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Usefulness of the Montreal Cognitive Assessment (MoCA) in Huntington's disease

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Abstract

The Montreal Cognitive Assessment (MoCA) is a brief screening instrument for dementia that is sensitive to executive dysfunction. This study examined its usefulness for assessing cognitive performance in mild, moderate, and severe Huntington's disease (HD), as compared to the MMSE. We compared MoCA and MMSE total scores and the number of correct answers in five cognitive-specific domains in 104 manifest HD patients and 100 matched controls. For the total HD sample, and for the moderate and severe patients, significant differences between both MoCA and MMSE total scores and almost all cognitive-specific domains emerged. Even mild HD subjects showed significant differences with regard to total score and several cognitive domains on both instruments. We conclude that the MoCA, although not necessarily superior to the MMSE, is a useful instrument for assessing cognitive performance over a broad level of functioning in HD.

Keywords

Huntington's disease; Montreal Cognitive Assessment (MoCA); Mini-Mental State Examination (MMSE); cognitive decline

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Introduction

Cognitive assessments are used clinically to diagnose and track individuals affected by disorders that impair cognition. However, comprehensive neuropsychological testing is unsuitable for most medical visits, when clinicians require rapid assessment of global cognitive functioning. Therefore, brief screening measures are useful tools to summarize information regarding the overall level of cognitive performance.

Although the Mini-Mental State Examination (MMSE) is the most frequently used brief cognitive instrument,¹⁻³ the extent of its usefulness has been questioned with regard to milder forms of cognitive impairment¹⁻³ and in dementing disorders characterized by executive, visuospatial, or complex attentional deficits.^{4, 5} The Montreal Cognitive Assessment (MoCA) is another brief screening instrument for dementia that is thought to assess a broader array of cognitive domains (e.g., attention/executive functioning, visuospatial, and language) compared to the MMSE.³ Although the MoCA has been shown to be sensitive to executive dysfunction in a variety of neurological conditions, including Alzheimer's disease (AD)³ and Parkinson's disease (PD),^{4, 6} studies in other subcortical dementias, such as Huntington's disease (HD), have been limited.^{5, 7, 8}

The objective of this study is to examine the usefulness of the MoCA as a brief screening measure in patients with HD, compared to the MMSE. To our knowledge, no study has assessed performance on the MoCA in a large sample of HD patients who exhibit a wide range of disease severity.

Methods

Subjects

The MoCA and MMSE were administered on the same day, in counterbalanced order, to 104 manifest HD subjects and 100 matched normal controls. The Unified Huntington's Disease Rating Scale (UHDRS),⁹ including the Total Motor score, Functional Assessment, Independence Scale, and Total Functional Capacity (TFC), was administered to quantify neurologic and functional ability of patients. The UHDRS TFC was used to stratify manifest HD subjects as mild (TFC=10-13), moderate (TFC=7-9), and severe (TFC=0-6). Burden of Pathology (BOP)¹⁰ scores were included as a measure of disease burden for HD patients. Patients were recruited from the University of California, San Diego (UCSD) HD Clinical Research Center and examined by a senior neurologist (JC-B). Manifest HD inclusion criteria included a definitive diagnosis of HD with family history and expanded trinucleotide CAG repeat of 40 or more, in addition to chorea. Normal control subjects consisted mainly of spouses and friends of patients seen through the UCSD HD Clinical Research Center and the UCSD Shiley-Marcos Alzheimer's Disease Research Center (ADRC). The remaining control subjects were recruited from the San Diego community as part of a convenience sample. Normal controls had no reported history of neurological or psychiatric disorders, and no use of psychoactive substances or medications. Signed informed consent was obtained from each subject.

Measures

Individual items on the MoCA were divided into five cognitive-specific domains (attention/executive function, visuospatial, language, memory, and orientation) based on previous research.¹¹ The attention/executive function items included Trail Making Test B (1 point), digit span (2 points), target detection (1 point), verbal fluency (1 point), abstraction (2 points), and serial seven subtraction (3 points). The visuospatial items included clock drawing (3 points) and cube copying (1 point). The language items included object naming (3 points) and sentence repetition (2 points). The memory items included recall of five previously presented words (5 points). The orientation items included six orientation-based questions (6 points).

Individual items on the MMSE were also divided into five cognitive-specific domains for comparison. The attention/executive function items included serial seven subtraction (5 points). The visuospatial items included design copying (1 point). The language items included object repetition (3 points), object naming (2 points), phrase repetition (1 point), 3-stage command (3 points), reading comprehension (1 point), and sentence writing (1 point). The memory items included recall of three previously presented words (3 points). The orientation items included ten orientation-based questions (10 points).

