HHS Public Access

Author manuscript

Mov Disord. Author manuscript; available in PMC 2023 April 07.

Published in final edited form as:

Mov Disord. 2018 February ; 33(2): 187–195. doi:10.1002/mds.27227.

Rating Scales for Cognition in Huntington's Disease: Critique and Recommendations

Tiago A. Mestre, MD, MSc[1,*], **Anne-Catherine Bachoud-Lévi, MD**[2], **Johan Marinus, PhD**[3], **Julie C. Stout, PhD**[4], **Jane S. Paulsen, PhD**[5], **Peter Como, PhD**[6,†], **Kevin Duff, PhD**[7], **Cristina Sampaio, MD, PhD**[8], **Christopher G. Goetz, MD**[9], **Esther Cubo, MD**[10], **Glenn T. Stebbins, PhD**[9], **Pablo Martinez-Martin, PhD**[11],

Members of the MDS Committee on Rating Scales Development

[1]Parkinson's Disease and Movement Disorders Center, Division of Neurology, Department of Medicine, The Ottawa Hospital Research Institute, University of Ottawa Brain and Mind Institute, Ottawa, Ontario, Canada

[2]Assistance Publique-Hôpitaux de Paris, National Centre of Reference for Huntington's Disease, Neurology Department; Université Paris Est, Créteil; INSERM U955 E01, Institut Mondor De Recherché Biomédicale, École Normale Supérieure, Créteil-Paris, France

[3]Department of Neurology, Leiden University Medical Center, Leiden, The Netherlands

[4]Institute of Cognitive and Clinical Neuroscience, School of Psychological Sciences, Monash University, Melbourne, Australia

[5]Departments of Neurology, Psychiatry, Psychological and Brain Sciences, Carver College of Medicine, University of Iowa, Iowa City, Iowa, USA

[6]Division of Neurological and Physical Medicine Devices, Office of Device Evaluation, Center for Devices and Radiological Health, United States Food and Drug Administration, USA

[7]Department of Neurology, Center for Alzheimer's Care, Imaging, and Research, University of Utah, Salt Lake City, Utah, USA

[8]CHDI Foundation/CHDI Management, Princeton, NJ, USA

[9]Department of Neurological Sciences, Rush University Medical Center, Chicago, Illinois, USA

[10]Department of Neurology, Hospital Universitário Hermanos Yagüe, Burgos, Spain

[11]National Center of Epidemiology and CIBERNED, Carlos III Institute of Health, Madrid, Spain

Abstract

Cognitive impairment is one of the main features of Huntington's disease and is present across the disease spectrum. As part of the International Parkinson's Disease and Movement Disorder

[*]**Correspondence to:** Tiago A. Mestre, Parkinson's Disease and Movement Disorders Center, Division of Neurology, Department of Medicine, University of Ottawa, 1053 Carling Avenue, Ottawa ON K1Y 4E9, Canada; tmestre@toh.on.ca.
[†]Deceased

Relevant conflicts of interest/financial disclosures: Nothing to report.

Supporting Data

Additional Supporting Information may be found in the online version of this article at the publisher's website.

Society-sponsored project to review all clinical rating scales used in Huntington's disease, a systematic review of the literature was performed to identify cognitive scales used in Huntington's disease and make recommendations for their use. A total of 17 cognitive scales were identified and evaluated. None of the scales met criteria for a "recommended" status. For assessing severity of cognitive dysfunction, the Montreal Cognitive Assessment was "recommended *with caveats*." The UHDRS Cognitive Assessment, the UHDRS-For Advanced Patients cognitive section, the Alzheimer's Disease Assessment Scale-Cognitive Subscale, the Frontal Assessment Battery, the Mattis Dementia Rating Scale, the Mini-Mental State Examination, and the Repeatable Battery for the Assessment of Neuropsychological Status were "suggested" for evaluating severity of cognitive impairment. The MoCA was "suggested" as a screening tool for cognitive impairment. The major challenge in the assessment of cognition in Huntington's disease is the lack of a formal definition of dementia and/or mild cognitive impairment in this disease. The committee concluded that there is a need to further validate currently available cognitive scales in Huntington's disease, but that it is premature to recommend the development of new scales. Recently developed Huntington's disease-specific scales, such as the Huntington's Disease-Cognitive Assessment Battery, hold promise but require the completion of more comprehensive clinimetric development.

Keywords

Huntington's disease; cognition; rating scales; validation; clinimetrics

Cognitive signs and symptoms are key features of Huntington's disease (HD) that contribute to significant disability.[1,2] Cognitive signs and symptoms are evaluated in both clinical practice and research. Several cognitive assessment instruments (subsequently referred to as scales), some of which were developed specifically for HD, are available and have been used to assess cognitive function in HD.[3–5] However, it is unclear which scales are appropriate for screening for the presence of cognitive impairment (or dementia), assessing the severity of cognitive dysfunction, or assessing cognitive change over time or after a therapeutic intervention.

