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Visuoconstructional Impairment in Subtypes of Mild Cognitive Impairment

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Abstract

Clock Drawing Test performance was examined alongside other neuropsychological tests in mild cognitive impairment (MCI). We tested the hypothesis that clock-drawing errors are related to executive impairment. The current research examined 86 patients with MCI for whom, in prior research, cluster analysis was used to sort patients into dysexecutive (dMCI, n=22), amnestic (aMCI, n=13), and multi-domain (mMCI, n=51) subtypes. First, principal components analysis (PCA) and linear regression examined relations between clock-drawing errors and neuropsychological test performance independent of MCI subtype. Second, between-group differences were assessed with analysis of variance (ANOVA) where MCI subgroups were compared to normal controls (NC). PCA yielded a 3-group solution. Contrary to expectations,

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clock-drawing errors loaded with lower performance on naming/lexical retrieval, rather than with executive tests. Regression analyses found increasing clock-drawing errors to command were associated with worse performance only on naming/lexical retrieval tests. ANOVAs revealed no differences in clock-drawing errors between dMCI versus mMCI or aMCI versus NCs. Both the dMCI and mMCI groups generated more clock-drawing errors than the aMCI and NC groups in the command condition. In MCI, language-related skills contribute to clock-drawing impairment.

Keywords

Boston process approach; clock drawing; cluster analysis; executive control; mild cognitive impairment; visuoconstruction

Introduction

Mild cognitive impairment (MCI) is thought to be a prodromal neurocognitive condition leading to the eventual emergence of dementia (Petersen, 2004). Neuropsychological assessment plays a key role in identifying patients with suspected MCI (Schmand et al., 2014). Several common clinical diagnostic criteria for the diagnosis of MCI have been proposed (Petersen, 2004; Winblad et al., 2004). Recently, literature has emerged using person-centered statistical modeling techniques to classify patients with MCI (see Bondi & Smith, 2014, for a review). Research using person-centered statistical modeling techniques to classify patients with MCI has generally been consistent in that patients with single-domain (amnestic/dysexecutive) as well as multi-domain syndromes can be identified (Delano-Wood et al., 2009; Libon et al., 2010). An advantage to using statistical modeling versus clinical criteria to diagnose and classify MCI subtypes is its objectivity (Bondi & Smith, 2014; Eppig et al., 2012; Libon et al., 2011).

Visuoconstructional impairment has long been recognized as an early feature of Alzheimer disease (Freeman et al., 2000; Mendez, Mendez, Martin, Smyth, & Whitehouse, 1990) and a significant predictor of patients with a rapid rate of disease progression (Buccione et al., 2007). Moreover, the parietal lobe is considered central in subserving the ability to assemble and draw objects (Critchley, 1953). Recent structural neuroimaging evidence emphasizes early temporoparietal involvement in early Alzheimer's disease (Mosconi et al., 2004; Whitwell et al., 2008). Visuoconstruction incorporates a wide array of neurocognitive abilities including the ability to coordinate fine motor skills, ability to understand visuospatial relationships, as well as planning and executive function skills (see Benton &Tranel, 1993, for a review). Visuoconstruction is commonly tested using block construction tests and tasks requiring the reproduction of geometric figures such as the Rey Osterreith Complex Figure (ROCF; Freedman et al., 1994; Rey, 1941) and the Clock Drawing Test (CDT). Indeed, performance obtained on the CDT has been shown to correlate with a wide array of neuropsychological tests (Cosentino, Jefferson,Chute, Kaplan, & Libon, 2004; Libon, Swenson, Barnoski, & Sands, 1993, Libon, Malamut, Swenson, Sands, & Cloud, 1996).

There has been considerably less research examining visuoconstructional deficits associated with MCI. De Jager, Hogervorst, Combrenck, and Budge (2003), used the CDT (CLOX;

Royall, Cordes, & Polk, 1998) and found that patients with MCI were significantly impaired compared with controls. Moreover, performance on this task allowed for reliably discriminating between participants with MCI and those with Alzheimer disease. Similarly, Thomann, Toro, DosSantos, Essig, and Schroder (2008) showed significant stepwise impairment in clock drawing between healthy controls, patients with MCI, and patients with Alzheimer disease, whereby all three patient groups significantly differed from each other. However, forging links between impaired performance on visuoconstructional tests such as the CDT and MCI is not necessarily straightforward. As noted earlier, like most, if not all, neuropsychological measures, tests assessing visuoconstruction, such as the CDT, rarely depend on one unitary cognitive function, but they require the integrity of a number of neurocognitive abilities (Benton & Tranel, 1993).