Statistical Analysis

The raw data were examined for outliers and parametric distribution requirements. Between-group comparisons of demographic characteristics were conducted using Independent samples t-tests or Chi-squared (χ^2) for nominal data. Because of significantly non-normal distributions, nonparametric Mann-Whitney U tests were used to analyze performance on MoCA and MMSE total scores and the number of correct answers in each of the five cognitive-specific domains between groups. A Bonferroni correction for multiple comparisons was used to maintain at least a .05 Type I error level. Effect sizes were calculated using Cohen's *d*.

Results

Demographics and clinical characteristics of HD cohorts are shown in Table 1. Normal controls, which were 57% female, had a mean age of 48.3 years (SD=15.7) and mean education of 14.4 years (SD=1.8). HD patients and normal controls were well matched with regard to age, gender, and education; except for the severe HD patients who had significantly lower education levels compared to normal controls ($t=-3.05$, $p<0.01$).

For the total HD sample, and for the moderate and severe HD groups compared to normal controls, there were significant differences between both MoCA and MMSE total scores and all five cognitive-specific domains (Table 2; all $p<0.001$), except for language on the MMSE in moderate HD patients after Bonferroni correction. Significant differences on the MoCA and MMSE emerged even for mild HD groups compared to normal controls with regard to total score (MoCA: $U=-5.29$, $p<0.001$; MMSE: $U=-5.56$, $p<0.001$), and three (attention/executive function, memory, and orientation) of the five cognitive-specific domains (MoCA: $U=-3.14$, $p=0.002$ -- $U=-4.98$, $p<0.001$; MMSE: $U=-3.07$, $p=0.002$ -- $U=-4.57$, $p<0.001$).

after Bonferroni correction. Additionally, the MMSE showed significant differences on the visuospatial domain in mild HD patients as compared to normal controls ($U=-3.88$, $p<0.001$). As shown in Table 2, the effect sizes for differences between normal controls and each of the HD groups on MoCA, and to a slightly lesser degree on MMSE, were large for total scores and most cognitive-specific domains.

Discussion

In the current study, we analyzed performance on the MoCA in a well-characterized sample of HD subjects followed at one academic institution to evaluate its usefulness for assessing cognitive impairment, as compared to the more commonly used MMSE. To our knowledge, this is the largest sample of HD patients, with the widest range of symptom severity, assessed on the MoCA. In addition, this is one of the first studies to examine specific cognitive domains on the MoCA and MMSE in HD. We found that moderate and severe HD patients, in addition to the overall HD cohort, performed significantly more poorly on the MoCA compared to normal controls, both with regard to total score and all five cognitive-specific domains. Even mild HD subjects showed significant differences with regard to total score and the cognitive domains of attention/executive function, memory, and orientation. We found similar results for the MMSE, except with regard to language. However, mild HD patients did show significant impairment on the visuospatial domain of the MMSE as compared to the MoCA.

These results are consistent with findings from recent smaller studies.^{8,12} One study of 20 mild-to-moderate HD patients found significantly lower scores on the MoCA total score and almost all cognitive domains, compared to normal controls.⁸ Another study of 41 HD patients found that the total HD sample scored significantly lower than normal controls on the MMSE; however, performance in each stage of the disease was not compared to normal controls.¹²

An earlier study from our institution using ROC analysis reported that almost all five cognitive-specific domains on the MoCA, but only two on the MMSE, significantly differentiated a sample of 39 mild to moderate HD patients from normal controls.⁵ One possible reason for this discrepancy is the smaller sample size and the fact that their study excluded serial sevens from the analysis. Finally, a study involving 53 moderately impaired HD patients with a mean UHDRS TFC score of 7.0, concluded that the MoCA, as compared to the MMSE, may be a more sensitive screening instrument for cognitive dysfunction in HD, based on cut points.⁷

This study is not without limitations. We used a convenience sample of HD patients from one academic center; however, this was a relatively well-characterized group of patients. We also did not consider the effects of mood, medication, or concomitant disease on cognitive testing since both tests were administered in the same sitting. Normal controls had no reported history of neurological or psychiatric disorders, and no use of psychoactive substances or medications; however, we did not use additional standardized assessments of functional or psychiatric performance to exclude subjects. However, the mean MMSE total

score for normal controls was 29.0, suggesting that these subjects were in the normal cognitive range.

Nonetheless, in the current study, we found that the MoCA was able to detect cognitive impairment across a wide range of severity in HD, suggesting it is a useful screening measure of cognitive performance in a non-selected HD population, although not necessarily superior to the more widely used MMSE. Whether the MoCA, as compared to the MMSE, would be more useful for assessing effects of a therapeutic agent for cognition in HD trials, remains unclear.

