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Review Article

Neurology

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ABSTRACT: Huntington's disease (HD) is an autosomal dominant neurodegenerative disorder caused by a repeat expansion of CAG trinucleotides in the huntingtin gene (HTT) on chromosome 4. It is characterized by motor, cognitive and psychiatric manifestations that severely affect the patient's quality of life. Its evolution is insidious and structural and functional brain changes are present several years before presenting clinical features. Treatment is currently symptomatic, as there are no disease-modifying treatments. The objective of this review is to present a wide investigation of this disease and the emerging techniques that have shown encouraging results in different studies.

KEY WORDS: Huntington disease, diagnose, treatments.

Introduction

In 1872, George Huntington described HD, which he called "Huntington's Chorea" (from the Greek "choreia", dance), as well as its progressive and hereditary nature, associated symptoms and age of onset (1). In 1983, Gusella et al. located the genetic marker on the short arm of chromosome 4 (2). The HTT gene causal mutation was identified until 1993

Methods

An extensive database review was searched for terms such as "Huntington's disease", "Chorea", "Neurodegeneration" on Pubmed and google schoolar, and subsequently in combination with terms related to the disease modifying treatments proposed and studied in recent years, such as "Treatment update", "Immunotherapy", "DNA and RNA targeting". The search was restricted to articles in the English language and preclinical and clinical randomised studies were chosen. The search identified 8,134 candidate publications. We excluded 8074 articles due to lack of relevance and distance from the central theme of the research; as well as cross-sectional studies and clinical case series. Finally, 40 articles were included.

Results

Epidemology

The average age at which symptoms and signs appear is 40 years old (3), with a range of presentation between 20 to 65 years old, a symptomatic 20-year evolution is the average progress to death. It affects both sexes equally and occurs worldwide, although it is more common in Northern Europe and in Hispanic Americans. These populations have a higher frequency of HTT A1 and A2 haplotypes, which are at greater risk of spreading (3). On the other hand, the incidence is much lower in countries such as Japan, Taiwan and China (1-7 per million) in relation to the length of the average CAG repeat for each ethnic origin (4). Between 5.4% to 10% of cases start before age 21, known as juvenile HD (JD) or the Westphal variant. Rare cases of late-onset HD occur in the seventh or eighth decade of life (5).

Etiology

Molecular pathogenesis

HD is an autosomal dominant disorder caused by abnormal expansion of CAG trinucleotide repeat in exon 1 of the HTT gene, which results in the expansion of the mutant HTT protein (HTTm), which contains polyglutamine that causes neurodegeneration. The range of normal CAG repeat length is less than 27, intermediate alleles (AI) repeats between 27 and 35, reduced-penetration causal mutations between 36 and 39 and fully penetration of 40 or more are considered. Reduced penetration is rare in the population (0.25%), while the frequency of population with AI is relatively high (6.2%) (6).

An inverse relationship has been studied between the number of CAG repeats with the age of onset of motor symptoms and the decrease in cognitive ability, especially when the CAG repeat expansion is

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very large (> 60) (7). Most cases of JHD have expansions of 60 to 100 CAG repeats (5).

The age of onset of the disease decreases from one generation to the next due to increased lengths of intergenerational CAG repeats, mainly when the affected parent is the father due to a greater expansion in the sperm than in the somatic tissues. 70 to 90% of cases with large CAG repeats are inherited by paternal transmission (7).

HTTm expansion results in dysfunction and neuronal death through various mechanisms, such as the propensity to form abnormal aggregates and subsequent effects on cell proteostasis, axonal transport, transcription, translation, mitochondrial and synaptic function and microglial activation (6).

Genes involved in DNA repair can alter the age of motor onset, such as the FAN1 and MTMR10 genes on chromosome 15, RRM2B and URB5 on chromosome 8 and the MSH3 gene, associated with the somatic instability of CAG 19/4. Genetic pathways involved in DNA repair, mitochondrial fission and oxidoreductase activity have also been implicated (8).

