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Review

Unawareness of Deficits in Huntington's Disease

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Abstract. People with Huntington's disease (HD) may show reduced awareness of physical and mental changes in themselves. This article reviews the evidence for loss of awareness (anosognosia) in an attempt to elucidate its characteristics and possible underlying mechanisms. It is shown that defective awareness occurs across domains. People with HD may under-report the presence or severity of involuntary movements, under-estimate cognitive impairment and deny behavioural change. Nevertheless, awareness is not all or none. Moreover, it may be affected differentially for different symptom domains and emerge at different stages of disease, raising the possibility of distinct contributory mechanisms. Findings of an inverse relationship between insight and severity of disease suggest that cognitive impairment, in particular executive dysfunction, may be an important contributory factor. Evidence has accrued to support this argument. However, cognitive impairment cannot fully account for patients' lack of awareness of involuntary movements. Findings that patients accurately report consequences but not the experience of involuntary movements, and better acknowledge their presence when watching videotapes of themselves suggests that physiological factors play an important role. The putative role of denial as a coping mechanism is discussed. Recognition by clinicians of deficient self-awareness is crucial because of its implications for diagnosis and optimal clinical management of HD.

Keywords: Huntington disease, anosognosia, chorea, awareness

INTRODUCTION

It is a common clinical observation that people with Huntington's disease (HD) show reduced awareness of the changes in themselves. They may deny choreiform movements, fail to report neuropsychiatric symptoms and underestimate cognitive difficulties. Such loss of awareness or 'anosognosia' is now a well-documented feature of HD. Nevertheless, findings across published studies are not entirely uniform. Moreover, impoverished awareness is open to a variety of interpretations.

This paper reviews the published evidence for anosognosia in HD with the aim of addressing the following questions: 1) Is anosognosia domain-specific

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or generalized? 2) Is it influenced by severity of illness/stage of disease? 3) Is it secondary to or independent of cognitive impairment? It is hoped that consideration of these questions will help to shed light on possible mechanisms underlying anosognosia in HD. Better understanding may in turn carry implications for medical care and education of caregivers.

IDENTIFICATION AND CLASSIFICATION OF STUDIES

To identify original studies of anosognosia we performed a combined Web of Science MEDLINE search using the following search terms: TITLE [anosognosia OR self-awareness OR aware(ness) OR unaware(ness) OR self-report OR denial OR non-recognition OR insight] and TITLE [Huntington('s)] AND article type [article OR review] AND RESEARCH AREA [neurosciences neurology OR psychiatry OR psychology OR behavioral sciences OR geriatrics gerontology]. Forty-one papers were initially identified. We excluded one case study, one review paper in Polish, one validation study of self-report scale and 25 papers in which the term "insight(s)" did not denote "self-awareness". Thirteen studies on self-awareness in HD remained (Table 1).

The course of HD is conventionally divided into 5 stages according to patients' functional abilities [1]: stage 1 (i.e. able to function at home and work), stage 2 (i.e. unable to perform work and household activities at premorbid level), stage 3 (i.e.unable to work and /or manage household duties), stage 4 (i.e. no longer independent in daily activities), stage 5 (i.e. 24-hour care). An additional 'preclinical' stage refers to people with the HD mutation who do not yet manifest overt clinical signs of disease. Awareness has been studied in both preclinical [2–4] and early-stage (stages 1–3) HD [2, 3, 5–14].

Most studies of awareness in HD have involved comparison of patients' self-ratings with those of caregivers/companions [2, 8–14] (see: Table 1). Other studies have compared patients' ratings with ratings or measurements made by clinicians [3–7].

INSIGHT INTO MOTOR IMPAIRMENT

Involuntary movements in HD are typically first reported by patients' proxies rather than patients themselves. In line with this clinical observation the five studies that have investigated awareness of movement disorder in HD have all demonstrated impairment [3, 4, 6, 7, 11]. In one of the first studies on anosognosia in HD, Snowden et al. [6] found that HD patients under-reported involuntary movements. Yet, those same patients acknowledged the consequences of motor impairment (e.g. spilling drinks, bumping into furniture), which correlated with standard objective measures of movement disorder. This phenomenon cannot be explained by the patient's failure to understand the types of movement in question, as Snowden et al. asked the questions about chorea using non-specialist terms (e.g. twitching, jerking, moving against one's will). Moreover, the underestimation of chorea in HD was confirmed by Sitek et al. [11], who used videos to illustrate the types of movement in question. HD patients not only underreport chorea generally, they may also fail to notice the presence of chorea during the performance of a motor task, as demonstrated by Vitale et al. [7], who asked HD patients about the presence of chorea just after executing a motor task.

