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Which figure copy test is more sensitive for cognitive impairment in Parkinson's disease: Wire cube or interlocking pentagons?

Jane E. Alty [a,b,*], Jeremy Cosgrove [a,b], Stuart Jamieson [a,b], Stephen L. Smith [c], Katherine L. Possin [d,**]

[a] University of York, Hull York Medical School, York, UK
[b] Department of Neurology, Leeds Teaching Hospitals NHS Trust, Leeds, UK
[c] Department of Electronics, University of York, York, UK
[d] University of California – San Francisco, USA

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ABSTRACT

Background: Performance on figure copy tests has been shown to predict progressive cognitive decline in Parkinson's disease (PD). Historically, the interlocking pentagons from the Mini Mental State Exam (MMSE) have been the figure copy test most commonly used during cognitive screening evaluations. However, the wire cube from the Montreal Cognitive Assessment (MoCA) is increasingly being used.
Objective: To evaluate which of these figure copy tests is more sensitive for cognitive impairment in PD.
Methods: Sixty-three PD patients from UK and USA completed the MMSE and MoCA. Logistic regression and sensitivity/specificity analyses were used to evaluate the utility of each figure copy test for detecting global cognitive impairment.
Results: The wire cube was a significant indicator of cognitive impairment (OR = 4.79, 95% CI = 1.63–14.07, p = 0.004), with a sensitivity/specificity of 0.74/0.63 in our sample. In contrast, interlocking pentagons were not a significant indicator of cognitive impairment (OR = 1.88, 95% CI = 0.54–6.50, p = 0.32), with a sensitivity/specificity of 0.26/0.84.
Conclusion: The wire cube is more sensitive to cognitive impairment in PD, most likely related to its greater complexity. The results have implications for clinicians who may have time for just one figure copying task as part of a brief screen for cognitive impairment in busy clinics and for researchers applying the PD mild cognitive impairment diagnostic criteria necessitating two tests of visuospatial function to be administered.

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1. Introduction

Decline in visuospatial abilities is a hallmark feature of cognitive impairment in PD [1] and longitudinal studies have shown that Parkinson's disease (PD) patients who cannot accurately copy the interlocking pentagons are at an increased risk for incipient dementia [2,3]. As such, figure copy tasks are an important component of cognitive screens in PD.

The interlocking pentagons have been the most frequently used figure copy task as it is part of the Mini Mental State Exam (MMSE)

[4,5] and the Addenbrooke's Cognitive Examination (ACE) [6]. However, clinical use of the interlocking pentagons task is declining due to MMSE copyright enforcement [7–9], publication of a new version of ACE (ACE-III) with all MMSE items replaced [10], and also because of mounting evidence that the Montreal Cognitive Assessment Scale (MoCA) [11], which uses the wire cube, is a sensitive screen for cognitive impairment in PD [12–17]. As such, the wire cube may increasingly supplant the interlocking pentagons in cognitive screens.

The purpose of this study is to determine whether this transition is valid by comparing the sensitivity of these two figure copy tests to global cognitive impairment in PD. The results have implications for test selection – both for clinicians who may have time for just one figure copying task as part of a brief screen for cognitive impairment in busy clinics, and also for researchers applying the new PD-MCI criteria that requires two tests from the visuospatial domain to be administered [18].

* Corresponding author at: Department of Neurology, G floor, Martin Wing, Leeds General Infirmary, Leeds LS1 3EX, UK.
** Corresponding author at: Department of Neurology, University of California – San Francisco, 675 Nelson Rising Lane, Ste. 190, San Francisco, CA 94158, USA.
E-mail addresses: jane.alty@hyms.ac.uk (J.E. Alty), kpossin@memory.ucsf.edu (K.L. Possin).

Table 1
Demographic characteristics and screening test scores.

