinary least squares (OLS) assumptions were tested. Visual inspection of the residual plots revealed heteroscedasticity within the full model predicting delayed free recall. However, the ratio of largest to smallest variance across three data slices ($\sigma^2 = 1.52$) suggested that the violation was small and that it was appropriate to proceed with analyses in an OLS framework (Cohen, Cohen, West, & Aiken, 2003). No other assumption violations were identified.

Table 3 provides a summary of the three P(r)VLT regression analyses. Non-MCI patients performed better than MCI patients for both immediate (aMCI: $t = 3.72$, $p < .001$; mixed/dys MCI: $t = 3.08$, $p < .003$) and delayed free recall (aMCI: $t = 2.63$, $p = .01$; mixed/dys MCI: $t = 4.12$, $p < .001$). aMCI and mixed/dys MCI patients did not differ. For delayed recognition performance, analyses revealed a three-group dissociation such that non-MCI patients performed better than aMCI ($t = 4.62$, $p < .001$) and mixed/dys MCI patients ($t = 2.24$, $p < .03$), and aMCI patients performed worse than mixed/dys MCI patients ($t = 2.37$, $p < .021$).

Brief Visuospatial Memory Test-Revised Test Performance

Group differences on BVMT-R immediate free recall, delayed free recall, and delayed recognition performance were analyzed using the same methods as described above. Residual plot inspection revealed heteroscedasticity for the full model predicting BVMT-R delayed recognition. Subsequent tests via data slicing ($\sigma^2 = 1.85$) suggested that the violation was small and that it was appropriate to continue within an OLS framework (Cohen et al., 2003).

The three BVMT-R regression analyses are summarized in Table 4. Non-MCI patients performed better than MCI patients for BVMT-R immediate (aMCI: $t = 3.83$, $p < .001$; mixed/dys MCI: $t = 3.99$, $p < .001$) and delayed free recall (aMCI: $t = 4.24$, $p < .001$; mixed/dys MCI: $t = 3.00$, $p < .004$). The two MCI groups did not differ. Consistent with the P(r)VLT analyses described above, delayed recognition performance continued to reveal a three-group dissociation such that non-MCI patients performed better than aMCI ($t = 4.92$, $p < .001$) and mixed/dys MCI patients ($t = 4.92$, $p < .001$), and aMCI patients performed worse than mixed/dys MCI patients ($t = 2.01$, $p < .049$).

Non-MCI Versus MCI Logistic Regression

BVMT-R logistic regression

Age, education, gender and BVMT-R delayed free recall and delayed recognition scores accounted for approximately 32.3% of the null deviance ($R^2_L = .323$). The full model containing all demographic and both BVMT-R variables correctly classified 75% of the patients (Table 6). Without any information from predictors, the null model provides a 50.8% chance of accurately predicting patients diagnosed with MCI. To acknowledge this base rate, these proportions were used to calculate the proportion of correct classification corrected for base rate. Approximately 50% of the patients who were not correctly classified by the null model (base rate model) were able to be correctly classified by the five predictor (full) model. Specifically, 16 of the 32 patients not initially correctly classified by the null model were able to be correctly classified by the full model. After controlling for demographic variables, both BVMT-R

Table 2. Unadjusted vs Adjusted Descriptive for BVMT-R and P(r)VLT Raw Scores

Measure and Score Form	Subtest	Non-MCI		aMCI		Mixed/dys MCI		Overall	
		M	SD	M	SD	M	SD	M	SD
BVMT-R: Unadjusted	Immediate Recall	6.88	3.10	3.71	2.37	3.63	2.41	5.25	3.17
	Delayed Recall	2.63	1.60	0.86	0.86	1.47	1.17	1.91	1.53
	Delayed Recognition	5.47	0.72	3.64	1.82	4.42	1.07	4.77	1.34
BVMT-R: Adjusted	Immediate Recall	6.89	0.79	3.72	0.74	3.64	0.41	5.26	1.75
	Delayed Recall	2.64	0.41	0.87	0.41	1.49	0.36	1.92	0.84
	Delayed Recognition	5.46	0.12	3.64	0.11	4.42	0.10	4.76	0.75
P(r)VLT: Unadjusted	Immediate Recall	37.75	7.98	28.29	6.35	30.63	8.67	33.63	8.80
	Delayed Recall	6.81	2.86	2.64	2.76	4.47	3.12	5.23	3.33
	Delayed Recognition	0.91	0.09	0.73	0.15	0.83	0.13	0.85	0.13
P(r)VLT: Adjusted	Immediate Recall	37.72	1.20	28.26	1.25	30.61	1.43	33.60	4.36
	Delayed Recall	6.79	0.35	2.62	0.32	4.45	0.28	5.21	1.73
	Delayed Recognition	0.95	0.02	0.76	0.01	0.86	0.12	0.89	0.08