Anosognosia of chorea has also been described in the case of choreic dyskinesias in PD [7, 11, 15] and drug-induced dyskinesias in schizophrenia [16]. Two studies compared awareness of chorea in HD and Parkinson's disease (PD). They showed that although anosognosia for choreic movements occurred in both, it was more frequent [7] and more severe [11] in HD. These findings suggest that choreic movements may generally be more difficult to perceive for the individual. However, HD patients may be more prone to anosognosia than PD patients.

Awareness is sometimes treated as an all-or-none phenomenon. Nevertheless, there is evidence that this is an oversimplification. The above findings suggest that people with overt chorea in the course of HD are more likely to underestimate than to deny chorea and they may lack the direct experience of involuntary movements while retaining awareness of their functional consequences.

INSIGHT INTO MEMORY IMPAIRMENT

It is observed clinically that people with HD may complain of memory problems. The question is whether they can accurately judge the extent of those difficulties. Two studies have compared subjective and objective measures of memory performance in HD [12, 14]. In the first study, involving patients at different stages of disease [12], patients underestimated their memory problems. It should be noted, however, that ratings by patients' proxies, as well as by patients

Table 1
Studies on anosognosia in clinical and premanifest Huntington's disease

	Participants	Methodology	General	ADL	Motor	Executive	Memory	Psychiatric	Results
Deckel & Morrison, 1996[1]	19 HD and 14 patients with non-HD diagnoses[3]	self-ratings and staff-ratings (8 questions)	x						patients with more severe anosognosia are more cognitively impaired
Snowden et al., 1998[1]	40 HD patients	self-report questionnaire (direct experience of involuntary movements and the consequences of movements) vs.objective motor assessment		x	x				patients more frequently report consequences of motor problems (e.g. spilling drinks) than involuntary movements *per se*
Vitale et al., 2001[2]	9 HD vs 13 PD patients	structured interview about the presence of involuntary movements while executing motor tasks vs. objective rating of motor symptoms			x				7/9 HD patients unaware of chorea; 5/13 PD patients unaware of dyskinesias, 4 partially aware and 4 totally aware
Chatterjee et al., 2005[2]	53 HD patients and proxies	patient's self-ratings and caregivers' ratings on questionnaires (mood, apathy, irritability)						x	apathy ratings showed greatest discrepancy; higher discrepancies were associated with lower cognitive status
Ho et al., 2006[2]	75 HD patients and 67 caregivers	patient's self-ratings and caregivers' ratings on a questionnaire				x			HD patients underestimated extent of dysexecutive behaviours by 26%, but able to correctly rate caregivers' behaviour
Hoth et al., 2007[1]	66 HD patients and proxies	patient's self-ratings and caregivers' ratings on a questionnaire		x		X			poor awareness of ADL, emotional and behavioral control; unawareness associated with memory impairment
Duff et al., 2010[1]	745 expansion-positive and 163 expansion-negative individuals and companions	self-ratings vs. companion-ratings on a questionnaire				x			participant- companion discrepancy greater in individuals closest to HD diagnosis
Sitek et al., 2011[1]	23 HD patients, 25 with advanced PD, 21 with mild PD, 20 with CD	self-ratings vs. proxy ratings on a questionnaire and objective assessment of motor function		x	x				self-awareness of choreic movements more severely affected in HD than advanced PD, despite comparable cognitive status; satisfactory patient-proxy agreement on ADL

Table 1
(*Continued*)