Although temporal-parietal regions of the brain are often associated with visuospatial/ visuoconstructional test performance, executive functioning has been shown to play a key role regarding successful performance on visuoconstructional tests. For example, Johnson, Gustafson, and Reisberg (1996) observed an association between impairment on block construction tasks and decreased cerebral blood flow to the frontal lobe. Similarly, Ober, Jagust, Koss, Delis, and Friedland, (1991) showed an increased anterior, compared with posterior, association with figure copy tasks in patients with Alzheimer disease. Impairment on executive tests has been correlated with errors produced on the CDT (see Cosentino et al., 2004; Libon et al., 1993, 1996, for a review).

Interestingly, previous research has also suggested that deficits associated with language and semantic memory contribute to deficits in clock drawing seen in dementia. Libon et al. (1996) found impairment on the Boston Naming Test (BNT) to be related to the production of clock-drawing errors to both command and copy. In a voxel-based morphometry study, Thomann et al. (2008) found that impaired clock drawing in patients with MCI and Alzheimer disease was associated with decreased grey matter densities in a number of frontal, parietal, and temporal structures. However, after correction for multiple comparisons, impaired clock drawing was significantly correlated only with reduced grey matter density in the medial-temporal lobe and temporal neocortex. These data are intriguing and suggest that impaired semantic memory, implicated by damage to these structures, may contribute to the retrieval of item and feature knowledge of a clock, knowledge that is necessary for successful task completion. Indeed, Caine and Hodges (2001) found that patients with minimal cognitive impairment (considered analogous to MCI based on a Mini Mental State Examination [MMSE] score >24 at presentation), as well as those with mild Alzheimer disease showed visuospatial deficits and impaired episodic memory but no semantic memory impairment (Ahmed, Arnold, Thompson, Graham, & Hodges, 2008). Although not specific to visuoconstruction, these findings suggest that circumscribed parietal damage, as well as cognitive abilities mediated by the parietal lobe, can occur early in the disease process (Murray et al., 2011), perhaps before well recognized impairment in declarative memory.

In the current research we studied a group of patients with MCI, for whom in prior research, cluster analysis was used to classify patients into amnestic (aMCI), dysexecutive (dMCI), and multi-domain MCI (mMCI) subtypes (Eppig et al., 2012; Libon et al., 2011). The relationship between clock-drawing errors and neuropsychological performance was investigated using a variety of statistical techniques. Our first goal was to determine how clock drawing errors are related to neuropsychological test performance independent of cluster subtype. This question was addressed with principal components analysis (PCA) where neuropsychological test performance, including clock drawing errors, was included in the solution. This same question was also addressed using linear regression analyses where clock errors were the dependent variables and neuropsychological test performance was employed as the independent variable. On the basis of prior research suggesting that visuoconstructional tests require considerable executive resources, we predicted that clock-drawing errors would load most strongly with executive tests.

Second, we addressed the association between clock-drawing errors and MCI subtypes. Cluster-determined MCI subtype and a normal control (NC) group were used as grouping variables, and relations between clock-drawing errors and MCI subtype were assessed with analysis of variance (ANOVA). We expected that MCI subgroups would show a stepwise impairment in visuoconstruction such that the dMCI subgroup would produce more clock-drawing errors than the other MCI subgroups. The analysis of the cognitive constructs that underlie MCI and MCI subtypes may lead to better diagnostic algorithms for this important neurocognitive disorder.

Materials and Methods

Participants

The sample included 129 non-demented older adults, grouped according to cognitive status (MCI, n=86; NC, n=43). The clock-drawing protocols analyzed in the current research were collected prospectively and were part of the neuropsychological protocol previously described by Eppig et al. (2012) and Libon et al. (2011). The diagnosis of MCI was determined using (a) criteria established by Petersen and Morris (2005) including subjective complaints of a decline in cognitive functioning and a score of ≥24 on the MMSE (Folstein, Folstein, & McHugh, 1975); (b) no impairment in activities of daily living (score 6/6; Lawton & Brody, 1969) and instrumental activities of daily living (score 15/17); and (c) performance at 1.5 standard deviation units below normative values on any single neuropsychological test as described by Libon et al. (2010, 2011). All patients with MCI were recruited on the basis of self-referral to an outpatient, university-affiliated memory clinic. Participants with MCI were ambulatory, medically well and stable, and living independently in the community on the basis of self-report and/ or information provided by a family member. All NC participants obtained scores on the MMSE ≥27 and obtained scores on the Geriatric Depression Scale (Yesavage et al., 1982) < 9. Informed consent was obtained consistent with institutional review board regulations and the Declaration of Helsinki.

