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Utility of the NeuroTrax Computerized Battery for Cognitive Screening in Parkinson's Disease: Comparison with the MMSE and the MoCA

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Abstract

To determine the utility of a computerized assessment in Parkinson's disease (PD), we compared the cognitive performance of 50 PD patients on the NeuroTrax computerized battery relative to the mini-mental state examination (MMSE) and the Montreal Cognitive Assessment (MoCA). The results revealed fair agreement between impairment on the NeuroTrax and the MMSE ($\kappa = .291$, $p = .031$) but only slight agreement between the NeuroTrax and the MoCA ($\kappa = .138$, $p = .054$) and between the MoCA and the MMSE ($\kappa = .168$, $p = .069$). The NeuroTrax identified 52% of the sample as average or above, 40% as below average, and 8% as impaired. The MoCA identified 54% of the sample as impaired (28% average or above and 18% below average), while the MMSE identified 66% as average or above (20% below average and 14% impaired). Several stepwise regressions revealed that executive and verbal functions were the best predictors of cognitive functioning on the NeuroTrax, while memory recall, serial sevens, naming, and abstraction were the best predictors on the MoCA. These results suggest that although the NeuroTrax may be useful in identifying executive cognitive deficits in PD, similar to the MMSE the NeuroTrax may lack optimal sensitivity. While the MoCA is sensitive, it may be too stringent in overclassifying PD patients as impaired.

Keywords

cognitive screening; computerized cognitive batteries; MMSE; MoCA; NeuroTrax; Parkinson's disease

INTRODUCTION

Cognitive deficits are often associated with Parkinson's disease (PD), although the prevalence and pattern of these deficits remain unclear (Janvin, Aarsland, Larsen, & Hugdahl, 2003). This, in part, is related to a lack of identification of effective routine cognitive screening tests in the neurologic clinic that are sensitive and specific to PD-related cognitive deficits. Prevalence studies of dementia in PD have reported wide variations on point prevalence, although an 8-year longitudinal study reported long-term cumulative prevalence of dementia in PD as high as 80% (Aarsland, Andersen, Larsen, Lolk, & Kragh-Sorensen, 2003). Identification of early cognitive deficits in PD is important, as this can predict future cognitive decline and development of dementia, health-related quality of life, and functional impairment (Marras et al., 2008; Martin et al., 2008; Williams-Gray, Foltynie, Brayne, Robbins, & Barker, 2007). Therefore, early screening and identification of cognitive deficits in PD is critical and necessary to assist with clinical decision-making including use of cognitive enhancing agents and referrals to neuropsychology.

Since comprehensive neuropsychological assessment is not practical for all patients, it is important to evaluate screening instruments in terms of utility in PD patients. Many commonly used cognitive screening instruments, such as the mini-mental state examination (MMSE; Folstein, Folstein, & McHugh, 1975), have not been validated for use in PD and may be insensitive to milder PD deficits partly related to a ceiling effect and a lack of sensitivity to executive deficits common in PD (Hoops et al., 2009; Tombaugh & McIntyre, 1992; Zadikoff et al., 2008). Most cognitive screening measures such as the MMSE fail to cover a range of cognitive domains, and therefore subjects with variable cognitive abilities may all score relatively well (Athey, Porter, & Walker, 2005; Hobson & Meara, 1999). Thus, there is a need for concise but more comprehensive cognitive screening for cognitive impairment in PD.

Another brief screening measure, the Montreal Cognitive Assessment (MoCA), has demonstrated high sensitivity to detecting mild cognitive impairment (MCI) in the elderly and Alzheimer's disease (AD) relative to the MMSE in a memory clinic (Luis, Keegan, & Mullan, 2009; Nasreddine et al., 2005; Nazem et al., 2009; Zadikoff et al., 2008). The MoCA's sensitivity has been specifically linked to the development of memory testing that involves more words, fewer learning trials, and longer delay than that of the MMSE, as well as sensitive executive, language, and visuospatial functions (Nasreddine et al., 2005). Furthermore, the MoCA has demonstrated test-retest reliability and convergent validity relative to comprehensive neuropsychological assessment in patients with PD (Gill, Freshman, Blender, & Ravina, 2008). However, despite the MoCA's demonstrated superior sensitivity, its specificity is only fair (35%) when utilizing the recommended cutoffs (Luis et al., 2009). Although the MoCA appears to have utility as a cognitive screening measure in

PD, further investigation is warranted to determine whether it is useful as a diagnostic tool as opposed to a screening measure (Hoops et al., 2009).

