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Visuospatial Performance in Patients with Statistically-Defined Mild Cognitive Impairment

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Abstract

Background and Objective: The Oblique Effect denotes superior performance for perceiving horizontal or vertical rather than diagonal or oblique stimuli (Appelle, 1972). The current research investigated the Oblique Effect in patients with mild cognitive impairment (MCI).

Research Design and Methods: Four statistically-determined groups were studied; patients with little to no cognitive impairment (non-MCI); subtle cognitive impairment (SCI); amnestic MCI (aMCI); and a combined mixed/dysexecutive MCI (mixed/dys MCI). The Oblique Effect was measured with the Judgment of Line Orientation Test (JOLO). Comprehensive neuropsychological assessment was also obtained. Between-group differences for JOLO oblique and non-oblique test stimuli were analyzed. Hierarchical linear regression models were constructed to identify relations between accuracy for oblique and non-oblique test items and neurocognitive domains.

Results: The mixed/dys MCI group demonstrated lower accuracy for oblique test items compared to non-MCI patients. Accurate responding to oblique test items was associated with better performance on tests measuring executive control, processing speed, naming/lexical

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retrieval, and verbal concept formation. No between-group differences were seen for non-oblique items and these items were not associated with cognition.

Discussion and Implications: Significant impairment on oblique test items distinguished patients with multi-domain/dysexecutive MCI from non-MCI patients. Accurate responding to oblique test items was associated with a complex array of neuropsychological tests suggesting that multidimensional neuropsychological skills underlie the visuospatial reasoning abilities necessary for successful oblique line identification. Research associating the Oblique Effect with additional test paradigms and MRI-defined neuroanatomical regions in MCI may provide more information about the brain-behavior relations that underlie MCI subtypes.

Keywords

mild cognitive impairment; Alzheimer's disease; judgment of line orientation; visuospatial ability; oblique effect

Introduction

Mild Cognitive Impairment (MCI) is considered to be a prodromal state that often precedes the emergence of dementia syndromes such as Alzheimer's disease (AD) and other forms of dementia. Thus, the identification of MCI is a useful for identifying patients who may be at risk for further cognitive decline (Belleville, Fouquet, Hudon, Zomahoun, & Croteau, 2017). Much of the neuropsychological research involving MCI has focused on disorders of episodic memory, language, and executive functions (Epping et al., 2012; Kirova, Bays, & Lagalwar, 2015; Hwang et al., 2017; Libon et al., 2011; McCullough et al., 2019; Saunders & Summers, 2011). However, there has been considerably less research examining deficits associated with visuospatial functions (Jacobs et al., 2015; Mapstone, Steffenella, & Duffy, 2003; Vannini, Almkvist, Dierks, Lehmann, & Wahlund, 2007).

A wide variety of visuospatial functions have been studied in patients with focal cerebral lesions including visual field deficits (e.g., hemianopia), achromotopsia, disorders of motor perception spatial navigation, visual object agnosia, prosopagnosia, simultanagnosia, constructional apraxia, location of objects in space, and topographical orientation (Benton, 1993; Capruso, Hamsher, & Benton, 2006. Depending on task demands, visuospatial dysfunction has been associated with temporal, parietal and occipital injuries. Mishkin, Ungerleider, & Macko, (1983) have divided the visual processing networks into a dorsal "where" network and a ventral "what" network. There are also hemispheric asymmetries in visuospatial processing. For example, right ventral temporal-occipital lesions cause prosopagnosia and left ventral temporal lesions object agnosia and alexia without agraphia.

There has also been considerable research on how focal lesions affect the processing of the direction and orientation of lines (see Benton, 1993 for a review). Consistent with the visuospatial research described above, much of this research links posterior right hemisphere lesions with poor test performance. An emblematic paradigm used to assess how well patients can process the orientation and direction of lines is the Judgment of Line Orientation Test (JOLO; Benton et al., 1994). The JOLO test was constructed, in part, based on observations of right-handed college students who demonstrated left visual field/right

hemisphere superiority in identifying the direction of lines presented to the left and right visual hemifield (Benton, Sivan, Hamsher, Varney, & Spreen, 1994). In addition, Benton and coworkers demonstrated worse JOLO performance in those patients with lesions located in right posterior parietal regions. In contrast, patients with left hemisphere damage perform comparably to controls (Benton et al., 1994; Benton, 1978; Hamsher, Capruso, & Benton, 1992). Ng and colleagues (2001) found that an impairment in JOLO performance can occur in patients with left parietal dysfunction; however a greater impairment was associated with right parietal damage. These researchers suggested that the global-gestalt features of the JOLO stimuli and coordinated spatial relationships are initially processed by the right parietal lobe with a subsequent detailed categorical spatial analysis mediated by the left parietal region.