The current review was commissioned by the International Parkinson and Movement Disorder Society (MDS) to assess all cognitive scales used in HD studies and to evaluate their context of use and validation in HD. Considering the significant number of cognitive scales available, we reached a consensus on how to pragmatically define the scope of this review. A consensus was reached to consider any clinical measurement tool assessing multiple cognitive domains applicable to HD that provided a meaningful summary score for "overall cognitive performance," with or without summary scores for each of those cognitive domains.

Methods

Organization and Critique Process

The Committee on Rating Scales Development of the MDS appointed a team of 8 members (subcommittee) to review scales used in HD to assess cognitive function; these members included neurologists and neuropsychologists (all specialists in HD) and an expert in scale

development and clinimetrics (J.M.). Two subcommittee members evaluated each scale. If a task force member had been involved in the development of a scale, he/she was not involved in its review. Data were extracted into a pro forma table provided by the MDS and adapted for the current review. Scale assessment included the description of the scale, its availability, its context of use, and its reported clinimetric properties in patients with HD. All subcommittee members jointly assessed the completed reviews of the scales. Any unresolved issues and limitations of the critiqued scales were identified for discussion and reporting. The final recommendations were based on consensus among the subcommittee members.

Selection of Scales

The methodology for this review was modeled on previously used procedures.[6] A literature search was performed using Medline on PubMed, Web of Science, EMBASE, and Psychinfo. The keywords used in the search included “Huntington*” OR “Westphal variant” OR “juvenile Huntington*” and the terms “scale” OR “questionnaire” OR “index” OR “measure,” as well as keywords selected for the purpose of the review: “cognitive,” “cognition,” “cogn*.” For each identified scale, a search was conducted for the terms “Huntington’s disease” or “Huntington disease” or “Huntington*” and the name of the scale. Manuscripts published before September 2016 were retrieved using the above search strategy and thoroughly screened by the chair of the subcommittee (T.A.M.) to ascertain which rating scale had been used in each study.

Inclusion/Exclusion for Review

Scales used at least once in HD samples were included. A scale was excluded from the review if (1) it was not available in English; (2) it was only mentioned in reviews but not used in an original study; (3) it had been created for the sake of a specific study without any information about its structure or use; (4) a full paper was not available (eg, abstract format only); or (5) no composite score of the scale was published. We also excluded scales not assessing cognitive function (inadequate construct) and cognitive scales presented as a set of neuropsychological tests/instruments that only provided information on the performance of the individual tests but lacked a meaningful summary score that could be calculated for “overall cognitive performance.”

Criteria for Rating

We followed the classification system for scale recommendations used by the MDS, which uses 3 criteria: (1) use in HD populations; (2) use in HD by groups other than the original developers and data on its use are available; and (3) the available clinimetric/psychometric data in HD support the goals of screening, diagnosis (e.g., evaluation of sensitivity/specificity, score cutoff points, and reliability) or measurement of severity (e.g., evaluation of reliability, construct validity, and score discrimination across levels of symptom severity), and measurement of a change in severity with time (e.g., responsiveness or sensitivity to change). For this review, we also considered the applicability of the scale to the profile of cognitive impairment present in HD and the ease with which it could be administered (i.e., expertise required, calculation of sum score); for further details, see Table 1.

Results

Identified Scales and Their Utilization in Clinical Research

We identified a total of 78 cognitive scales including various versions of the same instrument that have been used in HD studies. Fifty-one of these scales were excluded after abstract review, as they corresponded to individual cognitive tests or cognitive batteries that did not provide a meaningful summary score for "overall cognitive performance." Of the remaining 27 scales, 10 cognitive scales were excluded from further analyses for the following reasons: composite score used for a single study (n = 5), inadequate scale construct (n = 2), cognitive battery used as set of individual cognitive test scores (n = 2), and full article not available (n = 1); see supplemental material for names of scales. A total of 17 scales were identified and considered for in-depth assessment. After detailed review, three scales were excluded for the following reasons: cognitive battery used as a set of individual cognitive test scores (n = 2) and inadequate construct, for example, measuring other features besides cognition, such as behavior (n = 1); see Supplemental material for names of scales. No scales met criteria to be classified as "recommended." The Montreal Cognitive Assessment (MoCA) was considered "recommended *with caveats*" for the specific purpose of measuring severity of cognitive dysfunction and "suggested" for screening for the presence of cognitive impairment in HD. Eight scales were classified as "suggested" for the purpose of measuring severity of cognitive dysfunction, namely the UHDRS Cognitive Assessment, the UHDRS-For Advanced Patients (FAP) cognitive section, the Alzheimer's Disease Assessment Scale-Cognitive Subscale, the Frontal Assessment Battery, the Mattis Dementia Rating Scale, the Mini-Mental State Examination (MMSE), and the Repeatable Battery for the Assessment of Neuropsychological Status. Six scales were classified as "listed" (see supplemental material for names of the scales).