Neuropsychological Protocol

As described by Eppig et al. (2012), the neuropsychological protocol was administered to all participants. Tests were chosen to assess three neurocognitive domains: executive control, naming/lexical retrieval, and declarative memory.

Executive control was assessed with serial order recall from the Backward Digit Span Test (BDT; see Lamar et al., 2007, 2008, for full details regarding test construction). Serial order recall tallies the total number of digits correctly recalled in accurate serial position divided by the total possible correct and multiplied by 100, ([total # correct digits SERIAL-ORDER]/[total possible correct] × 100). This variable is believed to measure executively demanding aspects of working memory associated with mental manipulation such as disengagement and temporal reordering (Hurlstone, Hitch, & Baddeley, 2013; Lamar et al., 2007, Lamar, Catoni, Price, Heilman, & Libon, 2008). Executive control was also assessed with tests of letter fluency (letters "FAS"; Carew, Lamar, Cloud, Grossman, & Libon, 1997). On the letter fluency test, participants were given 60 s to generate words, excluding proper nouns, beginning with a specified letter. The dependent variable was the number of responses summed across each letter.

Lexical retrieval/ naming abilities were assessed with the 60-item version of the BNT (Kaplan, Goodglass, & Weintraub, 1983) and a test of semantic fluency ("animals"). The dependent variable derived from the BNT was the number of correct responses. On the "animal" fluency test, patients were given 60 s to generate exemplars (Carew et al., 1997). The dependent variable was the total number of responses excluding perseverations and intrusion errors.

Declarative memory was assessed with the Philadelphia (repeatable) Verbal Learning Test (P[r]VLT; see Price et al., 2009, for full details regarding test construction). The P(r)VLT is a 9-word serial list-learning test modeled after the California Verbal Learning Test (CVLT; Delis, Kramer, Kaplan, & Ober, 1987). The administration of the P(r)VLT is identical to the original 16-word CVLT and the 9-word experimental version of the CVLT (Delis et al., 1987). Two P(r)VLT variables were used in the current research - total delayed free recall and a delayed recognition discriminability index. The latter index was calculated using the algorithm originally described by Delis et al. (1987; [1 − (false positive + misses/ # possible correct) × 100]). The rationale for using these P(r)VLT indexes is based on research associating performance on these test conditions and volume of the hippocampus (Libon et al., 1998). The three statistically determined MCI subgroups and the NC group did not differ for age or education. The NC group produced a small but statistically higher score on the MMSE (Folstein, Filstein, & McHugh, 1975) compared with the three MCI groups, $F(3, 169)= 20.87$; $p < .001$. There were no differences on the MMSE between the three statistically determined MCI groups (Table 1). No gender differences were found for demographic variables.

The Clock Drawing Test

The CDT was administered according to procedures originally described by Goodglass and Kaplan (1982). All participants were asked to "draw the face of a clock, put in all of the numbers, and set the hands for 10 after 11." The "10 after 11" time setting was utilized for its sensitivity to detecting neurocognitive dysfunction (see Freedman et al., 1994, for a review). After the command condition was completed, a copy condition was administered. Errors to command and copy were scored separately using a 10-point scale ranging from 0 (best performance) to 10 (worst performance) for each condition. These criteria were based on a clock scoring system originally described by Rouleau, Salmon, Butters, Kennedy, and McGuire, (1992) and subsequently adapted by Libon et al. (1996). Each error received a score of either 1 (i.e., present) or 0 (i.e., absent). Full details regarding this system for scoring clock-drawing errors can be found in Libon et al. (1996). The sum of command and copy clock-drawing errors obtained from all participants with MCI and NC participants was symmetrically distributed (M= 3.60, median= 4.00, mode= 5.00, skew=.466; Table 3).