The Oblique Effect was originally described by Mach (1861) and is an anisotropy characterized by better visuoperceptual accuracy when stimuli are horizontally or vertically (i.e., cardinal) oriented, compared to when these stimuli are diagonally oriented (Kelly & Matthews, 2011). The Oblique Effect has been observed in children, adults and in a wide variety of animals, including invertebrates (Appelle, 1972). Several studies have examined the Oblique Effect assessed with the JOLO test in patients with neurodegenerative conditions such as AD and Parkinson's disease (PD). Ska, Poissant, & Joanette, (1990) compared patients with AD and a normal control group on the basis of errors made on the JOLO test. These researchers reported diagnosis discriminability, such that AD patients sometimes reported a line to be in one quadrant when it was in the other. This kind of error was absent in normal controls. Finton, Lucas, Graff-Radford, & Uitti (1998) administered the JOLO test to patients with AD, Parkinson's disease (PD, and normal controls. The analysis of total number of correct trials found no differences when comparing the AD group to PD or normal controls; however, PD patients scored lower when compared to normal controls. Using the same error nosology developed by Ska and colleagues (1990), it was found that PD patients made more errors on tests trials containing oblique lines compared normal controls. The pattern of errors produced by PD patients was thought to be due to degraded selective attention (Filoteo et al., 1997; Maddox, Fileteo, Delis, & Salmon, 1996). Libon and colleagues (Libon et al., 2007, 2011) reported that patients with Cortical-Basal Syndrome (CBS) were also disproportionally impaired on an abbreviated version of the JOLO test and difficulty on this test was associated with dysfunction of the bilateral posterior temporal-occipital and bilateral parietal-occipital areas of the brain (Avants et al., 2014).

Lamar at al., (2017) used JOLO test to study the Oblique Effect in 107 community-dwelling, non-demented, non-depressed older adults, along with tests measuring executive control and information processing speed. Imaging data was also collected. Increasing number of oblique errors was correlated with worse performance on tests of executive functions. There was no relationship between the production of non-oblique errors and neuropsychological test performance. Moreover, the production of fewer oblique errors was associated with a frontally-mediated structural network that included the left rostral middle and superior frontal gyri.

To our knowledge there has been no research that has described the Oblique Effect in patients with statistically-determined non-MCI and MCI subtypes. In the current research, the Oblique Effect was measured via the standard administration of the Judgment of Line Orientation Test (JOLO) to memory clinic patients diagnosed with non-MCI, subtle cognitive impairment (SCI), amnestic MCI, and a combined dysexecutive/mixed MCI (mixed/dys MCI) subtypes using Edmonds et al., (2014) and Jak, Bondi criteria (2009). Our goals were (1) to determine the presence and severity of the Oblique Effect using the JOLO test, and (2) to determine the relationships between the Oblique Effect and performance on tests measuring executive control, processing speed, naming/lexical retrieval, verbal concept formation, and episodic memory. In prior research, patients with mixed/dys MCI performed worse on executive tests (Emrani et al., 2018). On the basis of these data and the findings reported by Lamar et al., (2017), it is our expectation that mixed/dys patients will produced great numbers of oblique errors compared to other groups.

Methods

Participants

All participants (n= 112; 66.7% female) were recruited from Rowan University, New Jersey Institute for Successful Aging, Memory Assessment Program (MAP). This sample size was deemed sufficient for the analyses described further on based on guidelines for multiple regression described in Tabachnick & Fidell (2013). All these participants presented with subjective cognitive complaints but had preservation of general functional abilities and the absence of dementia. These participants underwent a comprehensive neuropsychological evaluation and evaluations provided by a social worker and a board certified geriatric psychiatrist. In addition, all had either a MRI or CT study of their brain; and appropriate serum blood tests to evaluate for reversible causes of cognitive decline or dementia. A clinical diagnosis was determined at a conference for each patient by an interdisciplinary team. Participants were excluded if there was any history of head injury, substance abuse, or major psychiatric disorders, including major depression, epilepsy, B12, folate, or thyroid deficiency. For all participants, a knowledgeable family member was available to provide information regarding functional status. This study was approved by the Rowan University institutional review board and conducted consistent with the Declaration of Helsinki.