Critique of Clinical Cognitive Rating Scales

We provide a summary description of the rating scales classified as "suggested" or "recommended *with caveats*." See Table 2 for included scales, Table 3 for clinimetric data of scales suggested/recommended *with caveats*, and supplementary material for full descriptions.

Unified Huntington's Disease Rating Scale Cognitive Assessment

The UHDRS Cognitive Assessment is a section of the UHDRS. The UHDRS was originally developed by the Huntington Study Group to prospectively assess the clinical features and course of HD.[7] The UHDRS Cognitive Assessment takes approximately 15 minutes to complete. It includes 3 tests: (1) the symbol digit modalities test (SDMT/sampled cognitive domains: visual attention, working memory, symbolic encoding, and psychomotor speed), in which the total score corresponds to the number of correct responses within 90 seconds; (2) the Stroop color word interference test (sampled cognitive domains: psychomotor speed, cognitive flexibility, response inhibition, and selective attention), which includes 3 conditions (word reading, color naming, interference), each one of which is scored as the total number of items accurately completed within 45 seconds; and (3) the phonemic fluency test (sampled cognitive domains: language and executive functioning), in which the score corresponds to the total number of correct responses a subject generates in three 1-minute

tests, each test corresponding to a different letter. The entire UHDRS Cognitive Assessment is typically reported using the individual score of each test because each score is associated with a particular aspect of cognitive function. However, in some cases, a single sum score has been reported for this battery of 3 tests,[7] thus meeting criteria for inclusion in the current review. For the UHDRS Cognitive Assessment total score, lower scores indicate worse cognitive function. The UHDRS Cognitive Assessment has been used in many studies in HD.[8–12] The limited clinimetric data available for the summary score demonstrate excellent internal consistency (standardized Cronbach's alpha, 0.93),[4] convergent validity with the UHDRS-FAP cognitive section, and divergent validity with the noncognitive sections of the UHDRS.[4,13] The scale has been reported to be sensitive to change in some clinical studies[4,8,9] but not in others.[10,11]

Recommendation: The UHDRS Cognitive Assessment is "suggested" for assessing severity of cognitive dysfunction in HD. The validity of a sum score requires further assessment and may benefit from weighting the contribution of the 3 tests that make up the UHDRS Cognitive Assessment. Because of a reduced number of tests, it is not considered to adequately capture all relevant cognitive domains in HD.

Unified Huntington's Disease Rating Scale For Advanced Patients Cognitive Section

The UHDRS-FAP was developed based on the UHDRS but with adaptations to take into account the limitations of late-stage HD patients (UHDRS-Total Functional Capacity ≤ 5). It retains the labels of motor, cognitive, and behavioral sections of the UHDRS and adds a somatic section, which assesses signs and symptoms emerging with disease progression, such as tendon retraction. The cognitive section includes the Stroop task[4] and various tests from the Protocole Toulouse-Montreal d'Evaluation des Gnosies Visuelles (pointing tasks, simple commands, temporal orientation questions, praxis evaluations, automatic series, rating of participation in daily activities, categorical and functional matching).[14] It takes approximately 30 minutes to complete the 38 items of the entire UHDRS-FAP, whereas the cognitive section has 8 subtests.[4] The UHDRS-FAP cognitive section has only been used in HD by the original developers in a single study.[4] The UHDRS-FAP has been shown to have excellent internal consistency (standardized Cronbach's alpha, 0.96).[4] Correlation analyses have shown strong correlation with both the somatic section ($r = -0.76$) and the motor section ($r = -0.73$), all $P < 0.001$, of the UHDRS-FAP.[4] In the same group of late-stage HD, the UHDRS-FAP cognitive section (annual slope, −4.9/year; $P < 0.0001$) has been shown to be more sensitive to change over time than the UHDRS cognitive section (annual slope, −0.6/year; $P < 0.05$).[4]

Recommendation: The UHDRS-FAP cognitive section is "suggested" for assessing severity of cognitive dysfunction in late-stage HD. Further clinimetric development and use of the scale beyond its developers are needed.

Alzheimer's Disease Assessment Scale-Cognitive Subscale

The Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog) is a scale that was initially developed for assessing cognitive function in Alzheimer's disease (AD) in clinical trials.[15] In addition, the ADAS-Cog was used as a primary efficacy outcome

measure in pivotal studies of drugs that are currently Food and Drug Administration-approved for the treatment of AD. It consists of 11 items that cover language, memory, praxis, and orientation, which are considered the core symptoms of AD. The greater the cognitive dysfunction, the higher the total score. The scale takes between 30 and 45 minutes to administer, and training is required.[16] The total score has been shown to be significantly lower in normal controls than in HD patients.[17] Data from placebo groups of clinical trials in HD document lack of sensitivity to change after 12 weeks.[18–20]

Recommendation: The ADAS-Cog is "suggested" for assessing severity of cognitive dysfunction in HD, as it lacks clinimetric testing in HD and does not include subtests for attention or executive functions.