Note: Non-MCI = 32, aMCI = 14, mixed/dys MCI = 19. aMCI = Amnesic mild cognitive impairment; BVMT-R = Brief Visuospatial Memory Test-Revised; Mixed/dys MCI = Mixed/dysexecutive mild cognitive impairment; non-MCI = Non-mild cognitive impairment; P(r).VLT = Philadelphia (repeatable) Verbal Memory Test.

delayed free recall and BVMT-R delayed recognition scores significantly predicted MCI diagnosis ($\chi^2 [2] = 27.935, p < .001$; section 2.1, Table 5).

P(r)VLT logistic regression

Age, education, gender, and P(r)VLT delayed free recall and delayed recognition scores accounted for approximately 19.8% of the null deviance ($R^2_L = .198$). The full model containing all demographic and both P(r)VLT variables correctly classified 66% of the patients. Without any information from predictors, the null model accurately predicted 50.8% of the patients diagnosed with MCI. These proportions were subsequently used to calculate the proportion of correct classification corrected for base rate. Approximately 31.3% of the patients who were not correctly classified by the null model (base rate model) were able to be correctly classified by the five predictor (full) model. Specifically, 10 of the 32 patients not initially correctly classified by the null model were able to be correctly classified by the full model. After controlling for demographic variables, both P(r)VLT delayed free recall and delayed recognition scores significantly predicted MCI diagnosis ($\chi^2 [2] = 17.134, p < .001$; see section 2.2 in Table 5). However, unlike the BVMT-R described above, and despite the significant omnibus effect, neither P(r)VLT scores uniquely predicted MCI versus non-MCI diagnosis ($p > .05$).

Logistic regression model comparison

The BVMT-R model yielded a smaller AIC value (AIC = 1.08) than the P(r)VLT model (AIC = 1.25), suggesting that BVMT-R scores provided greater utility in correctly classifying patients' diagnostic group membership (Table 6).

Within-Group Comparisons

In a series of paired-sample *t* tests to assess for within-group differences between visual and verbal modalities, non-MCI patients showed no differences in visual versus verbal test performance. aMCI patients scored approximately .35 *SD* lower on the P(r)VLT immediate free recall ($M = -1.23$) than BVMT-R immediate free recall ($M = -0.87; t [13] = -2.31, p < .04$, confidence interval [CI]: -0.02 to $-0.68, d = .62$), suggesting a medium effect size (Cohen, 1988) with no difference for delayed free recall or delayed recognition performance. Mixed/dys MCI patients performed approximately 0.23 *SD* lower on BVMT-R immediate free recall ($M = -0.92$) than P(r)VLT immediate free recall ($M = -0.69; t [18] = -2.67, p < .02$, CI: -0.45 to $-0.41, d = .61$), and approximately 0.20 *SD* lower on BVMT-R delayed recognition ($M = -0.46$) than P(r)VLT delayed recognition ($M = -0.26; t [18] = -2.54, p < .02$, CI: -0.37 to $-0.03, d = .58$), consistent with medium effect sizes (Cohen, 1988). No significant difference was found for delayed free recall performance.

Discussion

Prior research has shown that MCI patients may score lower on visual versus verbal episodic memory tests, suggesting that performance on visual episodic memory tests may be more sensitive in identifying emergent illness. The current research was interested in providing additional evidence (1) demonstrating that MCI patients may, in fact, score lower on visual versus verbal episodic memory tests; (2) that mixed/dys patients may score lower than other groups because of the diversity of their neuropsychological impairment; and (3) that visual versus verbal episodic