Gross pathogenesis

HD is a degenerative brain disease, involving diffuse and progressive atrophy of the brain. Macroscopic postmortem and imaging examinations show that the main and earliest site of the disease is the striatum, which includes the caudate nucleus and the putamen; there is loss of structural and functional connectivity with other parts of the brain, caudate, dorsoventral and mediolateral neurodegeneration and less variable involvement of the globus pallidus, white matter mainly from the corticostriatal connections, nucleus accumbens, thalamus, subthalamic nucleus, cerebellum and cerebral cortex. (9)

The classification system for HD pathology consists of 5 grades (10) (Table 1)

Medium spinal neurons in the striatum are selectively vulnerable. There is an initial loss in the indirect pathway, which manifests clinically as hyperkinesia, followed by loss in the direct pathway resulting in a hypokinetic phenotype. The dopaminergic D2 receptors they express may be an important factor, in addition to the loss of brain-derived neurotrophic factor (BNDF) and glutamate excitotoxicity from corticostriatal projections. (11)

Widespread cortical degeneration is probably expressed clinically as cognitive impairment and various behavioral abnormalities. Early loss of white matter may contribute to increased or pendulous reflexes. The loss of specific hypothalamic neuronal populations may lead to dysautonomic symptoms, sleep disorders and weight loss. Cortical thinning occurs early in the disease and comes from the brain areas downstream of the disease. White matter atrophy may initially be observed up to 15 years before the onset of motor symptoms (12). Cerebellar degeneration, associated with ataxia, is most often found in JHD (5).

Several volumetric imaging studies have found a correlation between striatal atrophy and the duration of the disease and the length of the CAG repeat (9).

Diagnosis

The gold standard for diagnosis is the use of the Unified Huntington's Disease Rating Scale (UHDRS) and the expanded HTT CAG repeat length genetic tests. Clinical diagnosis is made on the basis of the family history of HD, the onset of the characteristic movement disorder, and the confirmed genetic mutation in the affected patient or family member. The risk of inheriting the causal HD mutation depends on the family relationship and the number of CAG repeats: greater than 39 is 100% (6).

UHDRS assesses total motor, cognitive, behavioral and functional ability. Cognitive section includes verbal fluency, symbol digit mode test and Stroop test. Behavioral section covers the frequency and severity of depressed mood, apathy, low self-esteem, guilt, suicidal thoughts, anxiety, irritability, aggression, obsessive thinking, compulsions, delusions and hallucinations. UHDRS addresses core functional areas of work, financial tasks, household chores, rutine activities and living situation to functionally assess the patient.

Traditional screening measures such as Folstein's Mini-Mental State Examination (MMSE) are less reflective of disease progression compared to UHDRS, so less useful (13). Quantitative motor assessments (Table 2) including tongue strength, grip strength, accelerated tapping and self-pacing are sensitive to disease progression. Timed tasks that control motor deceleration such as verbal fluency, symbol digit mode and Stroop testing are particularly valuable because they provide information on cognitive speed independent of the overall deceleration of motor responses, as well as being more sensitive to the detection of early changes in premanifest HD and progression (Table 2.1) (14). The

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use of informant based behavioural measures, such as Functional Behavioural Assessment, contributes to the interpretation of cognitive test performance (Table 2.2) (15).

Motor, cognitive and psychological function disabilities present in this disease result in the loss of functional independence and a considerable decrease in life quality. Reduction in total functional capacity is observed after the onset of symptoms with the loss of employment and the need for work modification (Table 2.3) (1).

Clinic

Motor symptoms

The most characteristic feature of HD is chorea, rapid involuntary movements of the face, trunk and limbs. Dystonia, deceleration, bradykinesia and slow twisting and stiffening movements of the extremities occur. Patients with chorea are known to have a reduced awareness of chorea and its deficits in general caused by dysfunction of the frontal striatal connections. Other symptoms present are abnormal oculomotor and eye chase movements, dysarthria, difficulty in fine motor control, abnormal postural reflexes, impaired gait and coordination. Motor impersistence, inability to maintain tongue protrusion or hand grip, are manifestations of frontal cortical dysfunction. Tics and tourette's are atypical presentations of adult-onset HD (16).