Frontal Assessment Battery

The Fontal Assessment Battery (FAB) is a short (10-minute) bedside cognitive and behavioral battery that was developed to assess frontal lobe functions in patients with neurological disease. It consists of 6 items that cover conceptualization, word generation, literal fluency, motor sequencing, sensitivity to interference, inhibitory control, and environmental autonomy, with a total sum score of 18 points.[21] A higher score corresponds to better cognition. Internal consistency has been reported to be very good in HD (Cronbach's alpha, 0.83).[22] Interrater reliability has not been assessed in HD. Correlations have been reported with verbal fluency ($r = 0.79$), the SDMT ($r = 0.80$), Stroop interference ($r = 0.72$), MMSE ($r = 0.83$), and the UHDRS motor section ($r = -0.80$).[22] FAB scores have been shown to be significantly lower in patients with HD (6.5 ± 5.0) than in controls (13.3 ± 3.3); $P < 0.001$.[22] It is not sensitive to executive changes in premanifest and early-stage HD. A floor effect has been reported in stage IV HD patients.[22]

Recommendation: The FAB is "suggested" for assessing severity of cognitive dysfunction in moderate HD, as core clinimetric data are not available in HD, namely, interrater reliability.

Mattis Dementia Rating Scale

The Mattis Dementia Rating Scale (MDRS) is a scale designed to screen for dementia. It consists of 5 areas sensitive to behavioral changes in dementia: attention, initiation and perseveration, construction, conceptualization, and memory, with a maximal score of 144 points. Higher scores indicate better cognition. Items are addressed in descending order, with the most difficult first, thereby enabling the duration of the scale to be shortened from 45 minutes to 25 minutes for cognitively intact subjects. The MDRS has been used in studies in both premanifest and manifest HD.[17,23–30] Reliability and validity have not been tested in HD. An annual slope of -0.7 ± 9.9 in the score of the MDRS has been reported in 22 adult early-stage HD patients.[26]

Recommendation: The MDRS is "suggested" for assessing severity of cognitive dysfunction in HD. The MDRS has the potential for use in HD but lacks formal clinimetric assessment in HD.

Mini-Mental State Examination

The Mini-Mental State Examinaton (MMSE) is a 30-point test that is quick to use (5 minutes) and is widely used in both clinical and research settings to assess cognition globally and to screen for dementia. Higher scores indicate better cognition. The MMSE has been used in many studies in premanifest and manifest HD. Internal consistency of the MMSE has not been assessed in HD. Convergent validity has been shown between the different domains of the MMSE and many other cognitive tests (see supplemental material). The majority of HD treatment studies indicate that the MMSE is not sensitive to change over time.[18,26,31–33] However, the MMSE has better sensitivity in moderate to severe stages of HD than in early-disease stages, and it may be useful in monitoring progression from moderate to severe HD.[34] A ceiling effect has been reported across different studies.[35–37]

Recommendation: The MMSE is "suggested" for assessing the severity of cognitive dysfunction in moderately impaired HD patients. The MMSE has important content validity limitations, as it does not assess executive function.

Montreal Cognitive Assessment

The MoCA is a short (10-minute) 30-point test that was developed as a generic assessment of cognitive function. Higher scores indicate better cognition. The MoCA samples multiple cognitive domains: spatiotemporal orientation, sustained attention, visuospatial/executive, verbal memory, language, naming, and literacy/abstract thinking. The MoCA has been used in several studies in HD across disease stages.[38,39] A cutoff score of <24 was reported to be indicative of cognitive impairment in 1 study,[39] whereas another study reported a cutoff of <26 to have sensitivity of 94% and specificity of 84% in the detection of cognitive dysfunction in HD.[40] The MoCA is more sensitive to an abnormal cognitive performance in HD than the MMSE.[39] In HD, the MoCA has very good internal consistency (Cronbach's alpha, 0.82),[40] and retest reliability has been studied using correlation analysis (Pearson correlations; $r = 0.83$).[5] Convergent validity has been reported between the MoCA and many well-established measures of cognitive functioning (see supplemental material).[40] The MoCA has been shown to be more sensitive to executive dysfunction in a variety of neurological disorders, covers a broader range of cognitive domains than the MMSE, is better for mild to moderate (severity) impairment, and has greater range in such samples.[41]

Recommendation: The MoCA is "suggested" for the screening of the presence of cognitive dysfunction in HD, and "recommended *with caveats*" for assessing severity of cognitive dysfunction, as the MoCA has undergone sufficient clinimetric development, but as a brief global cognitive assessment, the inclusion of a very reduced number of items per each domains is seen as a limitation of this scale. Often, the use of such a brief cognitive assessment tool requires additional comprehensive testing for a complete validation to determine the severity of cognitive dysfunction.