Table 3. P(r)VLT Hierarchical Regression Analysis Summary

Outcome	Step	Predictor Variable	R ²	95% CI (R ²)	ΔR ²	95% CI (ΔR ²)	B	SE (B)	95% CI (B)	β	s ^{r2}
Immediate Recall	1	Age	0.02	(0.00, 0.09)	0.02	(0.00, 0.09)	0.06	0.20	(-0.33, 0.46)	0.04	0.00
		Education					0.46	0.41	(-0.37, 1.29)	0.14	0.02
		Gender ^a					0.73	2.52	(-4.30, 5.76)	0.04	0.00
Delayed Recall	2	Non-MC/mixed/dys MCI	0.25**	(0.03, 0.39)	0.24***	(0.01, 0.36)	7.28	2.37	(2.55, 12.02)	0.42**	0.12
		Non-MCI/aMCI					9.78	2.62	(4.49, 14.96)	0.56***	0.18
		aMCI/mixed/dys MCI					-2.45	2.86	(-8.16, 3.27)	-0.12	0.01
Delayed Recall	1	Age	0.04	(0.00, 0.14)	0.04	(0.00, 0.14)	0.11	0.07	(-0.03, 0.26)	0.20	0.04
		Education					0.04	0.16	(-0.26, 0.35)	0.03	0.00
		Gender ^a					-0.53	0.94	(-2.42, 1.36)	0.94	0.00
Delayed Recognition	2	Non-MC/mixed/dys MCI	0.27**	(0.05, 0.41)	0.23***	(0.02, 0.37)	2.32	0.88	(0.55, 4.08)	0.35*	0.08
		Non-MCI/aMCI					4.00	0.98	(2.05, 5.95)	0.61***	0.21
		aMCI/mixed/dys MCI					-1.69	1.06	(-3.82, 0.44)	-0.21	0.03
Delayed Recognition	1	Age	0.03	(0.00, 0.12)	0.03	(0.00, 0.12)	0.00	0.00	(-0.00, -0.02)	0.18	0.03
		Education					-0.00	0.01	(-0.02, 0.01)	-0.05	0.00
		Gender ^a					-0.01	0.04	(-0.09, 0.07)	-0.04	0.00
Delayed Recognition	2	Non-MC/mixed/dys MCI	0.30**	(0.07, 0.44)	0.26***	(0.04, 0.40)	0.08	0.04	(0.01, 0.15)	0.29*	0.06
		Non-MCI/aMCI					0.19	0.04	(0.10, 0.26)	0.67***	0.26
		aMCI/mixed/dys MCI					-0.10	0.04	(-0.18, -0.05)	-0.31*	0.07

Note: N = 65, Non-MCI = 14, mixed/dys MCI = 19, aMCI = Amnesic mild cognitive impairment; CI = Confidence interval; Mixed/dys MCI = Mixed/dysexcutive mild cognitive impairment; non-MCI = Non-mild cognitive impairment; P(r), VLT = Philadelphia (repeatable) Verbal Memory Test, s^{r2} = Squared semipartial correlation coefficient.

^a1 = female, 0 = male.

*p < .05; **p < .01; ***p < .001.

Table 4. BVMT-R Hierarchical Regression Analysis Summary

Outcome	Step	Predictor Variable	R ²	95% CI (R ²)	ΔR ²	95% CI (ΔR ²)	B	SE (B)	95% CI (B)	β	sr ²
Immediate Recall	1	Age	0.04	(0.00, 0.14)	0.04	(0.00, 0.14)	-0.06	0.07	(-0.20, 0.08)	-0.11	0.01
		Education					-0.01	0.15	(-0.31, 0.28)	-0.01	0.00
		Gender ^a					-1.07	0.90	(-2.87, 0.72)	-0.15	0.02
Delayed Recall	1	Non-MC/mixed/dys MCI	0.06	(0.00, 0.17)	0.06	(0.00, 0.17)	3.25	0.82	(1.62, 4.89)	0.52***	0.18
		Non-MCI/aMCI					3.46	0.90	(1.65, 5.26)	0.55***	0.18
		aMCI/mixed/dys MCI					-0.20	0.98	(-2.17, 1.77)	-0.03	0.00
Delayed Recognition	1	Age	0.01	(0.00, 0.06)	0.01	(0.00, 0.06)	-6.57	0.03	(-0.07, 0.07)	0.00	0.00
		Education					-0.10	0.07	(-0.24, 0.04)	-0.17	0.03
		Gender ^a					-0.64	0.43	(-1.49, 0.22)	-0.19	0.04
Delayed Recognition	2	Non-MC/mixed/dys MCI	0.30**	(0.07, 0.45)	0.24**	(0.03, 0.39)	1.18	0.40	(0.29, 1.97)	0.39**	0.11
		Non-MCI/aMCI					1.85	0.44	(0.98, 2.72)	0.61***	0.21
		aMCI/mixed/dys MCI					-0.66	0.48	(-1.62, 0.29)	-0.18	0.02
Delayed Recognition	2.1	Age	0.32***	(0.08, 0.46)	0.30***	(0.07, 0.45)	0.01	0.03	(-0.05, 0.07)	0.04	0.00
		Education					0.03	0.06	(-0.09, 0.16)	0.07	0.00
		Gender ^a					-0.25	0.39	(-1.02, 0.53)	-0.08	0.01
Delayed Recognition	2.1	Non-MC/mixed/dys MCI	0.32***	(0.08, 0.46)	0.30***	(0.07, 0.45)	1.04	0.34	(0.35, 1.72)	0.39**	0.10
		Non-MCI/aMCI					1.87	0.38	(1.12, 2.63)	0.70***	0.28
		aMCI/mixed/dys MCI					-0.83	0.42	(-1.67, -0.00)	-0.26*	0.05