Statistical Analysis—The relations between clock-drawing errors and neuropsychological test performance were assessed with two sets of analyses. The first group of analyses sought to assess clock-drawing errors independent of MCI subtype. This was done using a PCA with Varimax rotation. The variables used in this analysis were the group of six neuropsychological variables described earlier plus total clock-drawing errors generated in both the command and copy test conditions. Only participants with MCI were studied in this analysis. The relations between clock-drawing errors to command and copy and neuropsychological performance independent of MCI subtype were also assessed with two regression analyses. In both analyses, clock-drawing errors were the dependent variables. To limit the number of analyses conducted, three neuropsychological indexes were created: the Executive Index,

Lexical Retrieval/ Naming Index, and Declarative Memory Index—The three neuropsychological indexes were constructed by first calculating z scores on the basis of NC test performance and then averaging the two tests from each of the three neuropsychological domains as described in the "Methods" section. The second group of analyses employed ANOVAs followed by Tukey post-hoc tests to evaluate for group differences between the three statistically determined MCI subgroups and NCs in clock drawing to command and clock drawing to copy. Significance was set at $p < .01$.

Results

Clock Drawing Errors and Neuropsychological Test Performance

As displayed in Table 2, the PCA yielded a three-factor solution accounting for 62.34% of the variance in the model. Factor 1 contained both executive tests where relatively intact BDT serial recall was related to increasing output on the letter fluency test. However, a positive factor loading for the "animal" fluency test was also observed on this factor. Factor 2 can be described as a combined naming/lexical retrieval and clock-drawing factor. The inverse relationship with positive factor loading from both clock-drawing variables along with the negative factor loading from the BNT and "animal" fluency test suggest increasing clock-drawing errors were associated with poorer BNT and "animal" fluency performance. Finally, Factor 3 contained positive loadings from both P(r)VLT memory test parameters.

Regression Analysis

Two linear regression analyses were conducted associating clock-drawing errors to command and copy (dependent variable) and the Executive, Naming/ Lexical Retrieval, and Declarative indexes described earlier. For the command test condition, increasing errors were uniquely associated with worse performance only on lexical retrieval/ naming tests

(R=.373, R= .139, df=3, 82, F=4.42, $p < .006$, beta= −0.321, $p < .005$). Other neuropsychological indexes did not enter the model. The regression analysis for the copy test condition was not significant.

Clock Drawing Errors and MCI Subtypes

Analyses of between-group differences were carried out, examining for differences between the NC and the three MCI groups. Statistical differences were found for clock-drawing errors to command, $F(3, 125)=7.66$, $p < .001$, clock-drawing errors to copy, $F(3, 125)= 4.60$, $p < .004$, and total clock-drawing errors, $F(3, 125)= 7.85$, $p < .001$. Post-hoc (Tukey test) analysis for errors produced in the command condition found no difference between participants with dMCI and mMCI, although both groups produced more errors than participants with aMCI and NC participants (dMCI vs. aMCI, $p < .011$; dMCI vs. NC, $p < .006$; mMCI vs. aMCI, $p < .011$; mMCI vs. NC, $p < .003$). In the copy test condition, there was only a statistical trend suggesting participants with dMCI and mMCI produced more errors than NC participants (dMCI vs.NC, $p < .029$; mMCI vs. NC, $p < .024$). No gender-related differences were found.

Distribution of Clock-Drawing Errors

Libon et al. (1996) constructed three clock-drawing subscales scoring graphomotor errors: errors involving hand placement, errors involving number placement, and executive errors. Complete descriptions of all errors and the three clock error subscales are listed in Table 3. Because of possible restriction of range, nonparametric analyses were used to assess for between-group differences. Omnibus Kruskal-Wallis analysis for both command, $X^2(3)= 25.37$, $p < .001$, and copy, $X^2(3)= 10.97$, $p < .012$, test conditions were significant only for errors involving hand/ number placement.

Command condition—Pairwise comparisons were undertaken using Mann-Whitney tests. The dMCI and mMCI groups did not differ for any comparison. Both participants with dMCI and mMCI generated more errors than other groups (dMCI vs. aMCI, U= 51.50, z = −3.33, $p < .001$; dMCI vs. NC, U= 201.50, z= −4.04, $p < .001$; mMCI vs. aMCI, U= 175.00, z = −2.77, $p < .006$; mMCI vs. NC, U= 638.00, z= −3.67, $p < .001$).