Repeatable Battery for the Assessment of Neuropsychological Status

The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) is a 30-minute clinician-administered test that includes 12 subtests for assessing cognitive decline over 5 domains (immediate memory, visuospatial/constructional, language, attention,

delayed memory). Although not developed for use in HD, it has been used in several studies in manifest HD.[42–44] Significant correlations have been reported between the RBANS and various UHDRS subscales (Total Motor Score, Total Functional Capacity, behavioral score) and various cognitive tests (SDMT, Stroop, TMT A and B, phonemic fluency, Wide Range Achievement Test reading).[43] Some of the indices of the RBANS, but not the total scale, showed a decline over 16 months in 38 HD patients.[44] The RBANS has also been reported to discriminate between HD patients who did and did not drive.[45] Ceiling effects of > 15% have been observed for picture naming and list recognition, and a floor effect of >15% has been observed for list recall.[44]

Recommendation: The RBANS is "suggested" for assessing severity of cognitive dysfunction in HD. The RBANS lacks core clinimetric development in HD, namely, reliability. The presence of ceiling and floor effects is also relevant.

Discussion

Based on criteria established by the MDS for reviewing scales, the current review, focused on cognitive scales in HD, concludes that no scales could be classified as "recommended." Overall, the review of data available on the use and validation of the scales deemed "recommended with caveats," "suggested," or "listed" raises important points for discussion:

1. Regarding screening of cognitive dysfunction in HD, there is no "gold standard" tool against which scales can be compared. Therefore, any recommendation for screening made in this review should be handled with caution. It is our view that in the absence of a gold standard, the cutoffs used to identify cognitive dysfunction may be inappropriate for HD. A related topic is the challenge of providing a formal definition of mild cognitive impairment (MCI) or dementia in HD, highlighting an important limitation in measuring criterion validity in rating scales for cognition in HD. The adoption of the general neurological definition for dementia and MCI based on the presence of cognitive impairment and the presence or absence of functional impairment, respectively, carries the challenge of identifying functional impairment strictly associated with cognitive impairment in a complex disease such as HD, in which other clinical features may contribute to a functional limitation.
2. The MoCA samples several cognitive domains that are relevant to HD, although the extent of the evaluation of these same cognitive domains is very limited. One particular aspect to consider when validating scales such as the MoCA, usually labeled in neuropsychology as "screening" instruments for dementia, is establishing the advantages and limitations of assessing multiple cognitive domains with such a reduced number of items, as often a more comprehensive assessment is needed for more complete validation.
3. Clinimetric properties, such as test-retest and intrarater reliability of the included scales, were hardly ever assessed in HD.
4. The lack of positive clinical trials of cognitive treatment for HD poses a significant limitation in analyzing the dimension of responsiveness related to

a therapeutic intervention. The committee also acknowledges that this limitation applies to other scales capturing other symptom/sign clusters in HD. Along the same lines, there has been no formal assessment of responsiveness in the scales included in this review.

5. Although for this review there was a consensus to only assess clinical measurement tools that provide a summary score of cognitive performance, it remains to be discussed which is the optimal construct for the development of cognitive scales in HD, namely, the inclusion of multiple cognitive domains compared with the use of a single domain. We agree that the ultimate purpose of developing a scale is an important consideration to take into account when choosing a scale construct, and a clear rationale should be put in place at its inception. Because HD affects a specific range of cognitive functions, composite cognitive scores that consider those cognitive functions, rather than focusing only on individual areas of cognition, will be more relevant for characterizing both disability and response to a cognitive treatment. Ultimately, the most valuable scales for assessing cognition will sample across the relevant cognitive domains in a psychometrically robust manner. An effort should also be made to consider the variability in an HD population, namely, when cognitive dysfunction appears in the natural history of the disease, patterns of cognitive dysfunction, mood, motor features, and medications that can condition the performance of cognitive tasks. Cognitive scales that allow these influences to be parceled will provide better clarity regarding the severity and extent of cognitive deficit.

Finally, although no scale was sufficiently validated to be classified as “recommended,” the committee considers that certain scales specifically developed for use in HD are undergoing important validation processes and deserve closer scrutiny to assess their utility and validation. These efforts will determine whether such scales fill the needed role of assessing the presence or absence of cognitive impairment and the ranking of its severity if present. No new scale development is currently recommended. More importantly, the committee finds that the precise definitions of what constitute MCI and dementia in HD (scale construct) are among the most important unmet needs in this field.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments:

During this review project, Peter Como passed away unexpectedly. Peter Como made innumerous and highly valuable contributions to clinical research in HD. In the field of clinical measurement, Peter Como was a leader in the development of the cognitive and behavioral components of the UHDRS. We thank Anne-Marie Williams for editorial support and Theresa Bolton for assistance in the literature search of the current review.