Neuropsychological Assessment

The methods and neuropsychological protocol used to classify patients into non-MCI versus MCI subtype are identical as described by Emrani et al., (2018). Clinical classification regarding MCI subtype versus non-MCI was based on the assessment of three domains of neuropsychological functioning including executive control, naming/lexical access, and verbal episodic memory. As described by Emrani et al., (2018), nine neuropsychological parameters, three from each neurocognitive domain were used to classify patients as presenting with non-MCI versus the MCI subtypes described below. All test scores were expressed as z-scores derived from normative data. The rationale for using the protocol described above was based on prior research showing that these tests are able to illustrate key neurocognitive constructs that differentiate between MCI subtypes (Bondi & Smith, 2014; Libon et al., 2011; Thomas et al., 2018).

Executive Control

This cognitive domain was assessed with three tests including The Boston Revision of the Wechsler Memory Scale-Mental Control subtest (Lamar, Price, Davis, Kaplan, & Libon, 2002), the letter fluency test ('FAS'; Spreen & Strauss, 1990); and the Trail Making Test-Part B (Reitan & Wolfson, 1985). The dependent variable for the Mental Control subtest was the total non-automatized accuracy index (AcI; see Lamar et al., 2002 for full details). The dependent variables obtained from the letter fluency test and Trail Making Test-Part B were the demographically-corrected scores provided by Heaton et al., (2004).

Lexical Access/ Language

This domain was also assessed with three tests, including the 60-item version of the Boston Naming Test (Kaplan, Goodglass, & Weintraub, 1983); a test of semantic ('animals') fluency where participants were asked to produce as many names of animals in 60s excluding perseverations and extra-category intrusion responses (Carew, Lamar, Cloud, Grossman, & Libon, 1997); and the Wechsler Adult Intelligence Scale-III Similarities subtest (Wechsler, 1997), a test that assesses verbal concept formation (Giovannetti et al., 2001). The dependent variables for the Boston Naming Test and 'animal' fluency tests were also obtained from Heaton et al., (2004). The dependent variable obtained from the WAIS-III Similarities subtest was the age-corrected scale score.

Memory and Learning

This cognitive domain was assessed with the 9-word California Verbal Learning Test-short form (Delis, Kramer, Kaplan, & Ober, 2000). This test was scored and administered using standard instructions. The three CVLT-short form variables were used for classification included total immediate free recall, delayed free recall, and the delayed recognition discriminability measure.

Determination of Mild Cognitive Impairment Subtypes

Single and Multi-Domain MCI—Jak, Bondi et al., (2009) criteria were used to determine MCI subtype. Single domain MCI syndromes were diagnosed when participants scored >1.0 standard deviation 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 standard deviation below normative expectations on any of two of the three measures within two or more cognitive domains. On the basis of these procedures 28 patients were diagnosed with single domain amnestic mild cognitive impairment (aMCI), 7 patients were diagnosed with single domain dysexecutive mild cognitive impairment, and 23 were diagnosed with mixed or multi-domain mild cognitive impairment (mxMCI). Because of the small number of dysexecutive MCI patients, a combined mixed/dysexecutive (mixed/dys) MCI subgroup (n= 30) was constructed.

Subtle Cognitive Impairment—Fifteen patients produced neuropsychological test scores where two neuropsychological parameters across different domains of cognitive functioning were below 1.0 standard deviation. These patients were diagnosed with subtle cognitive impairment (SCI) following criteria outlined by Edmonds et al., (2014).

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Non-MCI Group—Among the patients who presented for clinical evaluation 39 patients did not meet either Jak, Bondi et al., (2009) criteria for MCI or Edmonds et al., (2014) criteria for SCI. Some of these patients (n= 20) performed such that all nine neuropsychological parameters were above 1.0 standard deviation. A second group of patients (n= 19) produced tests scores where only 1 of the 9 neuropsychological parameters was below the 1.0 standard deviation cut-off.

