Unified Huntington's disease rating scale for advanced patients: Validation and follow-up study.

Katia Youssov, Guillaume Dolbeau, Patrick Maison, Marie-Françoise Boissé, Laurent Cleret de Langavant, Raymund Roos, Anne-Catherine Bachoud-Lévi

Unified Huntington's Disease Rating scale for Advanced patients: Validation and follow-up study

Katia Youssov, MD (1,2,3,4), Guillaume Dolbeau, RI (1,2,4, 6), Patrick Maison, MD, PhD (2,3,4,5), Marie-Françoise Boissé, MSc (1), Laurent Cleret de Langavant, MD, PhD (1,2,3,4), Raymund A. C. Roos, MD, PhD (7), Anne-Catherine Bachoud-Lévi, MD, PhD (1,2,3,4)

[1]AP-HP, Centre de référence Maladie de Huntington, GHU Henri Mondor- Albert Chenevier, F- 94000 Créteil, France

[2]INSERM U955, Equipe 01 Neuropsychologie interventionnelle, F-94000 Créteil, France

[3]Ecole Normale Supérieure, Institut d'Etudes Cognitives, 29 rue d'Ulm, 75005 Paris, France

[4]Université Paris Est, Faculté de Médecine, F- 94000 Créteil, France

[5] Pharmacologie Clinique, APHP, Hôpital Henri Mondor, F-94000 Créteil, France

[6] Unité de recherche Clinique, APHP, Hôpital Henri Mondor,F- 94000 Créteil, France

[7] Department of Neurology, K-05-Q 112, Leiden University Medical Center, P.O. Box 9600, Albinusdreef 2, 2300 RC Leiden, The Netherlands

Corresponding author:

Anne-Catherine Bachoud-Lévi (bachoud@gmail.com)

Service de neurologie, Hôpital Henri Mondor

51 av du Mal de Lattre de Tassigny, 94010 Créteil, France

Fax +33 1 49 81 23 26

Tel +33 1 49 81 43 01

Word count of the paper = 2970 words, character count of the title = 95

Running Title: Assessment of Advanced-HD patients

Key Words: Huntington's disease, Outcome research, Neuropsychological assessment

The authors report no financial disclosure or conflict of interest related to this research.

Funding sources for study: This work was supported by the Centre of reference of Huntington's disease (Ministry of Health, France) and by a Contrat d'interface INSERM (ACBL). Additional support was provided through the NeurATRIS (European Advanced Translational Research Infrastructure in Neurosciences) project, the Groupement d'Intérêt Scientifique (GIS)- Institut des Maladies Rares and the" Biomarker program" AP-HP.

ABSTRACT

Background: The Unified Huntington's Disease Rating Scale (UHDRS) adequately measures decline in patients at early and moderate stages of Huntington's disease (HD). In advanced patients, floor effects hamper the evaluation, thus calling for an adjusted scale. We designed the UHDRS-For Advanced Patients (UHDRS-FAP), in order to improve longitudinal assessment of patients at advanced disease stage.

Methods: Sixty-nine patients with a Total Functional Capacity ≤ 5 were recruited in France and in the Netherlands. Among them, 45 patients were followed-up longitudinally (mean 1.6 year ± 1.2) with the UHDRS-FAP; 30 were also assessed with the UHDRS. Cross-sectional analyses evaluated psychometric properties and inter-rater reliability of the scale. Longitudinal analyses evaluated the sensitivity to decline compared to the UHDRS.

Results: Internal consistency was higher for motor and cognitive scores than for somatic and behavioural scores (respectively 0.84, 0.91, 0.70, and 0.49). Inter-rater reliability was ≥ 0.88 in all scores. The somatic score, specific to the UHDRS-FAP, declined over time, as well as motor and cognitive performance with both scales. Although performance with the two scales correlated, the UHDRS-FAP appeared more sensitive to change and was the only scale which detected decline in patients with a TFC ≤ 1. Neither scale detected a significant decline in behavioural scores.

Conclusion: The UHDRS-FAP is reliable and more sensitive to change than the original UHDRS for cognitive and motor domains. It offers items relevant for daily care. Behavioural scores tended to decline but this may reflect the decline in the communicative abilities of the patients.