There is a slowdown and failure in psychomotor automation, which occur at the onset of the disease and are good predictors of progression and functional capacity in the patient's daily life. Chorea at the onset of the disease tends to decrease and be replaced by more dystonia and rigidity. The choreic motor phenotype is associated with better cognitive functioning than rigid bradykinetic. Patients with late-onset motor symptoms have greater gait instability than those with early-onset disease. When chorea is severe it causes exhaustion and falls. Up to 50% have more than two events per year (16).

JD is associated with prominent bradykinesia than with chorea and is more likely to have a rigid akinetic syndrome or parkinsonism accompanied by dystonia. In childhood, 65-85% present this phenotype, and up to 55% of young adults. Myoclonus, motor tics and seizures are present in 40% of cases (5).

Cognitive impairment

They are progressive and of subcortical pattern, since the attention and visuospatial processing speed functions are affected. There is relative preservation of language and memory. Over time they lead to subcortical dementia and are most associated with functional impairment.

While inspecting motor skills, the patient has problems with planning, attention, organization and sequencing, cognitive flexibility and problems with changing sets, as well as reduced performance on verbal fluency tasks, multitasking and "automatic" tasks.

When the basal ganglia are affected and there is interruption of the striatal-frontal pathways, there are difficulties in recognition memory, source memory, prospective memory, explicit memory, processing memory and signal memory. Difficulties have been reported in learning motor skills, sequential learning and serial reaction time (17).

As for social cognition, they show early-onset deficits in processing emotions, mainly negative ones, attribution of intentions, beliefs and mental states, recognition of vocal emotions, socially inappropriate behavior and facial expressions, as well as their own emotional expression. These aspects and the reduction of sympathy and empathy contribute to the social breakdown and damage of interpersonal relationships (17).

Other cognitive domains affected are speech production, which is progressively less intelligible, understanding of complex syntax and general language tasks. In the visuospatial domain, problems are manifested in perceptual discrimination and integration, mental rotation or manipulation of information and execution of timed visual search and construction tasks (17).

Psychiatric symptoms

They can appear up to 10 years before the start of the motor anomalies. Apathy, irritability and depression are the central behavioural changes in HD. The three different trajectories, as loss of motivation and drive are early-onset and becoming more widespread, while irritability and loss of temper control initially worsen and then decrease, and depression may arise at any time.

Apathy is progressive and correlates with executive decline. Dysfunction of the medial prefrontal, anterior cingulate and anterior temporal

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paralytic cortical cortexes has been implicated with this, as has disinhibition and impulsivity. Irritability is clinically significant in more than 50%, temperament uncontrol in 40%, and behavior or violence in 22%. Family members and caregivers are encouraged to identify the triggers of these episodes and to implement behavioral strategies to avoid outbursts.

Depressive symptoms exacerbate apathy, social withdrawal and cognitive performance, and are associated with suicidal ideation in 8% to 20% of HD patients. Suicidal ideation occurs in 6.3% of those with the causal mutation and 4.3% of those without it. Periods of increased risk of suicide are immediately prior to receiving a formal diagnosis and when the level of independence decreases. Other psychiatric disorders present are anxiety, obsessive-compulsive behavior in 10% of patients, rigidity of thought, delusions. Psychosis occurs in 3-11% of adults and 39% of JHVs. Depression, OCD and other problems with emotion and behavior are related to degeneration in the striatal circuits involving the frontal lobe and the ventral-anterior and medial-dorsal nuclei of the thalamus (18).