Note: N = 65, non-MCI = 32, aMCI = 14, mixed/dys MCI = 19. aMCI = Amnesic mild cognitive impairment; BVMT-R = Brief Visuospatial Memory Test-Revised; CI = Confidence interval; Mixed/dys MCI = Mixed/dys executive mild cognitive impairment; non-MCI = Non-mild cognitive impairment; sr² = Squared semipartial correlation coefficient.

^a1 = female, 0 = male.

*p < .05, **p < .01, ***p < .001.

Table 5. BVMT-R/ P(r)VLT Hierarchical Nonnested Logistic Regression Analysis Summary

Step and Model	Predictor Variable	<i>b</i>	SE(<i>b</i>)	95% CI(<i>b</i>)	Wald	<i>P</i>	OR	95% CI (OR)
1	Age	-0.059	0.046	(-0.203, 0.032)	1.596	.206	0.943	(0.816, 1.033)
	Education	-0.080	0.095	(-0.267, 0.107)	0.701	.403	0.923	(0.766, 1.113)
	Gender ^a	0.782	0.593	(-0.382, 1.944)	1.735	.188	2.185	(0.683, 6.991)
2.1	BVMT-R-delayed	-0.545	0.276	(-1.085, -0.005)	3.909	.048	0.580	(0.338, 0.995)
	BVMT-R-recognition	-1.108	0.389	(-1.871, -0.345)	8.124	.004	0.330	(0.154, 0.708)
2.2	P(r)VLT-delayed	-0.186	0.144	(-0.468, 0.096)	1.670	.196	0.830	(0.63, 1.101)
	P(r)VLT-recognition	-6.030	3.928	(-13.816, 1.668)	2.357	.125	0.002	(0.00, 5.303)

Note: N= 65, non-MCI = 32, aMCI = 14, mixed/dys MCI = 19; b = logit; BVMT-R = Brief Visuospatial Memory Test-Revised; CI = Confidence interval; Delayed= delayed free recall; OR = Odds ratio; P(r).VLT = Philadelphia (repeatable) Verbal Memory Test; recognition = delayed recognition discriminability index; SE = Standard error.

^a1 = female, 0 = male.

Table 6. BVMT-R/P(r)VLT Logistic Regression Model Comparison

Model	-2LL (Deviance)	<i>k</i>	Cox & Snell R ²	Nagelkerke R ²	R ² _L	AIC	% Correct classification
BVMT-R	58.49	5	0.385	0.513	0.323	1.08	75.4
P(r)VLT	69.29	5	0.274	0.365	0.198	1.25	66.2

Note: N = 65, non-MCI = 32, aMCI = 14, mixed/dys MCI = 19; -2LL = -2(Log Likelihood); *k* = number of predictors in the model; AIC = Akaike's Information Criterion; BVMT-R = Brief Visuospatial Memory Test-Revised; P(r).VLT = Philadelphia (repeatable) Verbal Memory Test.

memory test performance may be more effective in classifying patients into their respective groups.

To extend prior research suggesting episodic memory material-specificity in MCI, the current research classified patients using statistically derived comprehensive neuropsychological diagnostic criteria (Jak et al., 2009) that provided clear operational definitions for MCI subtypes and non-MCI patients. Analytical strategies contributed to both between- and within-group analyses that assessed for material-specific effects, and logistic regression analyses that determined how well either test was able to classify patients into MCI versus non-MCI groups.