Demographic and clinical characteristics including age, education, Mini-Mental State Examination test performance (Folstein, Folstein, & McHugh, 1975), depression assessed using the Geriatric Depression Scale (Yesavage, 1986), Wide Range Achievement Test-IV Reading subtest performance, and instrumental activities of daily living (Lawton & Brody, 1969) are displayed in Table 1. Table 2 described performance on neuropsychological parameters index scores. As can be seen, aMCI patients obtained lower scores on CVLTshort form test. Mixed/dys MCI patients scored lower on executive tests. Patient groups did not differ on age, education, Geriatric Depression Scale scores (Yesavage, 1986), estimated pre-morbid 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). On the Mini-Mental State Examination (F [3, 111]= 7.57, p<.001), non-MCI patients scored marginally higher than aMCI (p<.001) and mixed/dys MCI (p<.015).

Judgment of Line Orientation

The Judgment of Line Orientation Test (JOLO; Benton et al., 1978) is a non-constructional visuospatial measure of spatial perception and orientation. The test consists of 5 sample trials and 30 test trials of two line segments presented above a response-choice display of eleven numbered possible line orientation evenly separated by an 18 degree angle. Patients are asked to identify the orientation of the two-line segments in each test trial by providing the number of the line in the response-choice display that has the same orientation.

There is no single or uniform means by which to operationally-define test stimuli that measure the Oblique Effect. In the current research we followed procedures used by Lamar et al., (20170 and Peven et al., (submitted). Of the 60 JOLO tests test items presented 19 items are considered to be obliquely oriented such that lines fell between 36–54 degrees (i.e., lines 3, 4, 8 & 9) and are the least cardinally-oriented lines. The remaining lines in the display were considered non-oblique. The outcome measures of interest obtained from the JOLO test were (1) the total of correct test trials as traditionally scored (range: 0–30); (2) the total number of correct test stimuli (range: 0–60), (3) the number of correct oblique test items (range: 0–19), and (4) the number of correct non-oblique items (range: 0–41), and (5) percentage of oblique and non-oblique correct responses.

Neuropsychological Index Scores

Index scores of episodic memory, executive functioning and naming/lexical retrieval scores were created by averaging the performance z-scores across all tests within each cognitive domain as described above.

Statistical Analysis

Between and Within-Group Analyses—Demographic differences and performance on the JOLO tests were assessed using 1-way ANOVA with Bonferroni corrections. This method was also used to analyze between-group differences regarding performance for total correct JOLO test trials (range 0–30), total correct JOLO test items (range 0–60), oblique items (range 0–19), and non-oblique items (range (0–41). Missing data were handled with listwise deletion. Co-variates included MMSE test performance and gender as past research suggests that woman generally perform worse than man on visuospatial tests and the JOLO test in particular (Fernandez-Baizan et al., 2019; Gur et al., 2002). Percent of oblique versus percent non-oblique correct responses were also assessed within-group with paired test tests.

Regression Analysis—Three hierarchical linear regression models with block-wise entry of predictors were performed to identify associations between accuracy for oblique and non-oblique items and neuropsychological index scores. Missing data for these analyses were handled with listwise deletion. Neuropsychological index scores were the dependent variable. In Step 1, MMSE and gender were entered into the model. In Step 2, oblique test and non-oblique test items were entered into the model together. The results produced from Step 2 were interpreted to assess for the amount of variance in each neurocognitive domain explained by either oblique and/or non-oblique performance above and beyond the variance explained by MMSE and gender.

Results

Total Performance, Oblique, and Non-Oblique Items on JOLO

No between group differences were found for the total number of trials (range 0–30) or the total number of test items (range 0–60) correctly identified. For oblique test stimuli, mixed/dys MCI patients scored lower than non-MCI patients (M non-MCI= 13.48 ± 3.51; M mixed/dys MCI= 10.66 ± 3.79; p< .029; η^2 = .082). There were no between-group differences for correct number of non-oblique lines. When percent correct oblique versus percentage correct non-oblique responses were assessed within-group all patients groups scored better on non-oblique compared to oblique test stimuli (all p values < .001).