Copy test condition—Pairwise comparisons revealed no differences when the dMCI and mMCI groups were compared. However, participants with dMCI generated more errors than other groups (dMCI vs. aMCI, U= 69.50, z= −2.65, p< .008; dMCI vs. NC, U= 2.84, z= −2.75, p< .006). For participants with mMCI, there were statistical trends suggesting more rrors than for other groups (mMCI vs. aMCI, U= 35.02, z= −1.81, p< .069; mMCI vs. NC, U= 896.00, z= −1.75, p< .079).

Discussion

In the current research, visuoconstruction was assessed with the CDT. Our first goal was to assess how clock-drawing errors are related to cognitive impairment in MCI independent from MCI subtype or clinical diagnosis. Our prediction was that increasing clock-drawing errors would load with poorer performance on tests tapping executive functioning. Contrary to our hypothesis, we found that increasing clock-drawing errors loaded with poorer performance on language tests that assess naming/lexical retrieval. Similar results were obtained from linear regression analyses where increasing clock errors in the command condition were associated with worse performance on naming/lexical retrieval tests.

It should be mentioned that Factor 1 obtained from the PCA described earlier indicated better performance on the “animal” fluency test (reflected by the positive factor loading) along with better performance on other executive tests. However, on Factor 2, animal” fluency output yielded a high but negative factor loading along with a negative loading obtained on the BNT and increasing command/ clock errors. The cross loadings for “animal” fluency output might be explained by the multi-dimensional nature of this test. While executive ability is necessary to generate output (Factor 1), the negative factor loading for “animal” fluency output seen on Factor 2 might reflect limited ability for lexical or semantic organization of the output that is generated. This dissociation between “animal” fluency output and concomitant semantic organization has been demonstrated in patients with dementia (Carew et al., 1997; Libon et al., 2014). A similar situation could be present in patients with MCI. Further research is necessary to test these hypotheses.

In the current research, we found that participants with dMCI and mMCI made more clock hand/number placement errors than did other groups, but the dMCI and mMCI groups did not differ on this measure. Unfortunately, the scoring system used to assess clock-drawing errors in the current research does not necessarily suggest the reason(s) for these findings. For patients with mMCI, several language-related mechanisms, acting in concert, might underlie these findings. First, it is possible that patients with mMCI might have subtle difficulty accessing clock-related semantic features as demanded by our test procedures. A second possibility is that patients with mMCI may have difficulty in disambiguating the syntactically complex proposition to set the clock hands to “10 after 11.” The notion that subtle language-related deficits underlie problems with clock drawing in MCI is consistent with data reported by Leye, Saur, Eschweiler, and Milian (2009). In their research, patients with MCI were not significantly impaired on the CDT overall. However, using a specifically developed clock questionnaire, they found that patients with MCI were significantly impaired in semantic knowledge of the relationship between the hour and minute hands when asked to set different times. Future research examining clock-drawing errors using a wider array of executive and language-related tests, including measures that assess comprehension of grammar and syntax, may help clarify these issues.

The results of the current research might also be interpreted as supporting the existence of a distinct visuospatial MCI subtype as described by Clark et al. (2013). However, it is likely the case that visuospatial/ visuoconstructional tests, as is the case with other domains of neuropsychological functioning, do not represent a single underlying cognitive construct. One of the unique features of the CDT is that the test, regardless of specific scoring procedures, is rich in semantic features. The various semantic attributes associated with clock drawing might explain why clock-drawing errors in the current research were highly related to language-related tests. An equally rich semantic network is likely not associated with other commonly used visuoconstructional tests such as block construction and complex figure copy. Thus, although our results are intriguing, different findings may have emerged if other less semantically rich visuospatial/visuoconstructional tests had been used.

A second goal of our study was to assess for between-group differences between MCI subtypes and NCs. Indeed, a key advantage of this study was the statistical determination of MCI subtypes using a core group of well researched neuropsychological tests (Libon et al., 2010, 2014). Thus, MCI subtypes were determined empirically using neurocognitive constructs well known to be affected in both dementia and MCI (Bondi & Smith, 2014; Libon et al., 2014). Previous research has shown evidence for the presence of both single-domain impairments (i.e., amnestic and dysexecutive) and multi-domain MCI subtypes (Delano-Wood et al., 2009; Libon et al., 2010). In the current research, our mMCI group was characterized primarily by language and memory deficits, a finding that is partially consistent with guidelines previously suggested by other researchers (Petersen et al., 2009; Winblad et al., 2004).

