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Tremor and Other Hyperkinetic Movements

Reviews

The Many Facets of Unawareness in Huntington Disease

Elizabeth McCusker[1,2*] & Clement T. Loy[1,2]

[1] Huntington Disease Service, Westmead Hospital, Westmead, Australia, [2] The University of Sydney, Sydney, Australia

Abstract

Background: Unawareness or diminished awareness is present when a patient's perception of obvious disease manifestations and impact differ from that of observers such as clinicians or family members.

Methods: We examined studies that specifically investigate unawareness in Huntington disease (HD).

Results: Unawareness of motor, cognitive, behavioral, and functional aspects of HD has been documented throughout the disease course. This can occur at motor and cognitive onset but is more pronounced as the disease progresses.

Discussion: We discuss the implications for diagnosis, symptom report at presentation, timing of diagnosis, acceptance of symptomatic care strategies, and reporting in clinical trials. Assessments of work place competency, discrimination, driving, and the particular challenges of isolated patients without caregivers are described. Engaging with a person who is unaware of their disease or its impact presents a number of conflicts, including maintaining the right to autonomy, privacy, confidentiality, and independence while recognizing concerns for the wellbeing of the vulnerable person with HD and their caregiver when the unaware person refuses assistance. Unawareness is seen increasingly as neurologically based due to the impairment of functional networks, predominantly in nondominant frontostriatal pathways.

Keywords: Huntington disease, awareness, agnosia, denial

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*To whom correspondence should be addressed. E-mail: elizabeth.mccusker@sydney.edu.au

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Introduction

Unawareness or diminished awareness is present when a patient's perception of obvious disease manifestations differs from that of objective observers. Unawareness often accompanies Huntington disease (HD) and is recognized by clinicians and family members alike. It becomes obvious as premanifest CAG (cytosine adenine guanine) repeat expansion carriers move toward a definitive diagnosis, but unawareness can be seen throughout the disease course. In the past, some have described this as denial of illness and a coping mechanism. However, unawareness is increasingly seen as neurobiological in origin, possibly a consequence of impaired nondominant frontostriatal pathways.[1–5]

Clinically, unawareness is witnessed across all disease domains (motor, cognitive, behavioral, and functional) and possibly for different disease features at different disease stages. For example, unawareness is not only seen accompanying involuntary movements, but can also be observed for dysphagia, falls, irritability, impaired organizational skills, and impaired ability to drive. It can be a difficult situation for the physician who recognizes signs and impact of disease before any acknowledgement by the unaware person. This is especially when an isolated person comes to clinic visits without an accompanying person and therefore a corroborative history and when disease changes pose a risk.

In this review, we examine studies that specifically investigate unawareness in HD. In addition, we review the means of assessment and pathophysiology and explore care implications and workplace, legal and ethical issues. We conclude by discussing patients with HD with preserved awareness and implications for future research.

Definition and illustrative case studies

The terms anosognosia (described first by Babinski), unawareness, lack of awareness and insight, and denial are often combined in the literature[2,4,6–8] for HD and other neurodegenerative diseases. Distilling these definitions, unawareness is present when: 1) the manifestations of