Regression Analyses

In three hierarchical linear regression models, accuracy for oblique and non-oblique lines were used to predict performance for all three neuropsychological domains; executive function, naming/lexical retrieval, and episodic memory. All regressions were constructed using block-wise entry to control for MMSE performance and gender. Table 3 provides a detailed summary of the three regression analyses (Steiger & Fouladi, 1992). Above and beyond MMSE and gender, performance for oblique test items was associated with better performance on indexes measuring executive functioning (F= 13.61., p<.001) and naming/lexical retrieval (F= 14.97, p<.001). Accuracy for non-oblique items was not significantly associated with any neurocognitive domain (p > .05).

Post-hoc Correlations

Simple product-moment correlations (Table 4) assessed which tests within the three neuropsychological domains were associated with oblique test items. Correct oblique responding was associated with better performance on the Mental Control subtest (Mental Control; r= .394, p< .001), the Boston Naming Test (r= .319, p= .001), and the WAIS-III Similarities subtest, r= .376; p< .001).

Discussion

As noted above, in patients with MCI there has been comparatively less research examining non-constructional visuospatial test performance than other cognitive domains. In addition, we are unaware of any research that that has examined non-constructional, visuospatial operations as related to statistically-determined MCI subtypes. Consistent with the results reported by Finton et al., (1998), the between-group differences described above were confined to JOLO test trials containing oblique test items. Also, consistent with our prediction, and the results described by Peven et al., (submitted), accurate responding to oblique test items was associated with better performance on executive tests. Simple correlations found relations between accurate oblique responding and the Mental Control subtest, a test of working memory. Less robust relations were also noted between accurate oblique responding and faster time to completion on the Trail Making Test-Part B and greater output on the letter fluency test. These results suggest that the neurocognitive skills contributing to accurate oblique performance are associated with working memory, information processing speed, and the capacity to sustain a complex mental set.

Unexpectedly, we also found that accurate oblique responding was associated with better performance on language-related tests involving naming and verbal concept formation. Although the JOLO is understood to assess visuospatial operations, all test materials are assigned a verbal label and the mode of responding is verbal. This likely explains the association between accurate oblique responding and better performance on the Boston Naming Test and the Similarities subtest. As pointed out by Peven et al., (submitted), past research has suggested that particularly complex visuospatial tasks are likely mediated by the analytic abilities associated with the left hemisphere (Berlucchi, Brizzolara, Marzi, Rizzolatti, & Umilta, 1979; De Renzi, Faglioni, & Scotti, 1971; Umilta et al., 1974). Thus, depending on the paradigm used to assess the Oblique Effect, naming and higher-order, linguistically-mediate neurocognitive skills appear to contribute to intact responding to oblique test items. The association between oblique responding and language-related skills as described above is also consistent with observations reported by Peven, et al., (submitted) such that oblique responding was associated with structural network modularity between regions within the left frontal lobe.

Two classes of Oblique Effects have been described (Essock, 1980). Class 1 is associated with comparatively basic upstream visual functioning related to acuity and contrast thresholds associated with the processing of visual information in the retina and Brodmann's area 17, the primary visual cortex (Furmanski & Engel, 2000; Kennedy & Orban 1979; Li, Peterson, & Freeman, 2003; Mansfield 1974; Orban & Kennedy 1979, 1981; Vogel & Orban, 1985, 1986; Wang, Ding, & Yunokuchi, 2003). More germane to the current research

is evidence for a class 2 Oblique Effect that is associated with downstream neurocognitive abilities involved in the subsequent processing of visual information, including visuoperceptional and other neurocognitive processes. Support for the class 2 Oblique Effect has come from research involving areas of the brain beyond the primary visual cortex, including Brodmann's area 18 (Liu & Pettigrew, 2003; Wang, Ding, & Yunokuchi, 2003a) and the inferior temporal cortex (Orban & Vogels, 1998). Vidyasagar and Urbas, (1982) found some preference for horizontal and vertical orientation involving the lateral geniculate nucleus (LGN) in cats. Interestingly, this preference remains even after areas 17 and 18 were lesioned. Additional support for the class 2 Oblique Effect has been observed when the recruitment visual cortex is reduced. Matthews, Rojewski, & Cox (2005) observed that, when stimuli were presented successively instead of simultaneously, the Oblique Effect has a larger impact on performance, such that more time was needed to accurately discriminate between differently oriented oblique lines. Additional time was not necessary to achieve a comparable accuracy for cardinally orientated stimuli. Westheimer (2003) demonstrated that the Oblique Effect was observable even in situations in which the line being judged is imaginary. This study observed a prominent Oblique Effect, such that accuracy for judging the angle of the imaginary line as the angle approached 45 and 135 degrees decreased compared to when the line was more cardinally oriented. All of this research suggests that the Oblique Effect is associated with a complex and diverse underlying neurocognitive network both within and outside the primary visual cortex.