	Participants	Methodology	General	ADL	Motor	Executive	Memory	Psychiatric	Results
Sitek et al., 2012[1]	23 HD patients, 25 with advanced PD, 21 with mild PD, 20 with CD	self-ratings vs. companion-ratings on a questionnaire and objective memory performance					x		HD patients underestimated memory dysfunction in comparison to CD; proxy ratings inconsistent with objective memory performance in HD
Justo et al., 2013[1]	28 early stage HD patients, 28 premanifest gene carriers, 12 controls	structured interview and objective rating of motor symptoms blind to clinical status while executing motor tasks			x				patients demonstrated poor concurrent awareness of chorea, controls also unaware of non-pathological involuntary movements
Sitek et al., 2013[1]	23 HD patients, 25 patients with advanced PD, 21 with mild PD, 20 with CD	self-ratings vs. companion-ratings on a questionnaire and objective executive performance				x			insight mildy affected in HD in comparison to PD and CD
Cleret de Langavant et al., 2013[1]	46 HD patients and 33 proxies	patient's self-ratings against caregiver's ratings of patient's memory and actual performance					x		HD patients at stage 1 accurately rate their memory; at stage 2 rate their memory less accurately; patients rate their memory more adequately than caregivers
McCusker et al., 2013	550 HD mutation carriers	One question: Since your last visit, have you noticed any symptoms that you feel are suggestive of HD? vs. results of clinical examination			x				About 50% of HD patients are unaware of early HD signs; unaware patients are less depressed

[1]extended/domain-specific neuropsychological assessment. [2]screening neuropsychological assessment. [3]mild traumatic brain injury ($n = 6$), alcohol-related dementia ($n = 1$), toxic exposure ($n = 1$), Lymes disease ($n = 2$), depression ($n = 2$), learning disability ($n = 1$), Alzheimer's disease ($n = 1$). ADL-activities of daily living; CD-cervical dystonia; HD- Huntington's disease; PD-Parkinson's disease.

themselves, correlated poorly with objective memory performance measures. Judgement of extent of memory deficit may therefore be inherently difficult and influenced by factors other than memory itself, such as overall functional disability. In the second study findings differed as a function of stage of disease [14]. At stage 1, patients were actually more accurate than their proxies in evaluating their memory deficits. Only at stage 2 did HD patients underestimate their memory problems. This finding suggests that HD patients may indeed underestimate memory deficits but not early in the disease course.

INSIGHT INTO BEHAVIOURAL AND EXECUTIVE IMPAIRMENT

HD patients may exhibit a wide range of neuropsychiatric symptoms: apathy, depressed mood, anxiety, irritability and aggression, perseveration and obsessive-compulsive features, as well as psychotic symptoms [17–19]. Our clinical experience suggests that awareness is not identical for each of these symptoms: there may be anosognosia for perseveration, limited insight into apathy, irritability and aggression and relative preservation of insight into depressed mood and anxiety. To our knowledge, a systematic comparative study of insight across the full range of psychiatric symptoms has not yet been undertaken in HD. Nevertheless, there is some support for the notion of differential breakdown in awareness across neuropsychiatric symptoms. The study by Chatterjee et al. [8] showed that HD patients' own ratings of depression and irritability were similar to those of their caregivers, whereas they underestimated the extent of apathy. It is pertinent, in this regard, that depression and irritability are "mood-based" symptoms of HD that correlate neither with disease severity [20] nor with cognitive impairment [21]. By contrast, apathy has been found to be a sensitive marker of disease progression [20] and correlates significantly with executive dysfunction [21]. The discrepancy in apathy ratings between patients and caregivers that was identified in the study of Chatterjee et al. [8] may be due to the fact that apathy is related to HD progression whereas irritability and depression are not.

A recognized method of assessing self-awareness of executive function and behavioural change is by comparison of patient/proxy ratings on behavioural inventories such as the Dysexecutive Questionnaire [22] and Frontal Systems Behaviour Scale, [23]. Two studies using the Dysexecutive Questionnaire demonstrated that HD patients could accurately rate proxies' but not their own behaviour [9, 10], providing evidence of reduced self-awareness of behavioural change that cannot be attributable to generalized deficient judgement. A third study [13], which used the same questionnaire to compare insight in HD and PD, revealed only mild reduction in awareness for executive symptoms in HD, based on differences in patient and proxy ratings. It is possible though that relatively small group numbers resulted in lack of power to elicit significant differences. The evidence for anosognosia of executive-type behavioural dysfunction (e.g. impulsivity or impaired planning in daily life) in the studies by Ho et al. [9] and Hoth et al. [10] is more robust, being based on larger samples.