Table 1. Studies of Unawareness in HD

Author	HD Stage/ Participants	Domain of Impairment	Tests	Outcome	Specific Tests
Deckel et al 1993[4] Prospective	19 affected HD pts Several years to>10 years 14 controls non-HD	Cog, motor, and emotional	8 item self-report rating cog and motor abilities cf staff ratings	One-third of HD patients had anosognosia cf controls and cf raters	WCST WAIS-R Verbal/performance split and picture completion
Snowden et al 1998 [5] Prospective	40 affected HD pts duration 1–20 years	Motor	Subjective report questionnaire of direct experience/ consequences and QNE	Unawareness of choreiform movement but aware of nonchoreic motor consequences	Cog test correlates expected for HD stage
Vitale et al 2001[19] Prospective	9 affected HD pts and 13 PD	Motor	Pts asked to rate dyskinesias	Unawareness in HD related to disease duration and severity	Score of unawareness of dyskinesias when performing four motor tasks
Chatterjee et al 2005[9] Prospective	53 affected HD pts 53 caregivers	Behav	Self-report cf Caregiver rating on BDI, apathy, and irritability scales	Moderate – good for depression, low for apathy and fair at best for irritability	Caregiver assessment for moods and apathy as cognition worsens
Ho et al 2006[11] Prospective	75 affected HD pts All stages 67 caregivers	Motor Functional Cog	DEX, BDI and Telephone interview of cog status. Pts and caregivers rated themselves and each other	Pts underestimate cf caregiver ratings, which correlated with disease severity on UHDRS	DEX
Hoth et al 2007[12] Prospective	66 patient and collateral pairs	Cog/ emotional and functional	Patient Competency Rating Scale UHDRS, BDI, and Cog measures including WCST	Pts rated themselves better and did not correlate with findings on any subscales; greatest variance was for emotional	WCST greatest correlation with patient/collateral disagreement
Kaptein et al 2007[22] Prospective	51 couples (HD pts early to mod and partner)	QoL	UHDRS MMSE IPQ Medical Outcome Study of SF-36	Spouses report of more symptoms than the HD pts correlated with QoL	IPQ and MOS SF-36 to HD pts and spouses/partners
Duff et al 2010[10] Retrospective Data set enquiry	Premanifest 745 HD mutation and 163 without	Cog/behav	FrSBe difference participant and companion	Participants rating of frontal behaviors were less at low and high probability of diagnosis than mid. In contrast, companion rating of frontal behaviors was proportionate to probability of diagnosis	Total FrSBe

Table 1. Continued

Author	HD Stage/ Participants	Domain of Impairment	Tests	Outcome	Specific Tests
Sitek et al 2011[18] Prospective Specific	HD (23) cf PD with dyskinesia (25), PD without dyskinesia (21) and cervical dystonia 20	Motor and ADL	MIS Self-Assessment Disability Scale Patient and proxy and cog scores	Disparity in motor reports but not IADL	MIS AVLT
Hocaoglu et al 2012[21]	105 HD pts (36 early/18 mod/50 adv) with proxies	QoL	Self and proxy report of HrQoL Proxy perception of QoL	Good correlation between raters. Proxys perception of pt QoLbetter than pts'	HrQoL
Justo et al 2013[16] Prospective	28 Early HD 28 premanifest and 12 controls	Motor	Self attribution of motor scores vs observer when looking at video of themselves and assessing movements including non pathological involuntary movements	Underestimated movments cf with observer but controls underestimate their non pathological movements	Self attribution of motor scores vs observer.
McCusker et al 2013[17] Retrospective Data set enquiry	Premanifest HD 550 cf 163 nonmutation	Motor	UHDRS motor Participant HD History of symptoms, self-report of progression, cog, behav, and imaging measures	~50% with new motor diagnosis had no symptoms or report of progression	UHDRS motor and symptom history, self-report of progression
Cleret de Langavant et al 2013[20] Prospective	46 Early to mild HD 33 proxies	Cog memory	Subjective memory questionnaires given independently and before cog testing	Early stage HD 1 aware of memory impairment, HD 2 less aware but more aware than proxies	FCSRT Subjective memory score

Abbreviations: ADL, Activities of Daily Living; AVLT, Auditory Verbal Learning Test; BDI, Beck Depression Inventory; Behav, Behavioral; cf, Compared to; Cog, Cognitive; DEX, Dysexecutive Questionnaire; FCSRT, Free and Cued Selective Reminding Test; FrSBe, Frontal Systems Behavior Scale; HD, Huntington Disease; HrQoL, Health-related Quality of Life; IADL, Instrumental Activities of Daily Living Scale; IPQ, Illness Perception Questionnaire; MIS, Motor impairment scale; MMSE, Mini-Mental State Examination; MOS, Medical Outcome Study of the 36-Item Short Form Health Survey; PD, Parkinson Disease; Pts, Patients; QNE, Quantified Neurologic Examination; QoL, Quality of Life; SF-36, Short Form (36) Health Survey; UHDRS, Unified Huntington Disease Rating Scale; WAIS, Wechsler Adult Intelligence Scale; WCST, Wisconsin Card Sort Test.