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Table 1

Demographic and Clinical Characteristics of HD Cohorts, mean (SD) *

Characteristic	Mild HD	Moderate HD	Severe HD	All HD
N	24	36	44	104
Age, years	44.9 (10.3)	52.3 (11.9)	50.7 (11.3)	49.9 (11.5)
Education, years	14.7 (3.5)	14.4 (2.4)	13.4 (1.9) [†]	14.1 (2.6)
Percent Female ^a	50.0	47.2	65.9	55.8
CAG Repeat Length	44.5 (3.1)	43.7 (2.9)	45.7 (4.7)	44.7 (3.9)
BOP Score	375.0 (106.5)	406.0 (80.5)	472.7 (125.2)	426.8 (113.9)
UHDRS Total Motor	21.1 (12.2)	37.5 (13.5)	47.6 (16.5)	37.9 (17.7)
Functional Assessment	22.4 (2.1)	19.0 (1.8)	13.1 (5.8)	17.3 (5.5)
Independence Scale	89.0 (9.3)	73.1 (5.8)	60.7 (8.7)	71.5 (13.6)
Total Functional Capacity	11.2 (1.0)	7.8 (0.7)	4.7 (1.8)	7.3 (2.8)

HD=Huntington's disease; BOP=Burden of Pathology; UHDRS=Unified Huntington's Disease Rating Scale

* Stratified on the basis of Total Functional Capacity

^a Chi-squared Test[†] p<0.01 vs. NC

Cognitive Performance of Patient Cohorts vs. Normal Controls on MoCA and MMSE Total Scores and Cognitive-specific Domains, mean (SD)

Table 2

	NC		Mild HD		Moderate HD		Severe HD		All HD	
	Mean	d	Mean	d	Mean	d	Mean	d	Mean	d
Total MoCA (30 points)	27.5 (2.2)	N/A	23.3 (4.3)*	1.2	20.9 (4.1)*	2.0	15.7 (5.6)*	2.8	19.3 (5.8)*	1.9
Executive Function (10 points)	9.3 (0.9)	N/A	7.5 (2.1)*	1.1	6.9 (2.2)*	1.4	3.7 (2.4)*	3.0	5.7 (2.8)*	1.7
Visuospatial (4 points)	3.6 (0.6)	N/A	3.1 (1.1)	0.6	2.7 (1.1)*	1.1	1.6 (1.2)*	2.1	2.3 (1.3)*	1.3
Language (5 points)	4.6 (0.6)	N/A	4.2 (1.0)	0.4	3.9 (0.8)*	1.0	3.5 (1.2)*	1.1	3.8 (1.1)*	0.9
Memory (5 points)	3.8 (1.2)	N/A	2.2 (1.3)*	1.3	1.4 (1.6)*	1.7	1.5 (1.6)*	1.7	1.6 (1.5)*	1.6
Orientation (6 points)	5.9 (0.3)	N/A	5.5 (1.3) [†]	0.5	5.6 (0.7)*	0.6	4.8 (1.3)*	1.1	5.2 (1.2)*	0.8
Total MMSE (30 points)	29.0 (1.1)	N/A	26.2 (3.0)*	1.2	25.2 (3.3)*	1.5	21.1 (4.6)*	2.4	23.7 (4.4)*	1.7
Executive Function (5 points)	4.6 (0.7)	N/A	3.3 (2.0)*	0.9	2.9 (1.9)*	1.2	1.2 (1.5)*	2.9	2.3 (2.0)*	1.5
Visuospatial (1 point)	1.0 (0.2)	N/A	0.7 (0.5)*	0.8	0.7 (0.5)*	0.8	0.4 (0.5)*	1.6	0.6 (0.5)*	1.1
Language (11 points)	10.9 (0.4)	N/A	10.6 (0.6)	0.6	10.6 (0.5)	0.7	9.9 (1.7)*	0.8	10.3 (1.2)*	0.7
Memory (3 points)	2.7 (0.6)	N/A	2.0 (0.8)*	1.0	1.6 (1.1)*	1.2	1.5 (1.2)*	1.3	1.7 (1.1)*	1.1
Orientation (10 points)	9.9 (0.4)	N/A	9.6 (0.7) [†]	0.5	9.3 (1.2)*	0.7	8.2 (1.9)*	1.2	8.9 (1.6)*	0.9

NC=Normal control; HD=Huntington's disease; MoCA=Montreal Cognitive Assessment; MMSE=Mini-Mental State Examination; d=Cohen's d statistic

[†] $p=0.002$ vs. NC

* $p<0.001$ vs. NC; significant after Bonferroni correction for multiple comparisons