There is some evidence that reduced awareness of "frontal" behaviours may be a relatively early feature of HD. In a large study of preclinical HD, the Predict-HD study, involving 745 participants, Duff et al. [2] demonstrated that people far from clinical onset show few frontal behaviours, reflected in both their own and companions' ratings. As people move closer to clinical onset both they and their companions report more executive symptoms. However, when they become closer still to clinical onset their own and their companions' ratings diverge. People with the HD mutation report progressively fewer frontal behaviours whereas companion ratings suggest a relatively linear increase in frontal deficits. This finding is of clinical importance in the setting of pre-symptomatic clinics, as decreasing awareness may be one of the first signs of HD.

INSIGHT INTO CONSEQUENCES OF SYMPTOMS IN ACTIVITIES OF DAILY LIVING

As previously noted, HD patients better acknowledge the functional consequences of motor impairment (e.g. dropping things) than the presence of motor symptoms (e.g. involuntary movements) [6, 11]. Moreover, patients' report of functional consequences has been found to correlate with objective measures of motor impairment [6]. However, there is some evidence that HD patients underestimate their degree of functional impairment in activities of daily living. It has been demonstrated that proxy ratings of activities of daily living (ADL) are more concordant with patients' Total Functional Capacity than HD patient ratings [10]. Moreover, limited awareness of functional impairment is suggested by the fact that many HD patients continue to drive when their driving performance is unsafe [24–26].

IS ANOSOGNOSIA IN HD DOMAIN SPECIFIC OF GENERALIZED?

Theoretical accounts of anosognosia (based on studies of patients with focal brain lesions) have drawn a distinction between generalised loss of awareness, affecting all aspects of disability, and selective loss, e.g. a patient might be aware of motor impairment but not of behavioural change [27]. The studies outlined above reinforce the view that anosognosia is a notable characteristic of HD, occurring across multiple domains. However, relatively few studies of awareness in HD have explicitly addressed several domains in the same patient, so that within-patient comparisons are currently limited. Hoth et al. [10] showed that HD patients' lack of awareness extended across the symptom domains of behavioural control, emotional control and activities of daily living. Sitek et al. [11–13] studied the same patient sample across different domains and found deficient insight for motor, executive and memory functions. These findings, taken at face value, might point to anosognosia as a generalized phenomenon. Yet, Hoth et al. [10] also drew attention to differences across domains. Awareness was determined by disparities between self-report of competency from patients and reports of collaterals. Patient-collateral disagreement was higher for emotional control than for behavioural control or activities of daily living. Moreover, there was greater patient variability on the emotional control subscale, with some patients overestimating and others underestimating their functioning. Such findings highlight two important points outlined by Hoth et al: unawareness in HD is not absolute (self-awareness should be seen as falling along a continuum) and it should not be regarded as a unitary construct.

There are additional grounds for considering insight pertaining to different domains to be dissociable. Patients may be better aware of depressive symptoms than of apathy [8]; they may fail to report involuntary movements yet complain of their consequences [6]; they may be aware of memory difficulties early in the disease course [14] but not involuntary movements [3]. Such dissociations raise the prospect that the factors underpinning loss of awareness may not be identical for all functional domains.

BRAIN MECHANISMS OF ANOSOGNOSIA IN HD

Huntington's disease is a basal ganglia disorder, associated with prominent changes in caudate and putamen. Subtle changes may be evidenced on neuroimaging many years before clinical diagnosis [28]. Early cerebral pathology in HD is not confined to the striatum, but is also present within prefrontal cortex [29], corpus callosum [30] and orbitostriatal white matter tracts [31]. The importance of prefrontal cortex for self-reflection and insight is exemplified by the profound loss of insight and acknowledgement of illness characteristic of behavioural variant of frontotemporal dementia (bvFTD) [32, 33], which is associated with degeneration of prefrontal cortex. The neuroimaging findings therefore offer the possibility for distinct contributions to the pathogenesis of anosognosia in HD.

Only two studies of anosognosia in HD have examined neuroimaging correlates, so inferences are limited. In the study by Justo et al. loss of insight into movement disorder was associated with striatal atrophy (caudate and putamen atrophy bilaterally) [3]. McCusker et al. found the opposite pattern in a preclinical cohort of "unaware" people, classified by raters as showing very mild signs of HD. So-called "unaware" individuals had greater striatal and white matter volumes than an "aware" subgroup. Nevertheless, it is instructive that the "unaware" group also had better motor function (speeded tapping) and fewer functional limitations [4], suggesting that they were less overtly affected than the aware group. The pathological significance of the apparent lack of awareness in that cohort might therefore be considered questionable.