disease and the consequences are obvious to and can be documented by an observer, but 2) the individual underestimates or does not report experiencing symptoms or notice these changes or the impact. The person with HD may also rate their own abilities better than another observer (companion, caregiver, or clinician) and be unconcerned (anosodiaphoria).[9–12] Unawareness may extend beyond the person's lack of awareness of self. This may include unawareness of others' needs and the changed relationship between the person and his/her environment. Unawareness compounds the effect of manifestations (e.g., disordered empathy and impaired Theory of Mind seen in HD).[13,14] Unawareness may impair the perception of symptoms unrelated to HD, including pain.[15]

These definitions of unawareness are best illustrated by case examples:

Case 1: A patient with behavioral, cognitive, and motor manifestations was diagnosed some years before they were admitted voluntarily to the HD unit. After a violent incident, staff counseled the person that the outburst was HD related. The person flew into a rage and declared that he/she did not have HD.

Case 2: A law enforcement officer with HD who knew the correct behavior chose to cross a six-lane highway away from a crossing on a number of occasions. This seems more than impulsivity or bad judgment and included unawareness of self and environment. The person was unconcerned and offered no explanation for his repeated jay-walking.

Case 3: A male well-acquainted with the course of HD in his family was diagnosed before an accident that caused paraplegia. He spent his

compensation money on a farm distant from services that he could never look after: an example perhaps that the unawareness of HD may extend to other afflictions affecting the person.

Summary of studies on unawareness in HD

Compared with Alzheimer disease (AD) and frontotemporal dementia (FTD), unawareness in HD is understudied. Table 1 lists chronological studies that can be grouped according to unawareness of motor features[4,5,16–19] and cognitive, behavioral, and functional manifestations.[4,9–12,20] Two studies examined patient and caregiver/proxy perceptions of disease impact on Quality of Life (QoL).[21,22] Most studies were designed to identify unawareness by finding discrepancies between the person with HD and an observer but, by definition, unawareness is superimposed on other disease features. Few compared the aware and unaware patients to controls for other disease features. Deckel et al[4] compared HD persons scoring high and low on an anosognosia scale, but the sample size was small. McCusker et al[17] analyzed awareness/unawareness at first motor diagnosis in PREDICT-HD (Neurobiological Predictors of Huntington Disease), a large cohort study of mutation carriers. Only the retrospective data analysis studies from PREDICT-HD[10,17] included imaging that could potentially identify the pathological substrate.

Tests used to measure unawareness

A number of test batteries were used in the prospective studies designed specifically to rate degree of unawareness.[4,5,9,11,12,18–22] These include the Free and Cued Selective Reminding Test (FCSRT), Wisconsin Card Sort Test (WCST), Dysexecutive questionnaire (DEX), total Frontal Systems Behavior Scale (FrSBe, participant and companion), the Motor Impairment Scale (MIS), and the subjective memory questionnaire scale given to patients and observers. In most studies, disease stage was established using the history, motor, behavioral, and Total Functional Capacity sections of the Unified HD Rating Scale (UHDRS).

Motor studies

Deckel et al administered a simple eight-item anosognosia scale to 19 HD patients. The scale, a self-report rating of cognitive and motor abilities, was compared with ratings by clinicians on two occasions and 14 non-HD controls who presented for neuropsychological testing for other reasons. Based on their score on this scale, 6 HD patients were identified with "high anosognosia" (HA) and 11 with "low anosognosia" (LA). The HA patients were found to be more impaired upon formal neuropsychological testing, although it was unclear whether the HA and LA groups were at different disease stages. The WCST separated the two groups. The authors suggested this might implicate involvement of the dorsal-lateral prefrontal pathway, which is activated by WCST.