References

1. Paulsen JS, Long JD, Ross CA, et al. Prediction of manifest Huntington’s disease with clinical and imaging measures: a prospective observational study. Lancet Neurol 2014;13:1193–1201. [PubMed: 25453459]

2. Ho AK, Gilbert AS, Mason SL, Goodman AO, Barker RA. Health-related quality of life in Huntington's disease: Which factors matter most? Mov Disord 2009;24:574–578. [PubMed: 19097181]
3. Huntington Study Group. Unified Huntington's Disease Rating Scale (UHDRS). Available at: http://huntingtonstudygroup.org/tools-resources/uhdrs. Accessed December 9, 2016.
4. Youssov K, Dolbeau G, Maison P, et al. Unified Huntington's disease rating scale for advanced patients: validation and follow-up study. Mov Disord 2013;28:1717–1723. [PubMed: 24166899]
5. Stout JC, Queller S, Baker KN, et al. HD-CAB: a cognitive assessment battery for clinical trials in Huntington's disease 1,2,3. Mov Disord 2014;29:1281–1288. [PubMed: 25209258]
6. Schrag A, Barone P, Brown RG, et al. Depression rating scales in Parkinson's disease: critique and recommendations. Mov Disord 2007;22:1077–1092. [PubMed: 17394234]
7. Huntington Study Group. Unified Huntington's Disease Rating Scale: reliability and consistency. Mov Disord 1996;11:136–142. [PubMed: 8684382]
8. Ravina B, Romer M, Constantinescu R, et al. The relationship between CAG repeat length and clinical progression in Huntington's disease. Mov Disord 2008;23:1223–1227. [PubMed: 18512767]
9. Dorsey ER. A randomized, double-blind, placebo-controlled study of latrepirdine in patients with mild to moderate huntington disease: HORIZON investigators of the huntington study group and european huntington's disease network. JAMA Neurol 2013;70:25–33. [PubMed: 23108692]
10. Piira A, van Walsem MR, Mikalsen G, Nilsen KH, Knutsen S, Frich JC. Effects of a one year intensive multidisciplinary rehabilitation program for patients with Huntington's disease: a prospective intervention Study. PLoS Curr 2013;5.
11. Busse M, Quinn L, Debono K, et al. A randomized feasibility study of a 12-week community-based exercise program for people with Huntington's disease. J Neurol Phys Ther 2013;37:149–158. [PubMed: 24232362]
12. Tabrizi SJ, Scahill RI, Owen G, et al. Predictors of phenotypic progression and disease onset in premanifest and early-stage Huntington's disease in the TRACK-HD study: analysis of 36-month observational data. Lancet Neurol 2013;12:637–649. [PubMed: 23664844]
13. Devos H, Nieuwboer A, Tant M, De Weerdt W, Vandenberghe W. Determinants of fitness to drive in Huntington disease. Neurology 2012;79:1975–1982. [PubMed: 23100397]
14. Agniel A, Joanette Y, Doyon B, Duchein C. Protocole Toulouse Montreal d'Evaluation des Gnosies Visuelles. Isbergues: L'Ortho Edition; 1992.
15. Rosen WG, Mohs RC, Davis KL. A new rating scale for Alzheimer's disease. Am J Psychiatry 1984;141:1356–1364. [PubMed: 6496779]
16. Wesnes KA. Assessing change in cognitive function in dementia: the relative utilities of the Alzheimer's Disease Assessment Scale-Cognitive Subscale and the Cognitive Drug Research system. Neurodegener Dis 2008;5:261–263. [PubMed: 18322407]
17. Mohr E, Walker D, Randolph C, Sampson M, Mendis T. Utility of clinical trial batteries in the measurement of Alzheimer's and Huntington's dementia. Int Psychogeriatr 1996;8:397–411. [PubMed: 9116176]
18. Kieburtz K, McDermott MP, Voss TS, et al. A randomized, placebo-controlled trial of latrepirdine in Huntington disease. Arch Neurol 2010;67:154–160. [PubMed: 20142523]
19. Cubo E, Shannon KM, Tracy D, et al. Effect of donepezil on motor and cognitive function in Huntington disease. Neurology 2006;67:1268–1271. [PubMed: 17030764]
20. Giuffra ME, Mouradian MM, Chase TN. Glutamatergic therapy of Huntington's chorea. Clin Neuropharmacol 1992;15:148–151. [PubMed: 1350513]
21. Dubois B, Slachevsky A, Litvan I, Pillon B. The FAB: a Frontal Assessment Battery at bedside. Neurology 2000;55:1621–1626. [PubMed: 11113214]
22. Rodrigues GR, Souza CP, Cetlin RS, et al. Use of the frontal assessment battery in evaluating executive dysfunction in patients with Huntington's disease. J Neurol 2009;256:1809–1815. [PubMed: 19536583]
23. Salmon DP, Kwo-on-Yuen PF, Heindel WC, Butters N, Thal LJ. Differentiation of Alzheimer's disease and Huntington's disease with the Dementia Rating Scale. Arch Neurol 1989;46:1204–1208. [PubMed: 2530966]