Other symptoms present are sleep disorders, dysautonomia, and metabolic changes. Increased motor activity has been reported in the stages of non-rapid eye movement sleep, restless sleep and insomnia (19). Autonomic dysfunction is reported in HD and JD. Profuse sweating, heat intolerance and progressive male sexual dysfunction may occur (21). The expression of HTTm throughout the body generates increased caloric requirements, even in very early prodromal or non-manifested stages, and progressive weight loss accompanied by altered gluconeogenesis and cholesterol homeostasis. Dysphagia due to swallowing problems contributes to weight loss and bronchial aspiration. A high basal BMI has been associated with a slower rate of functional, motor and cognitive impairment, independent of the size of CAG repeats (21).

Genetics

Genetic testing for HTTm mutation can be diagnostic or predictive. Predictive testing is performed before the onset of symptoms in adults at risk of inheriting the causal mutation 4. It has medical, psychological, ethical, social and financial implications for the person evaluated and his or her family members, so the delivery of a positive result must be done in person with the patient and family. It is usually performed for reproductive reasons. Referral to a genetic counselor is recommended prior to formal testing. On the other hand, predictive genetic testing is not recommended for children under 18 years of age (6).

Treatment

There is currently no known drug therapy with modifying effects in HD, so treatment is supportive. However, it is not fully effective, so studies to find alternative treatments are continuing.

Motor symptoms

Chorea only requires treatment when it affects quality of life, function or patient safety. The only medication specifically licensed to treat it is the vesicular monoamine transporter type 2 (VMAT2) inhibitor tetrabenazine, although it may increase the likelihood of depression. Less incidence of depression and suicidal ideation and impact on dystonia is reported (23). Deutetrabenazine is another VMAT2 inhibitor with a longer half-life and a lower risk of sedation. It is indicated in tardive dyskinesia, as is valbenazine (24).

Neuroleptics such as haloperidol, risperidone, sulpiride, olanzapine, and quetiapine have also been used, which also decrease depression and aggression, but side effects include weight gain, metabolic syndrome, drowsiness, and parkinsonism. Atypical antipsychotics such as aripiprazole and olanzapine are well tolerated. Benzodiazepines can adversely affect balance. Baclofen, benzodiazepines, botulinum toxin injections, lidocaine and non-steroidal anti-inflammatory drugs are useful in treating focal dystonia. Levodopa can be used to relieve the predominant bradykinesia and stiffness. Dopidines are dopamine stabilisers that are dependent on dopaminergic tone and may improve other aspects of motor dysfunction in HD (25).

Cognitive symptoms

Of the cholinesterase inhibitors, rivastigmine has been shown to improve cognitive tests (26). Bilateral deep brain stimulation of the globus pallidus interna could benefit cognitive functions and improve chorea without worsening bradykinesia. Research on both treatment is still ongoing (27).

Psychiatric symptoms

Valproate, aripiprazole and selective serotonin reuptake inhibitors (SSRIs) can be effective for irritability (28). Depression can be treated using SSRIs or tricyclic antidepressants (TCAs). Sedative antidepressants such as trazodone, mirtazapine or

TCAs can stabilize mood (29). Finally, medications such as methylphenidate, atomoxetine, modafinil, amantadine, bromocriptine, and bupropion have been used to treat apathy.

The evidence for non-pharmacological interventions in HD is limited. Formal neuropsychological assessment is recommended before starting therapies to coordinate multidisciplinary care. Physical and occupational therapy interventions promote safety and comfort to motor symptoms.

Several studies have reported improvements in executive and motor functions and gray matter structure after resistance training interventions, especially in combination with cognitive exercises, although randomized controlled trials are needed (30). Nutritional interventions such as prevention of weight loss improve motor symptoms. Advanced dysphagia can be treated with enteral nutrition (31).

Neuroprotective and disease-modifying therapeutics

The reason why HTTm expansion causes neurodegeneration is not yet fully known, research on treatments focus on possible pathways of neurodegeneration and reduction of HTTm levels.

HD is associated with early and prominent abnormalities within the immune system, immunomodulators treatments have intensified. In an ongoing study, it has been observed that laquinimod may improve motor function, behaviour, weight loss, longevity and the percentage of cells expressing mHTT. Another promising and equally ongoing study is the development of a humanised anti-SEMA4D monoclonal antibody (VX15 / 2503) from Vaccinex, as SEMA4D is highly expressed in HD. So far, behavioural and neuropathological phenotypic improvements have been seen in mouse models (32).