In contrast, Snowden et al[5] suggested that unawareness of chorea was a physiological phenomenon and not due to cognitive or psychological factors. Their conclusion was based on the observation that HD persons who were not aware of the chorea did recognize its consequences. The authors further postulated that patients may not receive internal feedback of the chorea and therefore had no subjective experience of it. In support of this, they reported that chorea was not generally reported over a range of disease stages or associated with a particular pattern of cognitive impairment. Contrary to this hypothesis is the observation that some people are aware of their movements whereas some seem unaware of consequences.

Vitale et al[19] explored this further by recording the self-reported Abnormal Involuntary Movement Score for people with chorea in HD versus people with dyskinesia in Parkinson Disease (PD). In HD, unawareness of chorea and the impact on motor function was related to disease duration. In contrast, unawareness of dyskinesia in PD was not related to the Unified PD Rating Scale score, dyskinesia score, or disease duration.

Sitek et al[18] also compared patients with HD patients with chorea and people with PD-related dyskinesia. People with HD were found to underreport motor deficits compared to the other group. This disparity was not as evident for perception of activities of daily living, a finding that supported the conclusions of Snowden et al.[5]

McCusker et al[17] retrospectively analyzed PREDICT-HD data and identified unaware and aware groups at the time of motor diagnosis. In this study ~50% of patients were unaware of motor features at motor diagnosis. However two groups, one aware at motor diagnosis and one with motor complaints prediagnosis, were aware at a time when mild motor signs would be unlikely to have an impact and this does not support the hypothesis that only motor features with impact are recognized. The unaware group reported significantly fewer depressive symptoms. Magnetic resonance imaging (MRI) striatal volume loss was greatest in the more aware and diagnosed group. The significance is uncertain, as the limited imaging of the PREDICT-HD study did not specifically incorporate the areas thought to be involved in unawareness.

Cognitive and behavioral

Chaterjee et al[9] explored caregiver and patient agreement for depression, apathy, and irritability using standardized scales. Agreement for depression was fair to moderate but less marked in milder disease. Agreement for apathy was worse for more advanced disease, and agreement for irritability was "fair at best" regardless of disease stage.

Ho et al[11] examined executive dysfunction using the Behavioral Assessment of the Dysexecutive Syndrome (BADS). Patients with HD were able to rate their caregivers' behavior in a similar manner to the caregivers, but their rating of their own behavior differed significantly from their caregivers. This suggests a deficit in self-awareness. However the caregiver usually would not have dysexecutive function and therefore would be likely to be rated in the same way. Impaired perception could be an alternate explanation for this disparity between patient self-rating and caregiver rating of the patient. When asked to rank three aspects of behavior (cognition, self-regulation, and insight), people with HD ranked impaired cognition as the greatest concern, while caregivers ranked cognition and lack of insight as equally problematic. Overall, caregivers' rating of patients correlated better with UHDRS clinical measures of disease severity.

Hoth et al[12] took a similar approach using the Patient Competency Rating Scale (PCRS)[23] and eight motor items generated for the study. Again, collaterals' ratings correlated with neurological examination scores, dementia ratings, memory performance, and some measures of executive function (WCST perseverative responses and symbol digit), but patients' self-rating did not. Interestingly, better rating of one's own impairments was associated with depression. The authors' conclusion was that unawareness protects against depression, and we reported a similar finding among a very early group of HD motor phenoconverters.[17]

Duff et al[10] compared ratings by 745 mutation carriers and 163 noncarriers and companions on the modified FrSBe (apathy, disinhibition, and executive dysfunction), from the PREDICT-HD study. The companion scores correlated with markers of disease progression, including MRI striatal volume, through the prodrome. In contrast, HD carriers regarded themselves as less impaired within 5 years of diagnosis, whereas the companions rated them as more impaired.