Interestingly, results obtained from both between-group ANOVAs demonstrated that the NC and aMCI groups made few clock-drawing errors and did not differ from each other. By contrast, both the mMCI and dMCI groups produced more clock-drawing errors than other groups. This pattern of performance is compelling in that impairment in visuoconstruction has long been recognized to be an important feature of Alzheimer disease (Mendez, Mendez, Mantis, Smythe, & Whitehouse, 1990) due, perhaps, to the presumption of parietal-lobe involvement. On the basis of prior research, it may have been reasonable to have expected that the aMCI group (i.e., patients thought to represent a prodrome of Alzheimer disease) would have demonstrated significant visuoconstructional or clock-drawing impairment. This was not the case. One reason for this may have been that the CDT was too easy for patients with focal impairment in the disease process where cognitive functioning was typically outside of declarative memory processes (Alladi et al., 2006). This is consistent with studies showing that visuoconstructional impairment evolves with the progression of disease (Guerin, Belleville, & Ska, 2002). More taxing tests such as the Wechsler Block Design or ROCF (i.e., tests that do not necessarily provide the patient with a familiar or semantically rich context) may have revealed a different pattern of deficits.

The dMCI and mMCI groups were equally impaired on both clock-drawing indexes suggesting pathology involving a complex cortical network subserving diverse neurocognitive abilities including visuoconstruction, language-related skills, and declarative memory. As suggested earlier, constructs underlying the production of clock-drawing errors in either group could be different. While our results suggest that language-related deficits typified by lexical retrieval/ naming and memory deficits might underlie clock-drawing errors in patients with mMCI, other neurocognitive problems could be responsible for clock-drawing errors generated by patients with dMCI. For example, the production of clock-drawing errors among patients with dMCI might implicate problems with the central executive and mental planning components of the test. Royall, Cordes, and Polk (1998) suggested that the command and copy conditions produce differing demands on executive control and "purer" visuoconstructional ability, respectively. However, this conclusion is not supported by others (Cosentino et al., 2004; Libon et al., 1996) who have shown that errors produced in the copy test condition were associated with visuoconstructional impairment as determined by the MMSE Interlocking Pentagons task.

Importantly, our results show a novel relationship between clock-drawing errors and problems on naming/ lexical retrieval tests. This finding is consistent with the few existing studies that have emphasized the role of semantic knowledge in the expression or representation of time as assessed with the CDT (Leyhe et al., 2009; Libon et al., 1993, 1996). Libon et al. (1996) found that performance in the command condition correlated with neuropsychological tests of semantic memory and language, whereas copy test performance was associated with executive and visuoconstructional measures. These findings are in accordance with evidence for significant semantic memory impairment in preclinical Alzheimer disease (Delano-Wood et al., 2009) as well as more recent evidence suggesting impaired lexical retrieval in preclinical Alzheimer disease (Ahmed et al., 2013). Other research examining performance on verbally mediated executive tests has clearly linked better performance on executive tests with relatively good performance on the BNT and the “animal” fluency tests, the language-related measures used in the current research (Bondi et al., 2002). Lou (1999) has also suggested that the alterations in response set can occur when verbally mediated executive tests require language-related abilities (Ahmed et al., 2013; Weakley, Schmitter-Edgecombe, & Anderson, 2013).

To summarize, visuoconstructional ability as examined by the CDT is not a unitary process. A variety of neurocognitive mechanisms are engaged to complete the task, suggesting the presence of complex underlying cognitive/ neuropathological relationships. Most convincingly, the simple CDT is useful in predicting salient language-related impairment and is sensitive to multidomain impairments in memory, language, and visuoconstruction. Based on the high probability of progression to Alzheimer disease in both aMCI and mMCI groups (Morris et al., 2001; Petersen et al., 2001), the latter finding may have clinical implications for disease staging, given that patients with aMCI remained unimpaired on this task. Although the findings described here are compelling in suggesting a role for simple tests of visuoconstruction to assess impairments in specific cognitive functions in MCI subtypes, several limitations must be acknowledged. First, the results may have differed if other neuropsychological tests assessing executive control as well as visuospatial operations were included. Future research would profit by including a greater number of tests within each neurocognitive domain that is assessed. Moreover, although education did not differ between our groups, general intellectual capacities as related to access to semantic attributes associated with clock drawing should be explored in future research. Third, the current research used clock-drawing procedures as described by Goodglass and Kaplan (1982). Different findings may have emerged if different clock-drawing administration procedures had been used. Fourth, given that we do not have pathological and/ or neuroradiological data, we are precluded from drawing firm inferences regarding the neuroanatomic substrates of visuoconstruction deficits across the different MCI phenotypes. Further work is needed to address these questions.