INTRODUCTION

Huntington's disease (HD) is an inherited neurodegenerative disease caused by a CAG extension in the *HTT* gene on chromosome 4 (1). The unquestionable genetic diagnosis makes it one of the best targets for therapeutic intervention among the neurodegenerative disorders. However, the manifestation of the disease covers various domains (motor, psychiatric, and cognitive) in which evolution is not always detected. The Unified Huntington's disease Rating Scale (UHDRS) (2) has shown its reliability and efficacy for follow-up in manifest patients, but ceiling and floor effects hamper the detection of changes in premanifest and advanced patients (3,4,5,6,7). Thus, in parallel to the development of new therapeutics, the development of adequate scales for patient assessment remains a major issue in HD.

Indeed, despite the increasing number of patients at advanced stage (38% in the Registry Study (8)), care guidelines and therapeutic interventions are limited by the lack of sensitive tools in this population (9,10). Inspired from the Alzheimer's disease field (11), the Behavior Observation Scale Huntington (BOSH) provides an inventory of the behavioural characteristics of advanced HD patients (12) but lacks a clinical assessment component which precludes it use for therapeutic intervention.

Therefore, we designed the UHDRS for Advanced Patients (UHDRS-FAP) for longitudinal follow-up of HD patients from stage 3 to 5 (13). Because the UHDRS is the universal reference in HD, we retained its structure, and designed the UHDRS-FAP as its complement. Thus, three sections capture motor, cognitive, and behavioural changes and an original section, the "somatic" subscale, assesses

symptoms emerging with the progression of the disease, for example, tendon retraction.

METHODS

Patients

Sixty-nine patients with HD confirmed by clinical, genetic and/ or family history, with a Total Functional Capacity (TFC) below or equal to 5 (13) were included. Twenty-four patients were assessed once and 45 at least twice. Forty-nine came from the outpatient clinics of the National Reference Centre for Huntington's disease (Créteil, France) including 14 patients from nursing home and 20 were institutionalized in the Huntington Centre Topaz Overduin, Katwijk. Demographic data are summarized in Table 1. The study started in 2001 in accordance with the bioethics laws in place at that moment in each country. All patients or their caregiver gave their informed consent for this study.

INSERT TABLE 1

UHDRS-FAP content

The construction of the scale followed several principles. First, we kept as much continuity with the original UHDRS, so the patients' evolution could be followed all lifelong. Second, we conceived the scale not only to capture the decline in patients but also to inform about their condition in order to adapt care. We thus established a provisional scale in 2001 by (i) identifying in the UHDRS items inadequate for scoring in the advanced patients, (ii) systematically reviewing the questions asked in these

patients by neurologists, nurses, speech therapists and physiotherapists to adapt their care, (iii) analysing the questionnaires for admission in long-term institutions. . Then, this scale was tested in a pilot, which conducted to the removing/addition/rephrasing of 50 questions (e.g. “3 = difficult, only possible with help”) and 7 items (e.g. “Capacity to transfer”) to constitute the present scale. Instructions were also adapted. Decisions were made both on statistical and clinical grounds.

The final version developed in French was then translated into Dutch and English (see addendum: the English version of UHDRS-FAP). Motor function, somatic domain, cognition, and behavior are assessed in 4 different sections. Administration takes about 30 minutes. The score in each subscale is the sum of all the ratings for each item. Like in the original UHDRS, a higher score indicates a more severe impairment in the motor, behavioural and somatic subscales whereas lower scores in the cognitive assessment indicate worse performance.

The motor subscale assesses 13 motor features with clinical ratings of gait, transfer capacity, dysarthria, risk of falls, deglutition, dysphagia, capacity of feeding, toileting, clothing, and other motor signs like cerebellar or pyramidal impairment, presence of synkinesia or tendon retractions (score range from 0 to 48). Somatic subscale includes nine items assessing digestion, continence for faeces and urine, pressure ulcers, hyperhidrosis, hypersalivation, and hypersomnia (score range from 0 to 32) Cognitive subscale includes pointing tasks, simple commands, temporal orientation questions, praxis evaluations, automatic series, daily activities participation rating, and categorical and functional matching of the Protocole Toulouse Montréal d'Evaluation des Gnosies Visuelles (PEGV) (14) and the Stroop task (15).

The behavioral subscale adapts the rating of the UHDRS for people with communication disorders. It transforms the 4 points score of each item of the regular UHDRS in binary yes/no answers about apparent sadness, anxiety, apathy, irritability, aggressiveness, agitation, obsession, and delirium. The rater is asked to provide a clinical impression and when a caregiver is available, to include also his/her impression during the previous month (score range from 0 to 8).

