SHORT REPORT

Assessment of simple movements and progression of Huntington's disease

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J Neurol Neurosurg Psychiatry 2007;78:405–407. doi: 10.1136/jnnp.2006.105338

Instrumental measurement of simple motion sequences reflects impairment in patients with Huntington's disease (HD). The objectives were to study the progress of symptoms of HD and tapping results in 42 patients with HD, without symptomatic drug treatment over 3 years. Assessment moments were at baseline, and at years 1, 2 and 3. Unified Huntington's Disease Rating Scale (UHDRS) total score and UHDRS arm score significantly increased. Motor test outcomes considerably worsened. Instrumental test results significantly correlated with both UHDRS scores at each assessment. Assessment of simple movement sequences is an additional simple method to follow impairment in patients with HD in addition to clinical rating.

Huntington's disease (HD) is a neurodegenerative, autosomal, dominantly inherited disorder, which manifests in early to middle adulthood and is associated with CAG repeat expansion in the first exon of a gene on chromosome 4. Characteristic clinical symptoms of HD are impaired cognition and behaviour, involuntary movements and bradykinesia, all of which influence initiation and execution of movement even in the early stages.¹ This results in a reduced performance of instrumental motor tests, which assess simple movements—that is, in patients with HD in comparison with healthy subjects.² Results of this motor task are not specific, but this kind of motion assessment does not require the services of an experienced clinician. In contrast with more complex alternate finger tapping tasks, this apparatus asks for repetitive performance of simple movements.² Results of this motor test support assessment of clinical symptoms in addition to clinical rating scales—that is, the Unified Huntington's Disease Rating Scale (UHDRS).^{2,3} This scale estimates behavioural, cognitive and motor dysfunction, but may have the physician's subjective impression.³ The objectives were to study the progress of symptoms in HD and tapping results in patients with HD, without symptomatic drug treatment over 3 years.

Subjects and methods

Patients with HD

In all, 21 female and 21 male patients with HD (mean (SD) age 48.79 (8.65) years; CAG 45.05 (2.95); age at onset of motor signs 40.74 (9.12) years; age at onset of psychiatric signs 39.1 (8.44) years) were enrolled. Patients with HD who had other medical conditions, which may affect the outcomes of the performed assessments, were excluded.

Design

Molecular analysis of the CAG expansion was performed as described elsewhere.⁴ We scored patients with HD with the UHDRS immediately before or after the motor test performance at each assessment moment at baseline (1), and at years 1, 2 and 3. The patients should receive no symptomatic drug treatment—that is, for involuntary movements, during the

observation period. All participating doctors and technicians were blinded to each other.

Unified Huntington's Disease Rating Scale

All patients with HD were scored with the UHDRS. Suitable items (6, finger taps; 7, pronate/supinate hands; 8, luria, fist-hand-palm test; 9, rigidity arms; 11, maximal dystonia b/c (right/left upper extremity); 12, maximal chorea d/e (right/left upper extremity)) of the motor part of the UHDRS were added to the UHDRS total score.²

Tapping

To execute the tapping test (Schuhfried Ges mbH, Mödling, Austria), the individuals were instructed to tap as quickly as possible on a computer-based contact board (3 cm×3 cm) with a contact pencil for a period of 32 s after the initial flash of a yellow stimulus light. The board was positioned at the centre of the table. When performing the task, elbows were allowed to be in contact with the table. The number of contacts was registered by means of a computerised device. First, the tapping rate of the right hand and then of the left hand were measured; the results of both were added for the statistical analysis. All patients were allowed to familiarise with this test.²

Statistics

Data showed a normal distribution. Consequently, parametric tests were performed. Analysis of variance with repeated measures design was used for comparisons in combination with Tukey's honest significant difference test for the post hoc analysis. Pearson product-moment correlation was used for correlation analysis.

Ethics

Informed consent was obtained from each patient. The local ethics committee of the university approved this study.

RESULTS

UHDRS total score ($F = 53.51$, $p = 7.3E-21$; fig 1A) and UHDRS arm score ($F = 28.1$, $p = 2.54E-13$; fig 1C) significantly increased. Tapping rates significantly decreased ($F = 5.8$, $p = 0.002$; fig 1B). Tapping rates were significantly correlated with both UHDRS scores at each assessment (UHDRS total score and tapping result: baseline, $R = -0.62$, $p < 0.001$ (fig 1D); year 1, $R = -0.43$, $p = 0.017$; year 2, $R = -0.74$, $p < 0.001$; year 3, $R = -0.67$, $p < 0.001$. UHDRS arm score and tapping result: baseline, $R = -0.55$, $p < 0.001$; year 1, $R = -0.42$, $p = 0.021$; year 2, $R = -0.78$, $p < 0.001$; year 3, $R = -0.62$, $p < 0.001$). The computed differences between the various assessment moments of the UHDRS and the tapping results were not related to each other (results not shown). Seven patients were lost to follow-up investigation at year 3 due to various reasons such as, lack of motivation, start of drug treatment and so on.

Abbreviations: HD, Huntington's disease; UHDRS, Unified Huntington's Disease Rating Scale

Figure 1 Head progression of Huntington's Disease (HD) after baseline (1), and at years 1, 2 and 3. For the definition of scores of Unified Huntington's Disease Rating Scale (UHDRS) and tapping outcomes see Methods section. p = p value of the post hoc comparison.

DISCUSSION

This study shows that both clinical UHDRS rating and assessment of simple movement behaviour reflect progression of HD. Earlier trials showed that tapping results correlate to severity of HD and standardised performance of complex movement sequences. But these studies did not follow the patients in the further course of HD.²⁻⁶ It took 3 years until the tapping test showed a significant difference from baseline, while the UHDRS showed differences much earlier. Thus the tapping test was less sensitive in our trial in detecting differences, probably as it mainly focuses on motor behaviour. By contrast, the UHDRS also captures additional aspects of HD. Therefore, we suggest the tapping procedure as an additional tool for tracking progression in HD.

Nevertheless, this study supports the value of this motor task for the assessment of symptoms of HD, although the tapping procedure is limited to the upper limbs. A positron emission tomographic study with repeat measurements of regional cerebral blood flow consistently located the functional neuroanatomy of tapping movements to the precentral and postcentral gyri and supplementary motor area in younger subjects.⁷ Thus deterioration of tapping rates may reflect abnormalities in basal ganglia outflow, to these motor cortical areas.⁷

We emphasise, that, although this computer-based test is more objective and could be used by assessors of motor function other than neurologists, it is difficult to think of a situation in which this test alone would be considered as an adequate assessment, as the UHDRS is proved to be a good tool. But the tapping rates may help to identify clinical changes and to follow the course of HD. Moreover, sequential tapping performance may help to detect

onset of clinical symptoms of HD much earlier. This would support the transformation of HD gene carriers into patients with symptoms of HD, which is complex from an ethical point of view.

Future studies will show whether this tapping test may monitor symptomatic drug effects—that is, the effect of neuroleptic or antidepressant compounds on the clinical presentation of symptoms of HD. A further future issue of research may be the variability of the tapping test in relation to inter-rater variability of UHDRS scoring.

In conclusion, the outcomes of the applied tapping procedure are not specific, but our results indicate that this assessment of simple movement sequences is an additional simple method to follow impairment in patients with HD.

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Competing interests: None declared.

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Received 25 August 2006

Revised 17 October 2006

Accepted 23 October 2006

Published Online First 10 November 2006

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