Gene silencing techniques are the most advanced in test development. They include negative regulation or complete deactivation of transcription or prevention of translation of the mutant gene. Orientation of mHTT DNA can be achieved using two approaches. Zinc finger proteins can selectively target CAG repeats to suppress their expression without suppressing other poly-CAG genes. In mouse models they have decreased 95% of mHTT production, 78% of mRNA and improved cognitive function (33,34). However, they have the potential to cause immune reactions. The CRISPR/Cas9 system edits the genome-wide mutation in pluripotent stem cells by cleaving the DNA and completely silencing the gene. It was successfully tested in a mouse model (35).

RNA targeting can be achieved through the use of antisense oligonucleotides (ASO), RNA interference (RNAi) or small molecule splicing inhibitors. ASOs are currently being tested. IONIS-HTTRx is a second generation 2'-O (2-methoxyethyl) ASO designed to reduce concentrations of HTT messenger RNA (mRNA). It has been shown to reduce HTTm concentrations in cerebrospinal fluid and central nervous system tissues by up to 63%, without adverse effects in humans (36); motor improvement in mouse models and reduction of light neurofilament protein, which shows correlation with progression of brain atrophy and neuronal injury (37). On the other hand, RNAi is more invasive, requiring intracranial injection into the striatum, but a single treatment can provide a permanent reduction in HTTm (38,39). Small molecule splice modifiers are promising in animal models of small muscle atrophy; we are currently seeking to identify small molecule splice modulators of mHTT (40).

Discussion

Huntington's disease (HD) is a neurodegenerative movement disorder characterized by involuntary and irregular movements of the limbs, neck, head and/or face (chorea). It is caused by mutations of a gene by autosomal-dominant inheritance. The onset of symptoms depends on the individual degree but the average is in adulthood. The ideal treatment is still under investigation, with current therapies being symptomatic management and supportive care.

Conclusion

Despite the discovery of the causal HD gene mutation more than 20 years ago, finding a cure for HD has been difficult. The few available treatments and failed clinical trials are not encouraging. However, the understanding of genetic mechanisms and their contribution to HD phenotypes has grown considerably. Numerous clinical trials focusing on experimental therapeutic intervention and therapies targeting pathogenesis have been conducted so far. Meanwhile, good communication with the HD patient and his/her family or caregivers is largely responsible for slowing down the progression of this devastating disease and improving quality of life as much as possible.

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Conflicts of interests

The authors state that there are no conflicts of interest.

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Figures

Grade 0	*Clinical evidence of HD but no macroscopic or microscopic abnormalities.*
Grade 1	No macroscopic abnormalities in the caudate or putamen, moderate fibrillary astrocytosis at the microscopic level.
Grade 2	Macroscopic changes in the caudate and putamen, but no macroscopic changes in the globus pallidus.
Grade 3	Lateral segment of the globus pallidus showing fibrillary astrocytosis with the medial segment unchanged.
Grade 4	Yellow-brown shrunken caudate, enlarged anterior horn of the lateral ventricle, and smaller nucleus accumbens.

Table 1. Neuropathological classification of Huntington's disease

UNIFIED HUNTINGTON DISEASE RATING SCALE (UHDRS)

MOTOR ASSESSMENT

OCULAR PURSUIT (horizontal and vertical)

0 = complete (normal)

1 = jerky movement

2 = interrupted pursuits/full range

3 = incomplete range

4 = cannot pursue

SACCADE INITIATION (horizontal and vertical)

0 = normal

1 = increased latency only

2 = suppressable blinks or head movements to

3 = unsuppressable head movements

4 = cannot initiate saccades

SACCADE VELOCITY (horizontal and vertical)