Procedure

Patients were assessed both with the UHDRS and the UHDRS-FAP in order to compare their sensitivity. In addition, 18 patients were independently assessed by two neurologists on both scales during the same visit to allow the evaluation of inter-rater reliability.

Analyses

We performed first a cross-sectional analysis of the whole cohort and second, a longitudinal analysis on the subgroup of patients who were tested at least twice. Analyses were first conducted with the UHDRS-FAP alone and then in comparison with the UHDRS. For each domain, only patients having fully completed the corresponding subscale were included in the analyses. Because the range of performance of the Stroop differs from the range of other cognitive items, we ran two analyses using either the raw performance of the Stroop or the log 10 performance of the Stroop in the cognitive subscale.

All tests were two-sided; p-values less than 0.05 were considered significant. Statistical analyses were performed using SAS 9.1 (SAS Institute, Cary, NC) and R for Windows.

Cross sectional analysis

Internal consistency of each subscale of the UHDRS-FAP was assessed through Cronbach's alpha analysis, using both raw and standardized values when available. We compared the UHDRS-FAP and the UHDRS using Spearman's rank correlation coefficients and convergent construct validity. Inter-rater reliability was assessed in all subscales of the UHDRS-FAP using the intraclass correlation coefficient (in the cognitive part, the Stroop and the PEGV which were already validated were excluded). In addition, in order to further support the consistency with the regular UHDRS, we ran several principal component analyses (PCA) with the Varimax rotation method. We first included all items of the UHDRS-FAP, and found that some items like dysphagia, vomiting or diarrhoea could not be grouped with others. In order to reduce the number of items regarding to the number of participants, PCA were ran within each section of the UHDRS-FAP alone and then both with the UHDRS and the UHDRS FAP (results not presented here).

Longitudinal analysis of the UHDRS-FAP

We evaluated sensitivity to change of the four UHDRS-FAP subscales using a mixed model to take into account both the variability in the number of measures and the delay between assessments for each patient. The UHDRS-FAP subscore was the dependent variable and time and subjects were entered as independent variables. Annual slopes were calculated for each component, and compared to 0 using a t-test; a slope of 0 indicates stability. Raw scores were converted to percent correct scores [0; 100] in order to compare the slopes by year of the UHDRS-FAP and the UHDRS. . The limits of the sensitivity of the two scales were further assessed by

conducting analyses both in the full cohort and in a selected subgroup of patients at TFC ≤ 1.

Finally, we calculated the statistical power with each scale for the determined number of patients and effect size to obtain a significant difference between two groups with different treatments. . Simulating different sample size (n=30, 50 and 100), we have estimated the gain of power with the UHDRS-FAP compared to the UHDRS. This gain is the ratio of the power of the UHDRS-FAP to the power of the UHDRS.

RESULTS

Cross sectional analysis

Sixty-nine patients were enrolled in the cross-sectional analysis. Baseline characteristics are summarized in Table 2. Because results were similar for the cognitive scale using either the raw values of the Stroop or their log10 values, we report here only on the log Stroop values.

.

INSERT TABLE 2

Internal consistency of the UHDRS-FAP (using standardized Cronbach's alpha values displayed in brackets) was higher in both the motor and the cognitive subscales (0.84 [0.82] and 0.91 [0.96]) than in the somatic and the behavioural subscales (respectively 0.70 [0.53] and 0.49). Results were similar to the Cronbach's

value calculated in the UHDRS for the motor 0.84[0.90] and the cognitive subscales 0.88 [0.93] but higher in the behavioural section of the UHDRS (0.82) than in the UHDRS-FAP. Intraclass coefficients (ICCs) showed high inter-rater reliability in both scales (UHDRS-FAP subscales: motor ICC=0.98, somatic ICC=0.99, cognitive ICC=0.88 and behavioural ICC=0.89 and UHDRS subscales: motor ICC=0.97 and behavioural: ICC=0.99).

Each section of the UHDRS-FAP correlated with the other sections ($p < 0.001$), with the exception of the behavioural score which did not correlate with any other score. Finally, each corresponding sub-scale of the UHDRS FAP and of the UHDRS correlated with each other (see Table 3).