Group	N	Age (years)	Male (%)	HY (stage)	Education (years)	LEDD (mg)	MMSE score	MoCA score
PD-NC	32	68.6 (8.8)	63	2.5 (0.6)	13.0 (2.4)	700 (475)	29.3 (0.7)	27.8 (1.2)
PD-MCI	23	70.9 (8.2)	65	2.6 (0.8)	12.9 (1.4)	725 (314)	28.1 (1.5)	24.4 (1.4)
PD-D	8	70.5 (5.9)	75	3.1 (1.3)	12.8 (1.8)	450 (397)	24.6 (2.1)	17.6 (2.6)

PD-NC, PD patients with MoCA score ≥26; PD-MCI, PD patients with MoCA score 21–25; PD-D, PD patients with MoCA score <21; MMSE, Mini Mental State Examination; MoCA, Montreal Cognitive Assessment; HY, Hoehn and Yahr stage; LEDD, levodopa equivalent daily dose.

2. Methods

Forty-nine PD patients were recruited from Leeds Teaching Hospitals NHS Trust (LTHT), UK, and fourteen from the University of California – San Francisco (UCSF) Memory and Aging Center, USA. Subjects completed the MMSE and MoCA consecutively during the same session whilst *on*. The order of assessments was randomly allocated and the scores of the orientation tasks in the first assessment were used to auto-complete the corresponding section in the second assessment. The study was approved by LTHT and UCSF ethics committees on human research and written consent was obtained from all subjects.

Patients were identified with normal cognition, PD-NC ($n = 32$), mild cognitive impairment, PD-MCI ($n = 23$), and dementia, PD-D ($n = 8$) using the previously validated MoCA ranges of ≥26, 21–25, and <21, respectively [12,13]. To avoid circular reasoning when predicting MoCA-defined global cognitive impairment using the MoCA cube item, total MoCA score was out of a maximum of 29 with the cube score excluded. We subtracted rather than added the cube point in order to increase sensitivity to cognitive impairment when classifying subjects. Compared to classifications based on MoCA scores out of 30, four additional cognitively intact subjects were classified as PD-MCI and no additional PD-MCI subjects were classified as PD-D.

Demographic and clinical variables were compared between the patients at different levels of cognitive impairment using one-way ANOVA with Games-Howell post hoc analysis for continuous variables, Chi-square for gender and Kruskal–Wallis test for Hoehn and Yahr (HY) stage. Using logistic regression and sensitivity/specificity calculations, we determined how well the cube and pentagon scores distinguished PD-NC from cognitively impaired PD (i.e. PD-MCI and PD-D combined), and PD-NC from PD-MCI.

3. Results

The groups did not differ in terms of gender, age, years of education, duration of disease, levodopa equivalent daily dose or HY stage (all $p \geq 0.1$) (Table 1). The wire cube was copied incorrectly by 66% of PD patients and the pentagons were copied incorrectly by 21% ($\chi^2 = 5.60$, $p = 0.018$). Regarding the individual cognitive groups, the cube copy was impaired in 39% PD-NC, 63% PD-MCI and 100% PD-D ($\chi^2 = 10.43$, $p = 0.005$). The pentagon copy was impaired in 16% PD-NC, 13% PD-MCI and 63% PD-D ($\chi^2 = 9.92$, $p = 0.007$) (Fig. 1).