0 = normal

1 = mild slowing

2 = moderate slowing

3 = severely slow, full range

4 = incomplete range

DYSARTHRIA

0 = normal

1 = unclear, no need to repeat

2 = must repeat to be understood

3 = mostly incomprehensible

4 = mute

TONGUE PROTRUSION

0 = can hold tongue fully protruded for 10 seconds

1 = cannot keep fully protruded for 10 seconds

2 = cannot keep fully protruded for 5 seconds

3 = cannot fully protrude tongue

4 = cannot protrude tongue beyond lips

MAXIMAL DYSTONIA (trunk and extremities)

0 = absent

1 = slighthntermittent

2 = mild/common or moderatehntermittent

3 = moderate/common

4 = marked/prolonged

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MAXIMAL CHOREA (face, mouth, trunk and extremities)	RETROPULSION PULL TEST	FINGER TAPS (right and left)
0 = absent 1 = slighthntermittent 2 = mild/common or moderatehntermittent 3 = moderate/common 4 = marked/prolonged	0 = normal 1 = recovers spontaneously 2 = would fall if not caught 3 = tends to fall spontaneously 4 = cannot stand	0 = normal) (21515 sec.) 1 = mild slowing and or reduction in amplitude (1 1-14/5 sec.) 2 = Moderately impaired. Definite and early amplitude (1 1-14/5 sec.) fatiguing. May have occasional arrests in movement (7-10/5 sec.). 3 = Severely impaired. Frequent hesitation in initiating movements or arrests in ongoing movements (345 sec.) 4 = Can barely perform the task (0-2/5 sec.)
PRONATE/SUPINATE-HANDS (right and left)	**LURIA (fist-hand-palm test)**	**RIGIDITY-ARMS (right and left)**
0 = normal 1 = mild slowing and/or irregular 2 = moderate slowing and irregular 3 = severe slowing and irregular 4= cannot perform	0 = ≥4 in 10 seconds, no cue 1 = <4 in 10 seconds, no cue 2= ≥4 in 10 seconds, with cues 3= <4 in 10 seconds, with cues 4= cannot perform	0 = absent 1 = slight or present only with activation 2 = mild to moderate 3 = severe, full range of motion 4 = severe with limited range
BRADY KINESIA-BODY	**GAIT**	**TANDEM WALKING**
0 = normal 1 = minimally slow (? normal) 2 = mildly but clearly slow 3 = moderately slow, some hesitation 4 = markedly slow, long delays in initiation	0 = normal gait, narrow base 1 = wide base and/or slow 2 = wide base and walks with difficulty 3 = walks only with assistance 4 = cannot attempt	0 = normal for 10 steps 1 = 1 to 3 deviations from straight line 2 = >3 deviations 3 = cannot complete 4 = cannot attempt

Table 2.1 The results of Stroop Test and the other tests are reported as the raw number of correct responses. Higher scores indicate better cognitive performance.

UNIFIED HUNTINGTON DISEASE RATING SCALE (UHDRS)
COGNITIVE ASSESSMENT
VERBAL FLUENCY TEST Raw score
SYMBOL DIGIT MODALITIES TEST Raw score

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STROOP INTERFERENCE TEST
Color Naming (number correct)
Word Reading (number correct)
Interference (number correct)

Table 2.1 The results of Stroop Test and the other tests are reported as the raw number of correct responses. Higher scores indicate better cognitive performance.