INSERT TABLE 3

Longitudinal analysis

Forty-five patients were enrolled in the longitudinal evaluation of the UHDRS-FAP with a mean follow-up duration of 19.7 months (SD = 15.1, range, 6.0 – 59.7 months). All scores declined over time with the exception of the behavioural score ($\beta = 0.2 \pm 0.1$, $t = 1.9$, $p = 0.06$, $n = 45$;motor annual slope $\beta = 2.3 \pm 0.3$, $t = 8.1$, $p < 0.001$, $n = 44$ both when excluding dysphagia which was omitted at the second evaluation in Leiden or when including dysphagia in the sole patients at Créteil ($\beta = 2.5 \pm 0.3$, $t = 8.3$, $p < 0.001$, $n = 28$); somatic: $\beta = 1.3 \pm 0.3$, $t = 4.4$, $p < 0.001$, $n = 44$;

cognitive: β = -5.0 ± 0.9, t = -5,6, p < 0.001, n = 26). . In some items, the variance was null (presence of delirium or hallucination, presence of pressure ulcers).

A subset of these 45 patients (mean follow-up duration :motor 24.2 ± 13.4 months, cognitive 21.3 ± 12.0 months and behavioural 26.5 ± 14.2 months with a range from 6.0 to 59.7 months) were also assessed with the UHDRS (N motor = 27, N cognitive = 26, and N behavioural = 30), thus allowing comparison of the original UHDRS with the UHDRS-FAP.

Both scales detected motor decline but the slope using the UHDRS-FAP was greater than the one obtained with the UHDRS (UHDRS-FAP: β = 5.1 ± 0.7 by year and t = 7.0, p < 0.001; UHDRS: β = 2.1 ± 0.6 by year and t = 3.8, p < 0.001); F = 13.4, p < 0.001. Results are displayed in Figure 1A. Likewise, cognitive performance declined with both scales. The slope was β = -4.9 ± 1.1 by year (t = -4.4, p < 0.0001), with the UHDRS-FAP and β = -0.6 ± 0.2 by year (t = -2.4, p < 0.05) with the UHDRS (F = 16.2, p < 0.0001) as seen in Figure 1 B. Performance in the behavioural score declined over time with the UHDRS-FAP (β = 2.9 ± 1.5 by year; t = 2.0, p <0.05) but not with the UHDRS (β = 1.4 ± 0.8 by year, t = 1.7, p = 0.1, F = 1.2, NS, Figure1C).

INSERT FIGURE 1

Seventeen patients had a TFC ≤ 1 and at least 2 assessments with the two scales (mean follow-up duration 25.4 ± 12.7 months). In this group, the UHDRS-FAP expressed a decline both in the motor (β = 2.7 ± 0.4 by year; t = 6.9, p < 0.001) and in the cognitive domains (β =: -3.8 ± 1.0; t = -3.7, p < 0.01) whereas the UHDRS did

not capture any change (motor $\beta = 0.3 \pm 0.7$; $t = 0.5$, $p > 0.1$NS; $F = 6.9$, $p = 0.01$ and cognitive $\beta = -0.1 \pm 0.1$; $t = -1.2$, NS with $F = 6.0$, $p < 0.05$). There was no difference between the two scales in the behavioural domain (UHDRS: $\beta = 2.0 \pm 1.0$; $t = 1.9$, $p = 0.06$; UHDRS-FAP: $\beta = 2.9 \pm 1.9$; $t = 1.5$, NS; $F = 0.3$, NS). Finally, the somatic score declined over time ($\beta = 1.2 \pm 0.4$; $t = 3.0$, $p < 0.01$).

According to these slopes, for a sample size of 30 patients with TFC ≤ 1 and an effect size of 20%, the gain of statistical power is increased with the UHDRS-FAP compared to the UHDRS by 16.5 and 7.5 for motor and cognition respectively. In other words, UHDRS-FAP cognitive part allows a power of 82% when the UHDRS cognitive part provides a power of 11%. The UHDRS-FAP does not improve the power for the behavior score (ratio=0.6). For a sample size of 50, the ratios of power are of respectively 14, 6.0 and 0.5 and for N=100, respectively 11, 3.4 and 0.7. For patients without any selection on the TFC, the gain of power is over 1.3 whatever the sample size and the score.

DISCUSSION

We designed the UHDRS-FAP with the aim of providing a tool for longitudinal assessment in patients at advanced stages of HD by adapting the evaluation provided in the regular UHDRS and adding new items specific to this population of patients. Here, we assessed its reliability for observational and interventional studies of patients with a TFC ≤ 5. We demonstrated that the UHDRS-FAP can measure changes over time in patients in all domains (motor, cognitive, somatic and behavioural) even at very late stages, in contrast with the UHDRS. In addition, it

provides insight about impairments and signs usually present when the disease has progressed but which are poorly assessed by the UHDRS, like tendon retraction for example. It also captures remaining abilities in those patients and thus could support care purpose.