Although results suggest that more comprehensive cognitive screening batteries may improve the sensitivity and specificity of early identification of cognitive deficits in PD, few predefined cognitive batteries have been previously evaluated (Athey et al., 2005; Hobson & Meara, 1999). The objective of this study was to evaluate the utility of a predefined computerized battery in providing cognitive profiles of PD patients compared with cognitive impairment on the MMSE and the MoCA. The NeuroTrax Mindstreams (Fresh Meadows, NY) computerized assessment was designed for clinical and research use for detecting MCI (Dwolatzky et al., 2003). Despite the validation of the NeuroTrax with neuropsychological assessment and for age-related cognitive decline, this system has not been validated on a PD population, although it has been previously utilized (Dwolatzky et al., 2003, 2004; Fillit, Simon, Doniger, & Cummings, 2008; Hausdorff et al., 2006). Thus, the practicality and utility of the NeuroTrax for cognitive screening in PD or as a diagnostic measure has yet to be determined.

METHODS

Subjects

Subjects were a sample of patients with a diagnosis of idiopathic PD confirmed by a movement disorder specialist (RP) and were selected from the Movement Disorder Clinic at the University of Kansas Medical Center. The subjects were being evaluated for deep brain stimulation surgery. The institutional human subjects committee of University of Kansas Medical Center approved data collection, and all subjects provided written informed consent.

Fifty patients with PD were administered the MMSE, the MoCA, and the NeuroTrax computerized battery to evaluate cognitive correlates of PD. The sample of patients ranged from 46 to 80 years of age (mean = 65.76) and was composed of predominately educated (mean = 15.28, $SE = 0.503$) White (98%) males (37 males and 13 females). All subjects with the exception of three were right-hand dominant. Clinical information for subjects including medication dosage, disease severity as measured according to the Hoehn and Yahr scale, and activities of daily living according to the Schwab and England scale were obtained from chart review. Overall patients were representative of patients with PD in specialty care settings, with mild to moderate disease severity (mean Hoehn and Yahr stage = 2.7; mean Schwab and England = 75.1; mean levodopa dosage = 890 ± 670.44 mg/day; and dopamine agonist use by 52% of subjects). The mean Beck Depression Inventory score was 10.16 ± 5.04 , with 22% of the patients having a score above the cutoff of 14 but only 8% of the sample having a score above 18, the suggested adjusted cutoff for PD (Tumas, Rodrigues, Farias, & Crippa, 2008).

Procedures

The MMSE, the MoCA, and the NeuroTrax were administered systematically in this fixed order to all patients, and performance ranges for individual patients were obtained from

published normative data (Crum, Anthony, Bassett, & Folstein, 1993; Smith, Gildeh, & Holmes, 2007). Patients were evaluated in their regular “on” state, and all subjects had taken their scheduled PD medications at the time of evaluation.

The MMSE is a popular measure to screen for cognitive impairment given it is brief, easily administered, and easily scored (Folstein et al., 1975). The MMSE includes a variety of items that assess orientation to time and place, attention/concentration, language, constructional ability, and immediate and delayed recall. The MMSE can typically be administered and scored in 5–10 min, with the score equal to the total number of correct answers and a maximum total score of 30.

The MoCA is a screening instrument with a total score of 30 containing the following 7 subscores: visuospatial/executive (5 points), naming (3 points), memory (5 points for delayed recall), attention (6 points), language (3 points), abstraction (2 points), and orientation (6 points). Scores are also adjusted for low educational attainment (1 point added if <12 years of education). The MoCA was originally developed to address the limitations of the MMSE and to improve diagnosis of MCI and mild AD (Nasreddine et al., 2005).