Wire cube failure significantly predicted cognitive impairment (OR = 4.79, 95% CI = 1.63–14.07, $p = 0.004$), with a sensitivity of 0.74 and a specificity of 0.63. Even when the cognitively impaired group was restricted to those with PD-MCI but not PD-D, cube copy remained a significant predictor (OR = 3.13, 95% CI = 1.02–9.55, $p = 0.046$), with a sensitivity of 0.65. In contrast, incorrect copying of the interlocking pentagons was not a significant predictor of cognitive impairment (OR = 1.88, 95% CI = 0.54–6.50, $p = 0.32$), with a sensitivity of 0.26 and a specificity of 0.84. When the cognitively impaired group was limited to those with PD-MCI, the sensitivity of the interlocking pentagons dropped to 0.13.
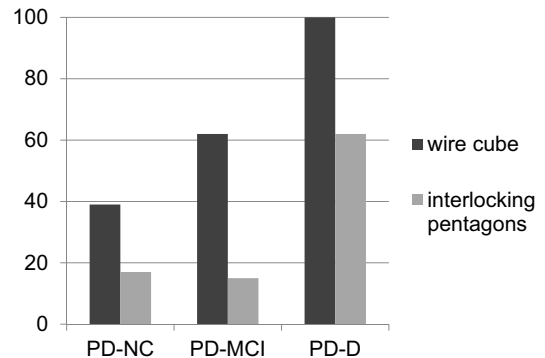
Fig. 1. The percentage of patients according to global cognitive status who incorrectly copied each figure.

4. Discussion

Visuospatial dysfunction is an early feature of PD-MCI [1], predicts a more aggressive rate of cognitive decline [2,3,19] and is severely affected in PD-D [1,20,21]. Historically, the most frequently used figure-copy test of visuospatial function has been interlocking pentagons incorporated into the MMSE and the ACE. However, use of the wire cube is increasing, in part because the MoCA is a recommended test of global cognition in PD [18].

The reason why one test of visuospatial function – copying a wire cube – predicted cognitive impairment but another – copying interlocking pentagons – did not may be explained by the relative complexity of the wire cube, evidenced by studies that have found a ceiling effect of interlocking pentagon scores when testing cognition in PD [22]. The wire cube is more complex because it is a 2D drawing of a 3D object. To perceive the 12 separate lines of the drawing as a 3D cube requires visual suppression and there is evidence that PD subjects lack the attentive resource [23] and perceptual flexibility [24] needed. Attention and visual perception difficulties in PD worsen with increasing cognitive dysfunction [25], mediated primarily by acetylcholine deficiency secondary to Lewy-body related infiltration of major brainstem nuclei [26]. This may explain the progressive difficulty of cube copying across the cognitive groups in this study and links with larger studies in PD subjects that have found significant correlations between cube copying and poor performance in a range of cognitive domains in addition to visuospatial function, including attention and memory [27].

Three limitations of this study are acknowledged. Firstly, using MoCA cut off scores to define MCI and dementia rather than considering functional dependence or performing detailed neuropsychological evaluations [18]. However, the MCI [14,15] and dementia [15] cut off scores have been validated previously and we did not include the cube item for classification. Secondly, our sample size is relatively small because assessments are from recruits to a trial of medical equipment and results may need to be confirmed in a larger sample. Thirdly, this is a cross-sectional rather than longitudinal study.

Despite limitations, this study suggests that copying a wire cube is a more sensitive detector of cognitive impairment in PD than

copying interlocking pentagons; a finding that has a clear, practical use for clinicians when working under time limitations such as outpatient clinics.

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References

[1] D.K. Johnson, J.E. Galvin, Longitudinal changes in cognition in Parkinson's disease with and without dementia, Dement. Geriatr. Cogn. Disord. 31 (2) (2011) 98–108.

[2] C.H. Williams-Gray, et al., Evolution of cognitive dysfunction in an incident Parkinson's disease cohort, Brain 130 (Pt 7) (2007) 1787–1798.

[3] C.H. Williams-Gray, et al., The distinct cognitive syndromes of Parkinson's disease: 5 year follow-up of the CamPaIGN cohort, Brain 132 (Pt 11) (2009) 2958–2969.

[4] M.F. Folstein, S.E. Folstein, P.R. McHugh, "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician, J. Psychiatr. Res. 12 (3) (1975) 189–198.

[5] K.I. Shulman, et al., IPA survey of brief cognitive screening instruments, Int. Psychogeriatr. 18 (2) (2006) 281–294.

[6] E. Mioshi, et al., The Addenbrooke's Cognitive Examination Revised (ACE-R): a brief cognitive test battery for dementia screening, Int. J. Geriatr. Psychiatry 21 (11) (2006) 1078–1085.