Like the UHDRS, the UHDRS-FAP demonstrates good internal consistency and inter-rater reliability, showing similar values through Cronbach comparison and the construct validity model (2,5). As expected, correlation between the two scales domain by domain is high. Behavioural symptoms are independent from other features in both scales whereas, cognitive, motor and somatic symptoms hamper functional capacity. However, the most important outcome of our study is the improved sensitivity to change in cognitive and motor subscales compared to the original UHDRS. The higher performance for tracking clinical changes longitudinally in advanced patients was particularly marked in very advanced patients (with a TFC ≤ 1), as it measures decline in motor and cognitive sub-scores which the original UHDRS failed to do. The UHDRS-FAP could then replace the UHDRS in patients longitudinally followed-up when their disease become more severe. The advantage of the cognitive sub-scale is that it allows the possibility to use the total score composed by the sum of the score at each item. The use of the Log10 Stroop score reasonably balances the cognitive score between various functions (language output, praxis, comprehension, orientation) and cancels the overweight of the raw Stroop values in the cognitive assessment. It provides a meaningful continuous measure from premanifest and early stages to the most advanced stages of the disease.

The somatic subscale focuses on very practical aspects of somatic disturbance like sleeping, sudation or pressure ulcers and still, showed sensitivity to change in the

longitudinal analysis. As it relates to the patients' comfort, it offers a strong basis for physiotherapy and daily care even in bedridden patients.

As expected the behavioural score of the UHDRS-FAP, like the UHDRS, did not correlate with the other subscales. They show an unusual trend for decline (16,17) in the full cohort (UHDRS-FAP) and in in the population of patients with TFC ≤ 1 (UHDRS). This might rather reflect the functional decline of the patients and their loss of communicative abilities (16,17) from the care-giver or the examiner impression. The PCA indicated consistency between items from UHDRS-FAP (e.g. "sadness") and those from the UHDRS (e.g. "depression") whereas the new scale is much easier to assess. However, the simplification of the scoring might have hampered the Cronbach value (0.49) but have limited the missing answers. Yet, as cognitive and behavioural changes, which are associated with functional decline drive the burden on families (18, 19), the behavioural part of the UHDRS-FAP might benefit from including items such as "cry", "opposition", "smile", "easy living for the caregivers" rather than "depression" or "anxiety".

The UHDRS-FAP is a sensitive scale which can be applied even in non-communicative patients. It results from a compromise between statistical results and the balance between clinical trial and care requirements. For example, we maintained in the scale two items without any variance (pressure ulcers, delirium/hallucination) because the lack of hallucinations here reflects its scarcity in the general HD population (1.6% in (20) Second, even if we did not found pressure ulcers in such well-followed-up cohort, their evaluation remains mandatory in bedridden patients. Finally, including dysphagia add a value (Cronbach score at .85) even in a smaller number of patients.

The time for evaluation is reduced for the motor and behavioural parts (less than 15 minutes) compared to the UHDRS. In contrast, cognitive assessment takes longer but is always applicable and thus more sensitive than the regular UHDRS. As therapeutic trials with advanced patients are difficult to conduct, it is noteworthy that the UHDRS-FAP requires fewer patients for clinical trials compared to the UHDRS, as shown by its effect size on motor and cognitive scores. Its ease of use will help in avoiding drops out as was the case in our study where none of our house-bound or institutionalized patients were lost to follow-up. A confirmation of the results of this study will be performed in a larger group of patients in the European Huntington Disease Network.

Acknowledgments:

Jenny Townhill corrected the manuscript for English.

Author roles:

KY, ACBL and RR designed the scales, ran the assessments of the UHDRS-FAP and contributed to the writing of the manuscript. GD was the data manager and ran statistical analyses and contributed to the writing of the manuscript. PM supervised the statistical analyses and contributed to the writing of the manuscript. MFB participated to the elaboration of the cognitive part of the UHDRS-FAP and ran the cognitive assessment. LCL contributed to the writing of the manuscript.

Financial Disclosures of all authors

KY, GD, MFB, and LCL report no disclosures. PM reports support from Eusapharma for analysing the RHLF cohort. RR receives project grants from CHDI and the Gossweiler Foundation. ACBL serves as an expert for the University of Sacramento, and receives institutional support from the Ministry of Health for the management of the Centre of reference for Huntington's disease. She benefits from a "contrat d'interface" by the INSERM for conducting her research.