The NeuroTrax is a set of Mindstreams tests developed to provide multiple predefined batteries containing different sets of tests (Doniger et al., 2006; Dwolatzky et al., 2004). All patients received the Global Assessment Battery that provides profiles in domains of memory, executive, visuospatial, verbal, attention, and information processing speed, and motor skills on the basis of the following subtest scores: Go-NoGo, verbal memory, problem solving, Stroop, nonverbal memory, finger tapping, catch game, staged information processing, visuospatial processing, and verbal function. Responses were recorded via a mouse and the number pad of the computer keyboard, and completion of the entire battery took approximately 1 hour. It is noteworthy that an information processing subtest score is not provided for subjects who fail the practice items or who do not complete the entire subtest, although incomplete performance can influence the total NeuroTrax score.

RESULTS

Age Correlations and Z-Score Conversions

The influence of age on cognitive performance was investigated and revealed a significant correlation as follows: MoCA, $r(48) = -0.386$, $p = .006$; MMSE, $r(48) = -0.322$, $p = .023$; and NeuroTrax, $r(48) = -0.296$, $p = .037$. Each subject's score on the MMSE and the MoCA was converted to a z-score based on published normative data (Crum et al., 1993; Nasreddine et al., 2005). Also, NeuroTrax standard scores, which were computer generated, were converted to z-scores. Performance ranges were derived from a standard psychometric conversion table that classifies subjects two standard deviations below the mean as falling in the impaired range of functioning. Comparison of z-scores revealed that overall the MoCA classified the sample of PD subjects as impaired ($z = -2.27$), while the NeuroTrax ($z = -0.712$) and the MMSE ($z = -0.478$) overall classified the sample as in the below average and average range, respectively. The NeuroTrax identified 52% of the sample as average or above, 40% as below average to borderline, and 8% as impaired. The MoCA identified 54% as impaired, while the MMSE identified 66% as average or above (see Table 1). While the

MMSE and the NeuroTrax classified 86% and 77% of the sample as below average or above respectively, the MoCA only classified 38% of the sample as below average or above. The screening measures classified 14%, 22%, and 62% of the sample as in the borderline to impaired range of functioning on the basis of the MMSE, the NeuroTrax, and the MoCA, respectively (Table 1).

Agreement Between MMSE, MoCA, and NeuroTrax

Cohen's kappa statistic was used to assess agreement between normal and impaired classifications of subjects for the MMSE, the MoCA, and the NeuroTrax. Kappa provides the percent agreement beyond chance between two methods, using the chi-square testing of significant association, with values ranging between 0 (slight agreement $<.2$) and 1 (perfect agreement $>.8$; Chmura Kraemer, Periyakoil, & Noda, 2002).

The results of the study revealed fair agreement between cognitive impairment identified by the NeuroTrax and the MMSE ($\kappa = .291, p = .031$) but only slight agreement between the NeuroTrax and the MoCA ($\kappa = .138, p = .054$) and between the MoCA and the MMSE ($\kappa = .168, p = .069$; see Table 2). Five subjects (10.9%) classified as within normal limits by the NeuroTrax were classified as impaired by the MMSE, while two subjects (50%) classified as impaired by the NeuroTrax were classified as normal by the MMSE. However, the MoCA classified 50% and 48% of the subjects in the within-normal-limits range on the Neuro-Trax and the MMSE (23 and 21 subjects), respectively, as impaired (Table 2). Conversely, only one subject who was in the normal range on the MoCA was classified as impaired on the MMSE.

Stepwise Regression and Subtest Predictors of Impairment

Several stepwise regressions were performed on the dependent variables of the MoCA and the NeuroTrax to identify the best subtest predictors of performance classifications (i.e., average, borderline, or impaired). A regression analysis was not conducted on the MMSE because it is not composed of distinct subtests. The first regression evaluated subtest z -scores as predictors and revealed that delayed memory recall [$F(1, 48) = 25.07, p < .0001$], serial sevens [$F(1, 47) = 25.94, p < .0001$], and naming [$F(1, 46) = 23.41, p < .0001$] were the best predictors of performance on the MoCA, explaining 34.3% and additional 18.2% and 8% of the variance, respectively (Table 3). On the NeuroTrax, information processing speed explained 45.3% [$F(1, 32) = 26.53, p < .0001$] of the performance variance, while the addition of verbal functions increased the variance by 17.1% [$F(1, 31) = 26.69, p < .0001$]. However, because many of the subjects did not complete the information processing subtest, they did not receive a subtest score eliminating them from the analysis.