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Table 1

Demographic Information and Clock Drawing Test (Means, Standard Deviation)

	Multidomain MCI	Dysexecutive MCI	Amnestic MCI	Normal Controls
Demographics				
Age	71.29	74.60	69.53	73.07
	(9.36)	(9.73)	(8.53)	(7.42)
Education (years)	13.78	12.52	13.94	13.61
	(2.38)	(2.45)	(2.58)	(2.58)
MMSE	27.27	26.96	26.53	28.91
	(1.71)	(1.76)	(1.92)	(1.23)
Clock Drawing Test				
Command errors	2.31	2.45	1.23	1.48
	(1.30)	(1.01)	(0.72)	(0.98)
Copy errors	1.92	2.09	1.15	1.21
	(1.38)	(1.10)	(1.06)	(0.90)
Total errors	4.19	4.45	2.38	2.75
	(2.15)	(1.73)	(1.60)	(1.75

MCI= mild cognitive impairment; MMSE= Mini Mental State Examination.

Table 2

Principal Components Analysis

	Factor 1	Factor 2	Factor 3
	Executive Tests	**Clock Drawing/Naming/ Lexical Retrieval Tests**	**Memory Tests**
BDT total serial order	**.733**	.128	−.211
Letter fluency	**.810**	−.110	−.046
"Animal" fluency	.586	**–.430**	.366
Boston Naming Test	.051	**–.701**	.043
P(r)VLT Delay Free Recall	.043	.051	.868
P(r)VLT Delay Recognition			
Discriminability	−.369	.156	.727
Clock total command errors	−.123	**.801**	.082
Clock total copy errors	.102	**.569**	.341
Eigenvalue	2.20	1.46	1.31
Percent variance explained	27.53	18.33	16.47

BDT= Backward Digit Span; P(r)VLT= Philadelphia (repeatable) Verbal Learning Test.

Table 3

Clock Scoring Criteria

Graphomotor Errors	
1	Clock size: In the command condition, a clock drawing was judged to be small if diameters were equal to or less than 34 mm or equal to or greater than 102 mm. In the copy condition, the cut scores were 39 mm and 73 mm, respectively. If one diameter was within the prescribed cutoff but the other diameter was slightly smaller or larger, the clock drawing was still judged to be small or large if the other diameter did not exceed the prescribed cutoff by more than 5 mm. 1. Clock size: In the command condition, a clock drawing was judged to be small if diameters were equal to or less than 34 mm or equal to or greater than 102 mm. In the copy condition, the cut scores were 39 mm and 73 mm, respectively. If one diameter was within the prescribed cutoff but the other diameter was slightly smaller or larger, the clock drawing was still judged to be small or large if the other diameter did not exceed the prescribed cutoff by more than 5 mm.
2	Shape of the clock face: clock face imprecisely drawn (i.e., face is oval or asymmetric, lopsided, or otherwise fragmented). 2. Shape of the clock face: clock face imprecisely drawn (i.e., face is oval or asymmetric, lopsided, or otherwise fragmented).
Errors in Hand/Number Placement	
1	Hands shifted either to one side or to the top/bottom or hands did not meet in the middle.
2	All numbers between 1 and 12 were not present or numbers were written in a form other than Arabic or Roman numerals.
3	Neglect of one side or quadrant or numbers in either side or quadrant were pulled away from the face regardless of their location within the clock face.
4	Deficits in spacing of the numbers: gaps between the numbers 12, 3, 6, 9, or numbers irregularly placed or otherwise not in their proper location.
5	One or more numbers written at least halfway outside of the clock face.
Executive Control Errors	
1	Turning the paper while writing the numbers.
2	Numbers written in counterclockwise order regardless of deficits in spatial layout or location within the clock face.
3	Perseverations: writing numbers beyond or in addition to the number 12 or drawing multiple hands with or without numbers present or perseverations in drawing the clock face.

Criteria for Evaluating Clock Drawing (Libon et al., 1996)