The results of between-group analyses found similar patterns of performance for both tests such that non-MCI patients outperformed both MCI groups. aMCI and mixed/dys MCI did not differ on any free recall test parameter. Both memory tests dissociated all three groups, with aMCI patients obtaining lower delayed recognition test scores than the other groups. The inclusion of within-group analyses extends prior research described by Bonner-Jackson and colleagues (2015). In the current research, within-group comparisons found no material-specific differences among non-MCI patients. Other within-group analyses found that aMCI patients obtained a lower P(r) VLT immediate free recall scored compared to the BVMT-R performance. However, mixed/dys MCI patients scored lower on BVMT-R immediate free recall and delayed recognition test parameters compared to the analogous P(r) VLT parameters. Subsequent logistic regression analyses

examining how well either test was able to classify patients into MCI versus non-MCI groups found that group classification was superior using BVMT-R parameters than analogous P(r)VLT parameters. In general, these data extend prior research and suggest that visual compared to verbal episodic memory tests may be troublesome for MCI patients, particularly for mixed/dys MCI patients who present with diverse neuropsychological deficits.

As noted above the neuropathology associated with both AD and MCI can involve not just the hippocampal regions, but cortical association area (Murray et al., 2011) as well as subcortical and neocortical white matter alterations (Brickman et al., 2012; Price et al., 2015). Widespread neuropathological alterations could negatively impact the diverse neurocognitive skills necessary for successful BVMT-R performance. Successful performance on the BVMT-R clearly requires a wider array of neurocognitive operations including memory for the test item, memory for the item's contextual place on the test page, visual scanning and visual attention; and the necessary motor skills to execute a proper response. In addition to memory, the diversity of these neuropsychological operations also requires considerable executive abilities including the ability to mentally plan all of these operations. Indeed, in prior research, also using Jak et al. (2009) classification method, Emrani and colleagues (2018) found that mixed/dys MCI patient performed worse on executive tests compared to other MCI groups. Thus, lower BVMT-R versus P(r)VLT serial list learning test performance among mixed/dys

patients MCI may be explained on the basis of the diversity of neurocognitive skills necessary for successful test performance, and the concomitant neurocognitive networks that support these neuropsychological operations. By comparison, the ability to encode a verbally presented “*shopping list*,” rich in semantic context, is likely related to a neurocognitive network drawing upon a relatively narrow range of operations circumscribed to left temporal regions.

This interpretation is consistent with prior neuropsychological and neuropathologic research. For example, Libon et al., (2011) found that the pattern of impairment produced by mixed MCI patients on verbal serial list learning tests was largely due to executive impairment. Researchers examining the brain regions associated with successful visual episodic memory performance found that memory for a recalled object was associated with right-sided hippocampal volume (Piekema, Kessels, Mars, Petersson, & Fernández, 2006; Toledo-Morrell et al., 2000). By contrast, memory for object location was associated with a wider neurocognitive network involving hippocampus, bilateral parietal, and bifrontal regions (Fujimori et al., 2000). Both memory for object and memory for object location are necessary for successful BVMT-R performance. Recent neuropathological research suggests that the diverse neuropsychological disabilities seen in mixed MCI patients is associated with a wider array of underlying neuropathological alterations compared to aMCI patients (Abner et al., 2017; Dugger et al., 2015). In sum, the results of the current research provide some support suggesting worse performance on visual, compared to verbal episodic memory tests in some MCI patients particularly when executive impairment is present.

The strengths of the current research include episodic memory assessment using well-known serial list learning paradigms, and well-validated comprehensive neuropsychological diagnostic criteria to classify non-MCI and MCI patients into their respective groups (Jak et al., 2009). However, several limitations must be acknowledged including our modest sample size; lack of ethnic diversity, and the fact that a visual episodic memory test was not included as a classification or diagnostic measure. Also, the CVLT-short form and the P(r) VLT are very similar. Thus, classifying patients using the CVLT-short form with outcome assessed with the P(r) VLT may have affected our results. Finally, the results of the current research were obtained on memory clinic patients. Different findings may have emerged using a community based sample. Thus, additional research is required before firm conclusions can be drawn about material-specific episodic memory test performance between non-MCI and MCI subtypes. Despite these limitations, the data reported suggest that visual episodic memory tests in general, and when assessed using the BVMT-R in particular, may be useful in identifying individuals who may be at risk for emergent illness.

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Conflict of Interest

None reported.

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