24. Rosser AE, Hodges JR. The Dementia Rating Scale in Alzheimer's disease, Huntington's disease and progressive supranuclear palsy. J Neurol 1994;241:531–536. [PubMed: 7799001]
25. Paulsen JS, Butters N, Sadek JR, et al. Distinct cognitive profiles of cortical and subcortical dementia in advanced illness. Neurology 1995;45:951–956. [PubMed: 7746413]
26. Bachoud-Levi AC, Maison P, Bartolomeo P, et al. Retest effects and cognitive decline in longitudinal follow-up of patients with early HD. Neurology 2001;56:1052–1058. [PubMed: 11320178]
27. Peran P, Demonet JF, Pernet C, Cardebat D. Verb and noun generation tasks in Huntington's disease. Mov Disord 2004;19:565–571. [PubMed: 15133822]
28. Davis J, Filoteo J, Kesner R, Roberts J. Recognition memory for hand positions and spatial locations in patients with Huntington's disease: differential visuospatial memory impairment? Cortex 2003;39:239–253. [PubMed: 12784887]
29. Frank E Central auditory and visual processing in Huntington's disease. J Med Speech Lang Pathol 2009;17:21–29.
30. Peavy GM, Jacobson MW, Goldstein JL, et al. Cognitive and functional decline in Huntington's disease: dementia criteria revisited. Mov Disord 2010;25:1163–1169. [PubMed: 20629124]
31. Ranen NG, Peyser CE, Coyle JT, et al. A controlled trial of idebenone in Huntington's disease. Mov Disord 1996;11:549–554. [PubMed: 8866496]
32. Randomized controlled trial of ethyl-eicosapentaenoic acid in Huntington disease: the TREND-HD study. Arch Neurol 2008;65:1582–1589. [PubMed: 19064745]
33. Zinzi P, Salmaso D, De Grandis R, et al. Effects of an intensive rehabilitation programme on patients with Huntington's disease: a pilot study. Clin Rehabil 2007;21:603–613. [PubMed: 17702702]
34. Klempir J, Klempirova O, Spackova N, Zidovska J, Roth J. Unified Huntington's disease rating scale: clinical practice and a critical approach. Funct Neurol 2006;21:217–221. [PubMed: 17367582]
35. Rothlind JC, Brandt J. A brief assessment of frontal and subcortical functions in dementia. J Neuropsychiatry Clin Neurosci 1993;5:73–77. [PubMed: 8428139]
36. Sanchez-Pernaute R, Garcia-Segura JM, del Barrio Alba A, Viano J, de Yebenes JG. Clinical correlation of striatal 1H MRS changes in Huntington's disease. Neurology 1999;53:806–812. [PubMed: 10489045]
37. Bonelli RM, Hodl AK, Hofmann P, Kapfhammer HP. Neuroprotection in Huntington's disease: A 2-year study on minocycline. Int Clin Psychopharmacol 2004;19:337–342. [PubMed: 15486519]
38. Gluhm S, Goldstein J, Brown D, Van Liew C, Gilbert PE, Corey-Bloom J. Usefulness of the Montreal Cognitive Assessment (MoCA) in Huntington's disease. Mov Disord 2013;28:1744–1747. [PubMed: 23798501]
39. Videnovic A, Bernard B, Fan W, Jaglin J, Leurgans S, Shannon KM. The Montreal Cognitive Assessment as a screening tool for cognitive dysfunction in Huntington's disease. Mov Disord 2010;25:401–404. [PubMed: 20108371]
40. Bezdicek O, Majerova V, Novak M, Nikolai T, Ruzicka E, Roth J. Validity of the Montreal Cognitive Assessment in the detection of cognitive dysfunction in Huntington's disease. Appl Neuropsychol Adult 2013;20:33–40. [PubMed: 23373682]
41. Mickes L, Jacobson M, Peavy G, et al. A comparison of two brief screening measures of cognitive impairment in Huntington's disease. Mov Disord 2010;25:2229–2233. [PubMed: 20721924]
42. Randolph C, Tierney MC, Mohr E, Chase TN. The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS): preliminary clinical validity. J Clin Exp Neuropsychol 1998;20:310–319. [PubMed: 9845158]
43. Duff K, Beglinger LJ, Theriault D, Allison J, Paulsen JS. Cognitive deficits in Huntington's disease on the Repeatable Battery for the Assessment of Neuropsychological Status. J Clin Exp Neuropsychol 2010;32:231–238. [PubMed: 19484645]
44. Beglinger LJ, Duff K, Allison J, et al. Cognitive change in patients with Huntington disease on the Repeatable Battery for the Assessment of Neuropsychological Status. J Clin Exp Neuropsychol 2010;32:573–578. [PubMed: 19882420]

45. Beglinger LJ, Adams WH, Langbehn D, et al. Results of the citalopram to enhance cognition in Huntington disease trial. Mov Disord 2014;29:401–405. [PubMed: 24375941]

TABLE 1.