Poor oblique responding in mixed/dys MCI patients and the association between oblique responding and executive test performance as described above could also reflect impairment involving the parietal dorsal visual pathways (Avants et al., 2014). This dorsal visual pathway, has been called the "where" pathway by Mishkin and Ungerleider (1982). However, it was Balint (1909; cited in Benton & Tranel, 1993) who reported that this parietal network is important in processing egocentric target location (optic ataxia). In addition, studies with patients who have focal lesions have revealed that right parietal injury most likely impairs performance on the JOLO.

The dorsal stream projects from posterior cortex to prefrontal, premotor, and medial temporal brain regions (Kosslyn et al., 1994; Miskin et al., 1983) and has been shown to be involved in a variety of visually guided neurocognitive operations (Kravitz, 1983). Recent MRI research documents degraded cortical thinning (Noh et al., 2014) and white matter (Brickman et al., 2012, 2013; Brickman, Zahodne, et al., 2015) involving parietal regions in both dementia and MCI patients. Using functional MRI technology, several studies have shown that parietal brain regions are associated with visuospatial operations related to oblique responding. For example, Jacobs et al., (2015) found that recognition of non-canonical objects resulted in increased recruitment of neurocognitive network involving parietal, temporal, and frontal cortical regions. Vannini and colleagues (2007) reported that reaction time and accuracy were similar for MCI patients and controls using an angle discrimination task very similar JOLO test stimuli. However, MCI patients who went on to develop AD demonstrated greater activation in dorsal visual pathways involving the superior parietal brain. Both of these studies suggest the need for compensatory recruitment in order to meet test demands in patients with MCI.

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The functional relationship between performance on the JOLO test and executive dysfunction is not well understood. Frontal-executive dysfunction involving visuospatial working memory skills involving the right frontal lobe might alter performance on this test (Smith et al., 1996, 1998). However, visuospatial working memory as separate from verbal working memory is not commonly tested in patients with MCI or dementia. In addition, when determining the angle of a line, horizontal or vertical lines are often used as references. Patients with frontal executive dysfunction might be impaired regarding their ability to disengage from these standards or be more distracted by these standards. Further research is needed to test these alternate hypotheses.

The current research is not without limitations. First, our sample size was modest. Second, as mentioned, in order to better understand the scope and parameters involving the Oblique Effect in MCI, paradigms other than commonly administered neuropsychological tests should be employed. A major strength of the current research is the use of newly proposed comprehensive diagnostic criteria to classify MCI subtype. Also, the current research suggests that paradigms assessing for an Oblique Effect may have considerable clinical utility in identifying MCI patients with multi-domain and/or dysexecutive impairment. In sum, in addition to performance on executive, episodic memory, and language tests, visuospatial operations measuring the Oblique Effect may be an important neurocognitive construct that can differentiate between MCI subtypes.

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Table 1:

Demographics and Judgment of Line Orientation Performance (means and standard deviations)

	non-MCI (N=39)	SCI (N=15)	aMCI (N=29)	mixed/dys MCI (N=33)	Significance
Age	74.54 (7.09)	77.13 (8.33)	74.18 (5.86)	74.67 (5.52)	ns
Education	14.97 (2.81)	15.47 (2.53)	13.61 (2.69)	14.90 (2.54)	ns
MMSE	28.59 (1.48)	27.20 (1.61)	26.46 (2.35)	27.17 (2.00)	aMCI < non-MCI; p< .001; mx/dys MCI < non-MCI; p= .02
GDS	3.23 (3.13)	2.27 (1.83)	3.14 (2.40)	3.20 (2.64)	ns
WRAT Reading	113.38 (16.59)	115.13 (16.07)	112.14 (15.10)	108.37 (17.06)	ns
IADL	15.51 (2.21)	14.40 (2.35)	14.66 (2.98)	14.67 (2.70)	ns
JOLO parameters	-		-		-
Total Correct (0-60)	51.56 (5.79)	50.47 (4.61)	49.39 (6.96)	47.37 (7.02)	mixed/dys MCI < non-MCI; p= .04
Total Score (0-30)	22.62 (5.14)	22.00 (4.00)	21.07 (6.09)	19.40 (5.56)	ns
Correct Oblique (0-19)	13.49 (3.52)	12.67 (3.52)	12.57 (3.60)	10.67 (3.80)	mixed/dys MCI < non-MCI; p= .01
Correct Non-Oblique (0–41)	38.08 (2.99)	37.80 (1.90)	36.82 (4.16)	36.70 (4.02)	ns
Percent Oblique Correct responses (0– 19)	75.26 (16.12)	68.42 (15.78)	68.88 (17.73)	58.53 (20.17)	correct oblique responses < correct
Percent Non-Oblique Correct responses (0– 41)	93.66 (6.09)	92.03 (4.91)	92.15 (8.95)	88.98 (10.10)	non-oblique responses, p< .001, all groups, within group t-tests