UNIFIED HUNTINGTON DISEASE RATING SCALE (UHDRS)
BEHAVIORAL ASSESSMENT
Use the following keys to rate both severity and frequency
Severity
0 = absent
1 = slight, questionable
2 = mild
3 = moderate
4 = severe
Frequency
0 = almost never
1 = seldom
2 = sometimes
3 = frequently
4 = almost always
Sad/Mood: feeling sad, sad voice/expression, tearfulness, inability to enjoy anything.
Low Self-Esteem/Guilt: self blame, self deprecation including feelings of being a bad or unworthy person, feelings of failure.
Anxiety: worries, anticipation of the worst, fearful anticipation.
Suicidal Thoughts: feels life not worth living, has suicidal thoughts, active suicidal intent, preparation for the act.
Disruptive or Aggressive Behavior: threatening behavior, physical violence, verbal outbursts, threatening, foul, or abusive language.
Irritable Behavior: impatient, demanding, inflexible, driven and impulsive, uncooperative.
Obsessions: recurrent and persistent ideas, thoughts or images.
Compulsions: repetitive, purposeful, and intentional behaviors.
Delusions: Fixed false beliefs, not culturally shared
Hallucinations: a perception without physical stimulus: Auditory, Visual. Tactile, Gustatory and Olfactory.
Does the investigator believe the subject is confused? Yes or No
Does the investigator believe the subject is demented? Yes or No
Does the investigator believe the subject is depressed? Yes or No
Does the subject require pharmacotherapy for depression? Yes or No

Table 2.2 The total behavior score is the sum of all responses; however, this score may have less usefulness than the individual subscale scores for mood, behavior, psychosis and obsessiveness which are created by summing the responses to the corresponding questions. Higher scores on the behavior assessments indicate more severe disturbance than lower scores.

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UNIFIED HUNTINGTON DISEASE RATING SCALE (UHDRS)

FUNCTION ASSESSMENT

OCCUPATION	FINANCES	DOMESTIC CHORES	ACTIVITIES OF DAILY LIVING	CARE LEVEL
0 = unable	0 = unable	0 = unable	0 = total care	0 = full time skilled nursing
1 = marginal work only	1 = major assistance	1 = impaired	1 = gross tasks only	1 = home or chronic care
2 = reduced capacity for usual job	2 = slight assistance	2 = normal	2 = minimal impairment	2 = home
3 = normal	3 = normal		3 = normal	

YES OR NO QUESTIONS

Could subject engage in gainful employment in his/her?

Could subject engage in any kind of gainful?

Could subject engage in any kind of volunteer or non?

Could subject manage his/her finances (monthly)?

Could subject shop for groceries without help?

Could subject handle money as a purchaser in a simple?

Could subject supervise children without help?

Could subject operate an automobile safely and independently?

Could subject do his/her own housework without help?

Could subject do his/her own laundry (washldry) without help?

Could subject prepare his/her own meals without help?

Could subject use the telephone without help?

Could subject take his/her own medications without help?

Could subject feed himself/herself without help?

Could subject dress himself/herself without help?

Could subject bathe himself/herself without help?

Could subject use public transportation to get places without help?

Could subject walk to places in his/her neighborhood without help?

Could subject walk without falling?

Could subject walk without help?

Could subject comb hair without help?

Could subject transfer between chairs without help?

Could subject get in and out of bed without help?

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Could subject use toilet/commode without help?

Could subject's care still be provided at home?

INDEPENDANCE SCALE

Please indicate the most accurage current level of subject's independence (only -0 or -5 selections are acceptable)

100: No special care needed.

090: No physical care needed if difficult tasks are avoided.

080: Pre-disease level of employment changes or ends; cannot perform household chores to pre-disease level, may need help with finances.

070: Self-care maintained for bathing, limited household duties (cooking and use of knives), driving terminates; unable to manage finances.

060: Needs minor assistance in dressing, toileting, bathing; food must be cut for patient.

050: 24-hour supervision appropriate; assistance required for bathing; eating, toileting.

040: Chronic care facility needed; limited self feeding, liquified diet.

030: Patient provides minimal assistance in own feeding, bathing, toileting.

020: No speech, must be fed.

010: Tube fed, total bed care.

Table 2.3 The functional assessments include the Huntington disease functional capacity scale (HDFCS*),* the Independence scale and a checklist of common daily tasks. For the YES/NO questions, the investigator indicates if the patient could perform the task. The checklist is summed by giving a score of 1 to all "yes" replies. The independence scale is rated from 0 to 100. Higher scores on the function scales indicate better functioning than lower scores.

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Erick Moreno Pizarro
University of Guanajuato
Guanajuato, Mexico
erickmpizarro@gmail.com

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