Cleret de Langavant et al studied individuals with early to mild HD.[20] On a subjective memory questionnaire, patients with cognitive impairment did not rate themselves differently from those without cognitive impairment. Reduced awareness of memory deficit was related to disease progression but not depression. The authors agreed with others that unawareness of deficit might vary for different domains at various stages of disease progression.

QoL

Kaptein et al[22] studied the impact of illness perceptions on QoL in 51 spouses/partners and patients with relatively early HD, using the Illness Perception Questionnaire (IPQ) and the Medical Outcome Survey (MOS) of the Short Form (36) Health Survey (SF-36). Spouses perceived more symptoms and reported less control than patients, indicating patient unawareness. Patients' illness perception and that of their partners had an impact on QoL. The vitality (energy and fatigue) subscale score for the MOS SF-36 was associated with partner belief in long duration and a cure, and the patient's belief of long disease duration.

Hocaoglu et al[21] investigated health-related QoL (HrQoL) by comparing proxy assessments and patient self-ratings for subjects at different disease stages. Proxy ratings were similar to patient ratings for the overall score on the HD QoL. The better the patient report of QoL, the better the proxy report. On some specific subscales (cognitive and specific physical and functional scales) proxies rated HrQoL worse than patients rated themselves. The discrepancy was greatest in moderate disease.

To date, most studies of unawareness have focused on establishing the presence of unawareness in HD by documentation of the discrepancies between patient and observer reports. Unawareness is documented across varying disease domains and with few exceptions correlates with disease progression but is evident at the earliest stages.

Unawareness and disease stage

In the premanifest group, the examiner may find definite but subtle motor signs that constitute a clinical diagnosis, including some signs without associated symptoms (e.g., early eye movement disorder). Fifty percent of people in some studies at this time in their HD course may be classified as unaware.[17] However, others with similar motor scores and another prediagnosis group reported motor symptoms. This would be evidence against the physiological hypothesis as these participants were aware of relatively subtle changes that would be unlikely to have a consequence. In contrast, Justo et al[16] found that some participants from each of the early HD, premanifest HD, and control groups were unaware of movements. This included some with nonpathological movements in the control group. However, these were undefined phenomenologically and only occurred intermittently and were likely less noticeable. This observation therefore may or may not support the concept that only a motor abnormality that impacts function produces symptoms.

Unawareness of executive dysfunction has been documented in the premanifest population in PREDICT-HD.[10] Cleret de Langavant et al[20] found those with early HD were more aware of their memory changes than proxies in the study, but patient awareness of memory impairment lessened with disease progression.

The degree and spectrum of unawareness in the HD population may not be fully captured in studies to date, as patients with unawareness are less likely to attend formal clinics or join research programs or patient and family support groups.

In the studies we reviewed, patient unawareness in a range of domains correlated with increasing HD severity. Reports of disease impact by the observer correlates well with objective measures of impairment.

Pathophysiology

To date, most knowledge of the pathophysiology of diminished awareness in the dementias comes from specific studies in AD and FTD.[24–28] Orbitofrontal, temporoparietal, and cingulofrontal changes have been identified on imaging studies. In HD, the likely neural substrate is implied from general imaging and pathological studies in which impairment of frontostriatal pathways is well documented, particularly in the studies of progression in the premanifest phase.[10,17,29–32] In addition, evidence from a number of reports that right basal ganglia infarction results in neglect and denial of deficit and lack of concern is well documented.[4] Unawareness covers a number of domains, so a different pathological substrate is likely for a particular deficit. [8] Specific imaging/pathological studies in those with and without impaired awareness in established HD have not been performed. The database inquiry studies in premanifest disease[10,17] included imaging but were not specifically designed to capture unawareness in detail. Taking these and other dementia studies into account, one must agree with the conclusion of Sitek et al: "attribution of deficient self-awareness of motor symptoms exclusively to the orbitofrontal-limbic atrophy in HD may be a simplification of this complex phenomenon and requires further empirical evidence."[18]

The pathophysiological substrate has not been studied for unawareness in HD but is inferred from studies of other disease states in which unawareness is prominent and includes frontostriatal pathology but may vary for different HD domains.