References

1. Huntington's Disease Collaborative Research Group. A novel gene containing a trinucleotide repeat that is expanded and unstable on Huntington's disease chromosomes. Cell 1993; 72:971-983.

2. Huntington Study Group. Unified Huntington's Disease Rating Scale: reliability and consistency. Mov Disord 1996; 11:136-142.

3. Siesling S, van Vugt JP, Zwinderman KA, Kieburtz K, Roos RA. Unified Huntington's disease rating scale: a follow up. Mov Disord 1998; 13:915-919.

4. Huntington Study Group. Tetrabenazine as antichorea therapy in Huntington disease: a randomized controlled trial. Neurology 2006; 66:366-372.

5. Hogarth P, Kayson E, Kieburtz K, et al. Interrater agreement in the assessment of motor manifestations of Huntington's disease. Mov Disord 2005; 20:293-297.

6. Tabrizi SJ, Scahill RI, Durr A et al. Biological and clinical changes in premanifest and early stage Huntington's disease in the TRACK-HD study: the 12-months longitudinal analysis. Lancet Neurol 2011; 10:31-42.

7. Busse M, Al-Madfai DH, Kenkre J, Landwehrmeyer GB, Bentivoglio A, Rosser A. Utilisation of Healthcare and Associated services in Huntington's disease: a data mining study. PLoS Curr 2011; 3:RRN1206.

8. Orth M, Handley OJ, Schwenke C, et al. Observing Huntington's Disease: the European Huntington's Disease Network REGISTRY. PLoS Curr 2010; 2: RRN1184.

9. Simpson SA. Late stage care in Huntington's disease. Brain Res Bull 2007; 72:179-181.

10. Moskowitz CB, Marder K. Palliative care for people with late-stage Huntington's disease. Neurol Clin 2001; 19:849-886.

11. Appollonio I, Gori C, Riva G, et al. Assessing early to late dementia: the TSI and BANS-S scales in the nursing home. Int J Geriatr Psychiatry 2005; 20:1138-1145.

12. Timman R, Claus H, Slingerland H, et al. Nature and development of Huntington disease in a nursing home population: The Behavior Observation Scale Huntington (BOSH). Cogn Behav Neurol 2005; 18: 215-22.

13. Shoulson I, Fahn S. Huntington disease: clinical care and evaluation. Neurology 1979; 29:1-3.

14. Agniel A, Joanette Y, Doyon B, Duchein C. Protocole Toulouse Montréal d'Evaluation des Gnosies Visuelles. Isbergues: L'Ortho Edition; 1992.

15. Trenerry M, Crosson B, Deboe J, Leber W. The Stroop Neurological Screening Test. Odessa, FL: Psychological Assessment Resources; 1989.

16. Craufurd D, Thomson,JC, Snowden JS. Behavioral Changes in Huntington's disease. Neuropsychiatry Neuropsychol Behav Neurol 2001; 14:219-226.

17. Kingma EM, Van Duijn E, Timman R, van der Mast RC, Roos RA. Behavioral problems in Huntington's disease using the Problem Behaviours Assessment. Gen Hosp Psychiatry 2008; 30:155-161.

18. Paulsen JS. Cognitive impairment in Huntington's disease: diagnosis and treatment. Curr Neurol Neurosci Rep 2011; 11: 474-483.

19. Ready RE, Mathews M, Leserman A, Paulsen JS. Patient and caregiver quality of life in Huntington's disease. Mov Disord 2008; 23: 721-726.

20. Marder K, Zhao H, Myers RH, Cudkowicz M, Kayson E, Kieburtz K, Orme C, Paulsen J, Penney JB Jr, Siemers E, Shoulson I. Rate of functional decline in Huntington's disease. Huntington Study Group. Neurology 2000; 54: 452-8.

Tables and figure

Table 1: Demographic data at baseline of patients with Huntington's disease

Table 2: Clinical characteristics at baseline of the whole cohort

Table 3: Comparison of UHDRS and UHDRS-FAP: Correlation analyses

Figure 1: Longitudinal comparison between UHDRS and UHDRS-FAP

(A) Motor scale; (B) Cognitive scale; (C) Behavioural scale; and (D) Somatic scale. Regression curves are shown with confidence interval curves (67% IC). In the UHDRS cognitive curve, the complete confidence interval is not represented, due to negative values

Additional data

UHDRS for Advanced Patients (UHDRS-FAP): English version. Translation and instructions were achieved with the support of the EHDN (European Huntington's Disease Network).