IS ANOSOGNOSIA INFLUENCED BY DISEASE SEVERITY?

HD patients who participate in studies on self-awareness do not encompass the whole spectrum of HD severity, but are typically in the mild or moderate stages of disease. Moreover, the very fact of their attendance at clinic might bias towards those patients with a degree of awareness. The data need therefore to be interpreted with this in mind. Poor insight has been linked to more pronounced motor [3, 7, 12, 14] and cognitive [8] change, as well as to greater functional impairment [12, 14], suggesting a relationship with disease severity. The relationship between insight and disease duration, as measured by years of illness, is less clear-cut. A negative association has been demonstrated in relatively advanced [7, 12] but not early stage HD [14]. HD is known to be highly variable in its rate of progression, so that years of illness may be a poor marker of disease severity and is not interchangeable with functional capacity.

Some studies failed to demonstrate an association between insight and disease severity (measured by Unified Huntington's Disease Rating Scale (UHDRS) motor score and Independence Scale), which may be due to small sample sizes [11, 13]. In other studies the relationship between the degree of awareness and disease severity was not addressed [6, 9].

Two studies examined awareness of very early HD signs [2, 4]. Duff et al. [2] showed that expansion-positive individuals who are close to clinical onset tend to underreport frontal behaviors [see section: Insight into behavioural and executive impairment]. Further, a longitudinal study of preclinical HD [4] also raised the possibility that reduced awareness may be present even in the very early stages of HD. HD gene carriers were asked the question "Since your last visit have you noticed any symptoms that you feel are suggestive of HD?" Their responses were compared with clinicians' judgement of whether they displayed unequivocal motor signs of HD, based on examination with UHDRS. Only about half of the patients judged to show clinical signs of HD reported symptoms. Interpretation of the findings is complicated. Motor raters were generally aware of people's gene status so potentially biased. Awareness was measured on the basis of responses to a single open-ended question only. The answer to the question asked by McCusker et al. [4] depended on people's prior understanding of HD, as in order to report something as a possible HD symptom the patient has to link his/her observations to the clinical picture of HD. In view of the generic nature of the question, the possibility cannot be ruled out that gene carriers did experience symptoms but simply did not ascribe them to HD. It is of interest in this regard that some of the preclinical cohort reported symptoms of HD, in the absence of clinical signs reported by raters. People in the prodromal phases of HD may, with justification, simply have difficulty knowing whether subtle alterations in their functioning are attributable to HD or not. There is a need for caution, therefore, in interpreting the data as evidence of impaired insight. Nonetheless, the study opens up the question of reduced awareness of change even in the very early stages of disease.

Thus, it seems, that disease severity contributes to the anosognosia to a more significant extent than disease duration. Moreover, insight may be affected early in the disease course.

POSSIBLE MECHANISMS OF ANOSOGNOSIA

Several factors might putatively contribute to loss of awareness of deficits in HD: cognitive (dementia, specific cognitive dysfunction), biological (physiological) and psychological (coping mechanisms) [34, 35]. Evidence for the contribution of these different factors is considered below.

COGNITIVE FACTORS

HD is associated with progressive cognitive decline [19, 36], which includes prominent changes in executive functions and memory. The findings of an inverse relationship between awareness of deficit and disease severity would be compatible with the notion that cognitive changes contribute to the decline in awareness. There is also some more direct evidence for the link. Reduced insight into motor symptoms was found to be associated with poor mental flexibility [3, 6] and reduced awareness of behavioral changes related to impaired sustained attention [10]. These findings suggest a role of executive skills in the capacity for awareness/self-reflection of deficit. In the study by Hoth et al. greater memory impairment, measured by the Memory subscale of the Dementia Rating Scale, was associated with lower level of awareness of ADL dysfunction and behavioral/emotional control, raising the possibility that memory impairment too might be a contributory factor. However, studies that have specifically addressed insight into memory impairment have yielded mixed results. In one study [12] insight into memory impairment, defined as patient-proxy disagreement, was not associated with the degree of memory dysfunction. By contrast, in another study [14] insight, defined as the discrepancy between subjective and objective memory performance, was found to relate to memory performance. The latter findings suggest that memory impairment, at least in mild degree, does not preclude the possibility of awareness.