Care implications

The primary ethical dilemma for neurologists and other care providers is the balance between a patient's family's concern regarding care and safety and maintenance of patient autonomy, privacy, and engagement in the context of unawareness.

Unawareness has a considerable impact on the timing of diagnosis, as well as caregiver and family relationships.[9,22] An unaware individual may not present for assessment or care. This may not be important unless the clinical changes pose a risk or are amenable to symptomatic interventions. However, among those without a known family history, delays in disclosure of risk to genetic family members can have significant consequences. Unaware individuals who do not want to disclose the risk of HD to other family members create another ethical conflict between confidentiality for the individual and the rights of those at risk to know.

Unawareness can also form a barrier to care delivery. People who are unaware tend not to attend clinics, and advice and support for the caregiver may not be optimal if the person with HD has not been assessed. We developed an outreach model of multidisciplinary care so that nursing staff and social workers trained in HD care, including behavior management, can visit at home or at the care facility. They act as "key workers" and liaise with the neurologists and members of the multidisciplinary care team. The situation is even more complex if these approaches are refused and when unawareness is superimposed on other behavioral and cognitive impairments including irritability, aggression, apathy, and depression.[3,9,33,34] A formal guardianship order may be needed as a duty of care.[4,35]

In patients with diminished awareness, some treatments may not be appropriate (e.g., when the person is unaware of chorea). However, many symptoms and manifestations of HD are amenable to interventions.[33] These include adoption of a healthy lifestyle; advice about diet; swallowing assessment and exercise therapy; treatment of depression and psychosis; home modifications and provision of aids for walking; and links to supportive care networks, a family physician, and research projects.

Lack of awareness also has substantial impact on caregivers. The patient may refuse intervention and assistance and have no perception that the caregiver needs respite or that they are unable to continue care. The caregiver usually initiates the patient's move to 24-hour inpatient care. This is particularly difficult if the person does not accept the need for later stage care. Caregivers may have difficulty in accepting this resistance to respite as part of the disease process.

In managing unawareness or diminished awareness, it is first important to recognize that this is frequent in HD and to encourage caregiver reports if the person with HD allows it. It is helpful to explain the nature of unawareness to caregivers and family members, including unawareness of cognitive impairment. Unawareness may be managed with a very gradual, nonconfrontational introduction of a care plan that preserves independence for the person with HD. Most studies have shown that unawareness has a greater impact with disease progression. Engaging the person early in the prodrome by offering assessments, review, research updates, and support and education is likely the best approach.

Unawareness delays diagnosis and care including treatment of modifiable symptoms and manifestations but also access to home services, caregiver support, and accommodation facilities if needed. Unawareness has a significant impact on the caregiver's ability to cope. An out-of-clinic outreach approach to care to engage with the unaware person is helpful.

Unawareness of functional and workplace competency and discrimination

To date, studies of discrimination in HD predominantly involve premanifest individuals. While a person's self-report of discrimination must be taken seriously and their employment protected, report of work performance and safety factors need to be considered. Some individuals with diminished ability to perform their usual employment safely may have reduced awareness and are unable to accept necessary changes to employment.

Both physical and cognitive impairments pose a risk in most occupations. While not a concern unless safety is compromised, the person with diminished awareness may not recognize the need for medical review with workplace duties in mind. The doctor's situation is even more difficult when a self-employed worker attends an appointment, especially if there is no companion and they refuse appropriate assessments.

This dilemma extends to a range of functions beyond the workplace that carry risks for the unaware person and others. These include impact on skills affected by cognitive decline (e.g., managing financial affairs). Driving is a particular concern if the possibility of reduced skill is unrecognized and the need for testing is rejected.[36,37] Driving restriction can make it very difficult to maintain an ongoing doctor–patient relationship.

Discrimination in the workplace must be guarded against. However self-report and even caregiver reports of workplace competency could be unreliable. Full assessment that takes into account the nature of the person's employment and other risk-prone activities (e.g., driving and financial management) can be difficult if unawareness is present and the need for assessment is not accepted.