MMSE= Mini-Mental State Examination; GDS= Geriatric Depression Scale; WRAT-IV= Wide Range Abilities Reading Subtest; IADL= Instrumental Activities if Daily Living; JOLO= Judgment of Line Orientation Test; non-MCI= non-mild cognitive impairment; SCI= subtle cognitive impairment; aMCI= amnestic mild cognitive impairment; mixed/dysMCI- mixed/ dysexecutive mild cognitive impairment.

Table 2:

Neuropsychological Test Performance (z-scores; means and standard deviations)

Neuropsychological Test Scores	non-MCI (n= 39)	SCI (n= 15)	aMCI (n= 28)	mx/dys MCI (n=30)	significance
Executive Functioning Index	0.05 (0.49)	-0.32 (0.26)	-0.23 (0.48)	-1.11 (0.76)	mixed/dys MCI < all groups; p< .001
Naming/Lexical Retrieval Index	0.17 (0.55)	-0.32 (0.50)	-0.19 (0.54)	-0.90 (0.78)	mixed/dys < non-MCI & aMCI; p< .001 mixed/dys MCI < SCI; p= .02
Memory Index	0.21 (0.62)	-0.61 (0.48)	-1.45 (0.44)	-0.73 (0.90)	aMCI < all group; p .001 mixed/dys MCI < non-MCI; p< .001

non-MCI= non-mild cognitive impairment; SCI= subtle cognitive impairment; aMCI= amnestic mild cognitive impairment; mx/dysMCI- mixed/ dysexecutive mild cognitive impairment.

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	lable 5.		

Domains of Cognition Index Performance Hierarchical Regression Analysis Summary

Executive Function 1 MMSE	*								
MMSE	.08	[.00, .19]	.08*	[.00, .19]					
					.10**	.03	[03, .16]	.28	.08
Sex					10	.14	[37, .17]	07	00.
2	23 ***	[.08, .35]	15 ***	[.03, .26]					
Oblique					.08	.02	[04, .12]	.39	.11
Non-Oblique					.01	.02	04, .05]	.04	00.
Naming/Lexical Retrieval 1	** 60 [.]	[.01, .20]	** 60°.	[.01, .20]					
MMSE					*80.	.03	[.01, .14]	.22	.05
Sex					35 *	.14	[63,07]	23	.05
7	21 ***	[.07, .33]	12 **	[.01, .22]					
Oblique					.08	.02	[04, .12]	.42	.11
Non-Oblique					03	.02	[08, .01]	16	.01
Episodic Memory 1	28 ***	[14, .42]	.28 ***	[14, .42]					
MMSE					.22 ***	.04	[14, .29]	.49	.23
Sex					44 **	.16	[-75,13]	23	.05
2	29 ***	29^{***} [13, .41]	.01	[.00, .03]					
Oblique					.02	.03	[-03, .07]	.07	00.
Non-Oblique					03	.03	[09, .02]	13	.01

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Mental Control	r= .394, p< .001
Trail Making Test-Part B	r= .238, p< .011
Letter fluency ('FAS')	r= .243, p< .010
Boston Naming Test	r= .319, p< .001
Similarities subtest	r= .379, p< .001
'animal' fluency	r= .188, p< .047
CVLT — Immediate Free Recall	r= .074, ns
CVLT — Delay Free Recall	r= .149, ns
CVLT — Delay Recognition	r= .003, ns

ns= not significant; CVLT= California Verbal Learning Test- Short Form