In order to include subjects with significant impairment in information processing, a second regression evaluating normal and impaired subtest performance was conducted on the MoCA and the NeuroTrax. All subjects with incomplete information processing performances (i.e., completed some part of the subtest but discontinued by the computer program because of inadequate performance) were classified as impaired, since incomplete performance influences the total NeuroTrax score. The second set of regressions revealed that the executive function subtest was the best predictor of cognitive impairment on the

NeuroTrax, explaining 59.7% of the variance [$F(1, 45) = 66.56, p < .0001$; Table 3]. The addition of verbal function (naming and word rhyming) increased the variance by 11.8%–71.5% [$F(1, 44) = 55.19, p < .0001$]. A final regression revealed that impairment in delayed memory recall explained 38.8% of the variance in impairment on the MoCA [$F(1, 48) = 30.48, p < .0001$], and the addition of serial sevens [$F(1, 47) = 20.74, p < .0001$], naming [$F(1, 46) = 8.41, p < .01$], and abstraction [$F(1, 45) = 6.48, p < .05$] increased the variance by 29.8%–68.6% (see Table 3).

DISCUSSION

To determine whether computerized assessment may be uniquely suited to early detection of cognitive changes associated with PD, we evaluated agreement between two commonly utilized cognitive screening measures, the MMSE and the MoCA, relative to the NeuroTrax computerized battery. Our results revealed fair agreement between cognitive impairment identified by the MMSE and the NeuroTrax but only slight agreement between the MoCA and the NeuroTrax and between the MoCA and the MMSE. Disagreement between screening measures was primarily related to the MoCA's tendency to classify subjects with normal profiles on the MMSE and the NeuroTrax as impaired. Specifically, utilizing the published normative data, the MoCA classified over half of the subjects who were classified as normal by the other screening measures as in the impaired range of functioning and the overall sample of PD subjects as in the impaired range (62% of the sample was classified as borderline or impaired by the MoCA). Conversely, the NeuroTrax and the MMSE classified the sample as in the below average to average range, with only 22% and 14% of the sample in the borderline or impaired range, respectively.

Our results concur with what has been previously reported regarding the less than optimal sensitivity and ceiling effect of the MMSE (Hoops et al., 2009; Nasred-dine et al., 2005; Nazem et al., 2009). This is evident from the MMSE classification of 30% of the PD sample as above average and 36% as average. While the NeuroTrax and the MMSE had fair agreement, the NeuroTrax only identified 2% of the sample as above average and provided a greater distribution across performance classifications, with 24% in the below average range and 16% in the borderline range of impairment. Unlike the other screening measures, the NeuroTrax better characterized mild cognitive deficits in PD patients with 40% of the sample falling in the below average to borderline range (compared with the MMSE that did not classify any subjects as borderline and the MoCA that classified 8% as borderline). Therefore, our results indicate that both the MoCA and the NeuroTrax emerge as sensitive screening measures capable of detecting early cognitive impairment in PD, although the two measures might disagree as to whether the patients are displaying MCI or reflect an actual dementia.

Similar to previous studies, our results indicate that the MoCA is a very sensitive screening measure for detection of early cognitive changes in PD (Gill et al., 2008; Hoops et al., 2009; Nazem et al., 2009; Zadikoff et al., 2008). However, our findings suggest that the MoCA may be too stringent in impairment classifications for PD patients, relative to their performance on both the MMSE and the NeuroTrax. A related study found similar results and reported that as much as 50% of patients with PD with a normal MMSE score had

demonstrated cognitive impairment based on the MoCA's recommended cutoff score of 26 (Nazem et al., 2009). The MoCA was developed on an MCI and AD population, and it appears to be more sensitive to age-related cognitive declines (Nazem et al., 2009). Thus, this normative data may not translate to a PD population. The reported specificity of the MoCA has been enhanced considerably when using a lower cutoff of 23 in older adults (Luis et al., 2009). However, the appropriate cutoff score for PD remains unclear (Gill et al., 2008; Hoops et al., 2009; Zadikoff et al., 2008). Although the MoCA may provide utility as a sensitive screening measure, clinicians should be cautious in diagnostic conclusions based on impairment classifications for PD patients.