Legal and ethical aspects of unawareness

The effect of impaired awareness on competency and capacity to make decisions needs to be recognized as an integral part of life and care decisions. Most of the discussions of the ethical implications of impaired awareness are in the Alzheimer's disease and dementia literature.[8,38] The multifaceted nature of competency, capacity, and awareness is emphasized in these studies.[8,38] The HD person is very vulnerable, especially when isolated. Errors of judgment in relation to life decisions are in part related to diminished awareness of the disease

process. An early power of attorney agreement is advised, as well as an up-to-date will and care directives, with the provision for periodic review. Poor planning and apathy compounded by unawareness may require appointment of a legal guardian or surrogate decision maker. Even then, the guardian may be powerless to act for an unaware person with major behavioral disturbance and withdrawal from medical and social contact.

The relatively long disease duration adds another layer of complexity. Earlier in the disease course, a person with HD may indicate through living wills and other predetermined directives how they wish to be treated in the future. However, they may not view HD in the same way as the disease progresses. With progression, their perception of QoL may also differ from others', including those entrusted with making decisions for them. For instance, some very advanced HD patients, with little awareness of disease impact, lead a relatively happy and content life that they may not have imagined earlier. It is important that the person is involved when care decisions and end-of-life plans are discussed, and if possible included in a routine review process.[22]

Finally, the authors of studies of unawareness of motor features in HD, in particular chorea, emphasize that it may not be ethical to offer antichoreic agents when the person is not aware of or bothered by movements. This is particularly so when medications cause side effects. The treatment of behavioral manifestations and depression or other disease features with a potential for harm is a different matter, and a duty of care could be argued.

Unawareness has a significant effect on decision making and must be considered when competency and capacity are assessed. Unawareness may change the person's perspective of disease impact and requires regular revision of care directives.

People with HD and preserved awareness

While unawareness poses significant problems, there is a group with more acute awareness of disease manifestations, even at early stages.[5,16,17] People aware of motor signs at phenoconversion in prodromal HD were more likely to experience depression and a greater perception of progression than the unaware group.[17] This link between depression and awareness has also been reported in other neurodegenerative diseases and is associated with a greater risk of suicide.[39,40] Most instances of suicide in our clinic population, including some very violent deaths, occurred in people with preserved awareness of disease and the consequences for themselves and others.

There is also a clinically observed group that is hyperaware. After testing positive as mutation carriers, they suspect HD onset with any movement or memory lapse. Anxiety is the most frequent outcome to impact on QoL after genetic testing.[41] In some people, this interferes with daily life over years, despite pre- and posttest counseling. For others, this may represent nonmotor onset.

Some people, usually in earlier stages of HD, retain awareness that is associated with anxiety, depression, and greater suicide risk.

Implications for research

Currently, there is no specific inclusion of unawareness in the HD behavior scales (UHDRS for Behavior and Problem Behavior Assessment [PBA]). There are provisions to include a corroborative history, but it is important to take unawareness into account. Otherwise, assessment of disease onset, symptoms, progression, and trial outcome could be affected. Based on the studies listed, self-report of history and progression is inaccurate in 30–50% of cases. Thus, self-report of treatment response from trial medication or placebo may be misleading and result in inaccurate trial outcomes because up to 50% of people will be unaware of disease manifestations and impact.

Conclusion

Unawareness in HD requires further specific studies to define the best tools for assessment, pathophysiology, and associations with the disease features at different disease stages. Our current motor-based diagnostic criteria need review[42,43] because cognitive and behavioral symptoms and manifestations often precede motor onset,[10,17,44] and unawareness is often included in these symptoms. Maintenance of patient autonomy by avoiding patronizing intrusions while still recognizing the impact of diminished awareness is a major challenge in caring for people with HD. When the many facets of unawareness compound the challenges of care, HD is indeed a confronting, complex condition.

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