The foregoing suggests that cognitive factors may contribute to loss of awareness, yet are unlikely to explain it fully. Impaired cognition as an isolated factor would have difficulty accounting for disparities in insight, i.e. that a patient might show awareness in one domain and not another. Moreover, both cognitive impairment and poor self-awareness may be related to the disease severity and just co-occur without direct impact of cognition on insight.

PHYSIOLOGICAL FACTORS

HD patients may fail to report the direct experience of involuntary movements, whilst retaining the ability to report their functional consequences [6].

This disparity has been interpreted as evidence for physiological mechanisms underpinning the loss of awareness of chorea and contrary to an explanation in terms of cognitive impairment. It has been observed, moreover, that choreic patients may fail to perceive their choreic movements in daily life, yet acknowledge their presence when they are videotaped and watch themselves on screen [15, 37]. Again, such findings point to fundamental deficiencies in the physiological experience of chorea, rather than a general cognitive incapacity for self-reflection.

HD is characterized by a variety of neurophysiological abnormalities [38] and deficient motor control in HD may be related to an abnormal processing of sensory inputs [39]. Of note, the absence of a pre-movement cortical potential before chorea [38] might explain why the subjective perception of chorea is impaired when based on sensory information. HD patients may have altered perception of movement/limb position, which is suggested by the early dysfunction in error feedback control [40], altered sensation of effort [41] and movement imprecision under blindfolded conditions [42]. However, a recent study by Justo et al. [3] demonstrated that mild choreic movements are no more difficult to perceive for HD patients than are non-pathological involuntary movements for healthy controls. That is, even healthy individuals lack the subjective experience of self-generated involuntary movements, raising the question as the degree to which 'unawareness' of chorea is in fact pathological. Nevertheless, with disease progression the choreic movements in HD are substantially greater than self-generated involuntary movements in healthy individuals both in terms of frequency and intensity. There is therefore a need for caution in generalizing this finding to HD patients with moderate and severe chorea.

PSYCHODYNAMIC FACTORS

As HD is a hereditary and fatal disorder, underestimation of symptoms might be regarded as an understandable coping mechanism. Psychological defense mechanisms such as denial (in case of complete anosognosia) or rationalization (in case of underestimation or misinterpretation of symptoms, e.g. attributing them to stress, age or other factors rather than HD) may potentially help the individual to cope with the disease burden. Most HD patients have witnessed the HD course in several family members (grandparents, parents, aunts, uncles, cousins or siblings) and at the time of diagnosis may have relatives in the advanced stages of disease.

Evidence for denial as form of defence mechanism is limited. In terms of motor function, the preserved ability to perceive the consequences of movement disorder despite failure to report experience of abnormal movements [6] is not consistent with a psychodynamic explanation. Furthermore, a psychodynamic hypothesis of "denial of illness" does not explain the fact that the patients may not report involuntary movements, but acknowledge their presence when they see themselves on video [37]. However, psychodynamic factors might still feasibly contribute to poor self-awareness of non-motor symptoms.

If underestimation of symptoms helps adaptation to the disease, it should be associated with better mood, whereas more depressed mood would lead to overestimation of symptoms. Such a pattern of results was found in only one study [10], whereas several others failed to confirm this relationship [3, 11–14]. In a preclinical cohort, comparison between people aware and unaware of early HD signs showed that the unaware group reported fewer depressive symptoms. Mood was slightly lowered in people who reported symptoms, regardless of whether they showed clinically identifiable signs of HD [4]. This finding would seem to indirectly support the relationship between insight and coping, although it must be viewed in the context of the methodological limitations of that study described earlier.