Our results concur with previous studies that have suggested that there may be multiple advantages to computer tests, including their ability to cover a wider range of ability, minimize floor and ceiling effects, and provide precise record of accuracy and speed of response (Wild, Howieson, Webbe, Seelye, & Kaye, 2008). In particular, the NeuroTrax may provide critical information on speed of response relevant to bradykinesia and well-characterized executive deficits evident early in PD. However, the rules of discontinuation on the information processing subtest may limit the usefulness to subjects with greater impairment, and the influence on the total score is unclear because the method for derived scores is not transparent in a computerized program (Dwolatzky et al., 2003, 2004). The feasibility of a computerized system for cognitive assessment has some support as being a practical clinical option for the elderly, although the utility in a PD population has been unclear (Fillit et al., 2008). This, in part, is related to the requirement that subjects provide a motor response on timed computerized tasks, which might be problematic in PD subjects, as it has the potential to confound cognitive and motor deficits of the disorder. Furthermore, because of the cost and time required for administration, it is unclear if the NeuroTrax is ideal for screening. Therefore, the MoCA may be a more practical screening measure, provided that subjects in the borderline to impaired range are followed up with a more comprehensive neuropsychological assessment when possible.

Interpretation of our results is limited. First, the majority of patients were in the mild to moderate range of motor impairment (i.e., Hoehn and Yahr stages 1–3). Second, we did not include an age-matched control sample without PD. Third, we did not include a comprehensive neuropsychological battery for comparison or establishment of clinical classifications. Finally, since the prevalence of dementia versus mild cognitive deficits in PD is unclear, it is difficult to compare the number of impaired cases in our study population in terms of being representative of other populations in movement disorder centers elsewhere. Consequently, we were not able to validate the optimal cutoff points for use of the MoCA in PD. Therefore, future studies should compare performance classifications on the MoCA, the Neuro-Trax (comparing differences between patient and experimenter computer responses), and standardized neuropsychological assessments.

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TABLE 1

Subject classification by screening measure (number and percentage of subjects)

Classification	MMSE	MoCA	NeuroTrax
Above average	15 (30%)	2 (4%)	1 (2%)
Average	18 (36%)	12 (24%)	25 (50%)
Below average	10 (20%)	5 (10%)	12 (24%)
Borderline	0	4 (8%)	8 (16%)
Impaired	7 (14%)	27 (54%)	4 (8%)

TABLE 2

Cross-tabulation and agreement comparing the NeuroTrax with the MoCA and the MMSE (number and percentages)

	MoCA		MMSE	
	Normal	Impaired	Normal	Impaired
NeuroTrax				
Normal	23 (50%)	23 (50%)	41 (89.1%)	5 (10.9%)
Impaired	0	4 (100%)	2 (50%)	2 (50%)

Note: NeuroTrax and MoCA, $\kappa = .138$; NeuroTrax and MMSE, $\kappa = .291$.

TABLE 3

Subtest predictors of performance based on stepwise multiple regressions

	B	SE (B)	β
MoCA Step 1			
Delayed recall	0.410	0.074	0.623
MoCA Step 2			
Delayed recall	0.305	0.067	0.463
Serial sevens	0.309	0.068	0.461
MoCA Step 3			
Delayed recall	0.292	0.062	0.443
Serial sevens	0.348	0.065	0.519
Naming	0.218	0.075	0.262
MoCA Step 4			
Delayed recall	0.254	0.061	0.386
Serial sevens	0.350	0.061	0.523
Naming	0.205	0.071	0.247
Abstraction	0.174	0.068	0.220
NeuroTrax Step 1			
Executive function	0.431	0.053	0.772
NeuroTrax Step 2			
Executive function	0.309	0.053	0.555
Verbal function	0.199	0.047	0.407

Note: MoCA, $R^2 = .388$ for Step 1 and $R^2 = .187$ for Step 2, .066 for Step 3, and .045 for Step 4 ($p < .05$); NeuroTrax, $R^2 = .597$ for Step 1 and $R^2 = .118$ for Step 2 ($p < .0001$).