[7] J.C. Newman, R. Feldman, Copyright and open access at the bedside, N. Engl. J. Med. 365 (26) (2011) 2447–2449.

[8] S. Powsner, D. Powsner, Cognition, copyright, and the classroom, Am. J. Psychiatry 162 (3) (2005) 627–628.

[9] R. Martin, D. O'Neill, Taxing your memory, Lancet 373 (9680) (2009) 2009–2010.

[10] C. Zadikoff, et al., A comparison of the mini mental state exam to the Montreal cognitive assessment in identifying cognitive deficits in Parkinson's disease, Mov. Disord. 23 (2) (2008) 297–299.

[11] D.J. Gill, et al., The Montreal cognitive assessment as a screening tool for cognitive impairment in Parkinson's disease, Mov. Disord. 23 (7) (2008) 1043–1046.

[12] Addenbrooke's Cognitive Examination – ACE-III English Version A. Available from: http://neura.edu.au/sites/./ACE-III Administration (UK).pdf [cited 26.02.13].

[13] Z.S. Nasreddine, et al., The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment, J. Am. Geriatr. Soc. 53 (4) (2005) 695–699.

[14] S. Hoops, et al., Validity of the MoCA and MMSE in the detection of MCI and dementia in Parkinson disease, Neurology 73 (21) (2009) 1738–1745.

[15] J.C. Dalrymple-Alford, et al., The MoCA: well-suited screen for cognitive impairment in Parkinson disease, Neurology 75 (19) (2010) 1717–1725.

[16] S. Lessig, et al., Changes on brief cognitive instruments over time in Parkinson's disease, Mov. Disord. 27 (9) (2012) 1125–1128.

[17] S. Nazem, et al., Montreal cognitive assessment performance in patients with Parkinson's disease with "normal" global cognition according to mini-mental state examination score, J. Am. Geriatr. Soc. 57 (2) (2009) 304–308.

[18] I. Litvan, et al., Diagnostic criteria for mild cognitive impairment in Parkinson's disease: movement Disorder Society Task Force guidelines, Mov. Disord. 27 (3) (2012) 349–356.

[19] D.K. Johnson, et al., Onset of Mild Cognitive Impairment in Parkinson Disease, Alzheimer Dis. Assoc. Disord. (2015).

[20] C.C. Janvin, et al., Cognitive profiles of individual patients with Parkinson's disease and dementia: comparison with dementia with lewy bodies and Alzheimer's disease, Mov. Disord. 21 (3) (2006) 337–342.

[21] E.Y. Uc, et al., Incidence of and risk factors for cognitive impairment in an early Parkinson disease clinical trial cohort, Neurology 73 (18) (2009) 1469–1477.

[22] S. Lord, et al., Cognition and gait show a selective pattern of association dominated by phenotype in incident Parkinson's disease, Front. Aging Neurosci. 6 (2014) 249.

[23] K.M. Bennett, U. Castiello, Three-dimensional covert attentional functions in Parkinson's disease subjects, Exp. Brain Res. 112 (2) (1996) 277–288.

[24] M. Diaz-Santos, et al., Perceptual, cognitive, and personality rigidity in Parkinson's disease, Neuropsychologia 69 (2015) 183–193.

[25] A. Yarnall, L. Rochester, D.J. Burn, The interplay of cholinergic function, attention, and falls in Parkinson's disease, Mov. Disord. 26 (14) (2011) 2496–2503.

[26] A.A. Kehagia, R.A. Barker, T.W. Robbins, Neuropsychological and clinical heterogeneity of cognitive impairment and dementia in patients with Parkinson's disease, Lancet Neurol. 9 (12) (2010) 1200–1213.

[27] X.Y. Bu, et al., Usefulness of cube copying in evaluating clinical profiles of patients with Parkinson disease, Cogn. Behav. Neurol. 26 (3) (2013) 140–145.