INSIGHT IN HD AND MODELS OF ANOSOGNOSIA

There are two quite comprehensive models of anosognosia in the literature [27, 43]. The Prigatano model, based on the functional organization of the cerebral cortex, makes a distinction between types of awareness, attributed to different cortical brain regions: frontal heteromodal (anosognosia of executive, emotional and behavioral changes), parietal heteromodal (anosognosia of hemiplegia or neglect), temporal heteromodal (anosognosia of amnesia and/or language impairment) and occipital heteromodal (anosognosia for visual impairment). The severity of anosognosia may vary from complete to partial, the complete syndrome being assumed to correspond to bilateral and partial syndrome to unilateral pathology [27]. Taking into account the fact that anosognosia in HD may affect several modalities and that early dysfunction of frontostriatal loops in HD may be treated as a sign of frontal

pathology, it is closest to the frontal heteromodal syndrome according to Prigatano's model. However, as Prigatano's model was designed to address loss of awareness associated with focal, cortical brain lesions, it has limited applicability to HD because of the progressive, bilateral and mixed pattern of atrophy in HD with important implication of the subcortical structures both prior to the clinical onset and during the disease course [29].

The Crosson model distinguishes between levels of awareness: intellectual awareness (being able to acknowledge the deficits), emergent awareness (being able to perceive deficits while they interfere with the execution of a given activity) and anticipatory awareness (being able to predict the consequences of the dysfunction) [43]. Most studies in HD addressed intellectual awareness as they used questionnaires asking about symptoms [2, 4, 6, 8–14]. Only two studies addressed emergent awareness [3, 7]. To our knowledge none of the HD studies addressed the capacity for anticipatory awareness; however, given the demonstrated deficits in intellectual awareness and emergent awareness, it would seem reasonable to suppose disturbance of anticipatory awareness. As many studies evidenced deficient intellectual awareness in HD, external compensatory strategies seem most applicable in the HD context.

NEGATIVE AND POSITIVE CONSEQUENCES OF POOR INSIGHT

There are a number of negative consequences of poor insight. Anosognosia may delay diagnosis and lead to poor medication compliance. Patients may be at risk of engaging in potentially dangerous activities, e.g. driving despite compromised driving ability [24–26].

There might also, however, be some potential benefits, as implied by psychodynamic explanations of anosognosia. Anosognosia might be construed as a way of reducing symptom-related anxiety and coping with progressive loss of function. HD is associated with increased rates of depressed mood [18, 44]. Higher degree of insight seems to be related to more depressed mood [4], however to our knowledge no studies addressed the relationship between insight and anxiety in HD.

PRACTICAL IMPLICATIONS OF ANOSOGNOSIA IN HD

From the clinician's perspective anosognosia has relevance throughout the course of the patient-clinician relationship. At the diagnostic stage poor self-awareness of problems (e.g. behavioural) may lead to under-reporting of symptoms by the patient, necessitating greater reliance by the clinician on information from informants. Anosognosia may have practical and ethical implications for patients' management. Potential benefits of medications need to be weighed against their side-effects. The side-effects of anti-choreic agents, for example, may outweigh their benefits in patients who have no subjective complaints of involuntary movements [45]. For psychiatric symptoms such as apathy or aggression, which the patient is unlikely to report spontaneously, interview with the caregiver is crucial when planning treatment [46].

ASSESSMENT OF ANOSOGNOSIA IN HD

Methodology for assessing awareness in neurodegenerative conditions is more complex than in other disorders as it is usually limited by the patient's cognitive dysfunction. Clare et al. [47] identified five main approaches to assessing awareness in dementia: clinician rating methods, questionnaire-based methods, performance-based methods, phenomenological, and multidimensional or combined methods. Most of the HD studies reviewed here used either questionnaire-based methods [2, 8–10], or a combination of performance and questionnaire-based techniques [3, 4, 6, 7, 11–14].

Two main methodological issues in studies on anosognosia in HD hinder the generalization of results and formulation of clinical implications: failure to report stage of disease, and focus on one (e.g. motor or cognitive) or few domains. Moreover, elucidation of the pathological mechanism of anosognosia in HD requires extensive use of cognitive and neuroimaging techniques as a supplement to insight assessment.

CONCLUSIONS

Patients with HD may have limited insight into motor, behavioural and cognitive deficits. Breakdown in awareness is not all-or-none, and it may occur in one domain more than another. The available evidence suggests that distinct factors may contribute to loss of awareness. Physiological factors appear, at least in part, to underpin the appreciation of involuntary movements whereas cognitive factors have relevance for other domains. However, more systematic, prospective studies are needed to parcel out the components of loss of awareness. Loss of awareness is of major practical

importance as its recognition by clinicians is crucial for optimal patient management.

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