Classification system for scale recommendation

Category	Criteria
"Recommended"	(1) Scale has been used in HD populations. (2) Use in HD by groups other than the original developers and data on its use were available.[a] (3) The available clinimetric/psychometric data in HD support the goals of screening (eg, evaluation of sensitivity/specificity, score cut points, and reliability) or measurement of severity (eg, evaluation of reliability, construct validity, and score discrimination across levels of symptom severity), or measurement of a change in severity (eg, responsiveness or sensitivity to change).
"Suggested"	(1) Scale has been used in HD populations. (2) Only one other criterion (2) or (3) from the above recommended category applies.
"Listed"	(1) Scale has been applied to HD populations, but no further criteria met.

HD, Huntington's disease.

[a]For rating scales not originally developed for use in HD, criterion 2 was fulfilled if used in at least 1 group in HD that reported any kind of clinimetric/psychometric data in HD.

TABLE 2.

Summary of all included scales in HD

Scale	Developed for use in HD	Scale has been applied to HD populations	Used by other groups beyond the original developing group[a]	Appropriate clinimetric testing in HD	Recommendation level	Comments
UHDRS-cognitive assessment	Yes	Yes	Yes	No	Suggested for assessing severity of cognitive dysfunction in HD	
UHDRS-FAP cognitive section	Yes	Yes	No	Yes	Suggested for assessing severity of cognitive dysfunction in late-stage HD	
Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)	No	Yes	Yes	No	Suggested for assessing severity of cognitive dysfunction in HD	
Montreal Cognitive Assessment (MoCA)	No	Yes	Yes	Yes[1]/no[2]	[1] Recommended *with caveats* for assessing severity of cognitive dysfunction in HD [2]Suggested for screening for presence of cognitive impairment in HD	
Mattis Dementia Rating Scale (MDRS)	No	Yes	Yes	No	Suggested for assessing severity of cognitive dysfunction in HD	
Frontal Assessment Battery (FAB)	No	Yes	Yes	No	Suggested for assessment of severity of frontal lobe dysfunction in moderate-severe HD	
Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-cog)	No	Yes	Yes	No	Suggested for assessing severity of cognitive dysfunction in HD	
Mini-Mental State Examination (MMSE)	No	Yes	Yes	No	Suggested for assessing severity of cognitive dysfunction in moderate-severe HD	
HD-Cognitive Assessment Battery (HD-CAB)[b]	Yes	Yes	No	No	Listed	Data from ongoing clinical trials needs appraisal in the near future
Neuropsychiatry Unit COGnitive assessment tool (NUCOG)[b]	No	Yes	No	No	Listed	Very limited use
Wechsler Adult Intelligence Scale-Revised (WAIS-III)[b]	No	Yes	No	No	Listed	More recent version (WAIS-IV) has not been used in HD
Computerized Drug Research Cognitive Assessment System (CODGRAS/CDR)[b]	No	Yes	No	No	Listed	Very limited use
Addenbrooke's Cognitive Examination-Revised (ACE-R)[b]	No	Yes	No	No	Listed	
Brief Cognitive Rating Scale (BCRS)[b]	No	Yes	No	No	Listed	Very limited use

[a] For those not developed for use in HD, if used in 1 group.

[b] Note: References for scales categorized as "listed" are included in the online supplementary data.

TABLE 3.

Summary of clinimetric data of all scales used in HD with a recommendation level of “suggested” and “recommended *with caveats”*

Scale	Internal consistency	Test-retest reliability	Interrater reliability	Construct validity	Discrimination across disease stages/severity	Responsiveness	Ceiling/floor effect	Sensitivity/ specificity
Unified Huntington’s Disease Rating Scale (UHDRS)-cognitive assessment	+	NR	NR	+	+	+/−	NR	NR
Unified Huntington’s Disease Rating Scale for Advanced Patients (UHDRS-FAP)	+	NR	+	+	NR	+	No floor or ceiling effect (for TFC ≤ 5)	NR
ADAS-Cognitive subscale (ADAS-cog)	NR	NR	NR	NR	NR		Ceiling effect	NR
Frontal Assessment Battery (FAB)	+	NR	NR	+	+	+/−	Floor effect	NR
Mattis Dementia Rating Scale (MDRS)	NR	NR	NR	+	NR	+	Floor effect	+/−
Mini-Mental State Examination (MMSE)	NR	NR	NR	+	+	+/−	Ceiling effect	NR
Montreal Cognitive Assessment (MoCA)	+	+	NR	+	+	−	Ceiling effect	+/−
Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)	NR	NR	NR	+	R	+/−	Floor and ceiling effects	NR

NR, not reported; +, good performance; +/−, contradictory data or very limited data; −, poor performance.

Note: data regarding minimally clinically important difference was not assessed in any of the scales.