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Depression in the early stages of Huntington disease

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Summary

Huntington disease (HD) has traditionally been considered a movement disorder, but cognitive and psychiatric symptoms also prominently factor into its clinical presentation. Depression is one of the most common psychiatric disturbances in HD, with its prevalence highest in manifest disease during stage 2, but it is also present during the illness prodrome (the period before manifestation of motor symptoms). Identification and treatment of depression in individuals with the HD mutation is an essential part of clinical management in this population, especially owing to the high risk of suicide. This article summarizes what is currently known about the presentation and treatment of depression in the early stages of HD and provides advice to clinicians treating this population.

Huntington disease: beyond motor symptoms

Huntington disease (HD) is a neurodegenerative disorder caused by an increased number of DNA trinucleotide repeats in the Huntingtin (*HTT*) gene on chromosome 4 [1,2]. When the number of cytosine–adenine–guanine (CAG) repeats on at least one copy of this locus is increased to more than 35, an individual will develop HD. It is a dominant mutation; therefore, the chances of offspring inheriting the mutation are 50%. Affected individuals develop gradual destruction of neurons in the striatum and cortex, leading to the motor symptoms of chorea, rigidity and bradykinesia, with degeneration over 20 years leading to death. The length of the CAG repeat is inversely correlated with the age of onset of motor symptoms, which on average occurs between the ages of 35–45 years. No treatments are available to prevent or reverse neurodegeneration in HD. The diagnosis of HD is traditionally based on the presence of motor symptoms; however, the cognitive and behavioral symptoms constitute a significant aspect of HD morbidity, affecting the ability to work, manage finances and perform other daily activities [3]. Early mortality may also occur due to increased risk of suicide. Cognitive deficits affect memory, visuospatial abilities and executive function, often resulting in dementia.

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Various psychiatric and behavioral symptoms can occur in HD, including irritability, aggression, obsessions, compulsive behaviors, anxiety or psychosis, with depression being one of the most common [4]. Depression has a significant effect on quality of life in individuals with HD [5]. Apathy is also common and may be confused with depression. Psychiatric symptoms, including depression, can develop several years prior to motor or cognitive deficits [6]. In contrast to other domains of HD, psychiatric symptoms are not correlated with disease progression; however, depression has been observed to occur more frequently during specific periods of the illness, especially during the early stages.

Presymptomatic genetic testing allows the ability to identify whether a person at risk for HD will develop the illness. Several longitudinal studies are underway in order to better understand the timing and progression of HD, including the international multisite PREDICT-HD study [7]. Over 900 individuals with the HD mutation and 300 gene-negative participants have enrolled in the PREDICT-HD study since 2002, and in this study we are continuing to characterize the course of illness in what is currently defined as the HD prodrome (prior to a motor diagnosis), including depression [101]. These projects will improve our understanding of neuropsychiatric symptoms such as depression in HD, with the goal of identifying more effective treatments for all domains of HD.

Diagnosis of depression

In the *Diagnostic and Statistical Manual for Mental Disorders* (DSM), depression can be classified into one of several disorders depending on the symptoms present (Box 1), severity, causal factors, and duration [8]. Many patients will only have some depressive symptoms with lesser severity or temporality, but they can still suffer significant impairment and require treatment even if they do not meet the criteria for major depression. An adjustment disorder is diagnosed instead if symptoms do not reach the level of major depression and the depressed mood is directly due to a recent stressor. Other possible causal factors must also be evaluated, including medical conditions such as hypothyroidism or substance-induced if medication, alcohol or illicit drugs are important contributing factors.

In contrast to depression, patients with manic or hypomanic episodes (Box 1) are diagnosed with bipolar disorder, as they will typically also have episodes of depression. Recent studies using DSM-based criteria have found low rates of mania or hypomania in HD [9]. Irritability is a common symptom in HD, but in most cases it is not mania, as the presence of other manic symptoms are also necessary. Older studies reporting higher rates of mania may have used less rigorous criteria.

Prevalence of depression in the stages of HD

The rate of depression in HD has been measured using many assessments across the stages of illness with a wide range of sample sizes. Although this makes interpretation across studies challenging, depression is common in HD. Prevalence results from recent studies in the literature are summarized in Table 1. In patients given a motor diagnosis of HD, 33–69% also present a depressed mood [4]. Our group stratified a sample of 2835 subjects from the Huntington Study Group (HSG) by the HD stage and found that depressive symptoms were highest in stage 2 (45% with sad mood) and lowest in later stages [10].

Depression in the HD prodrome has also been found to occur at varying rates based on proximity to diagnosis of manifest disease, highlighted in Table 1. In a sample of 89 gene-positive and 115 gene-negative individuals, Julien *et al.* administered the DSM-based Composite International Diagnostic Interview (CIDI) at the time of initial evaluation when both research participants and raters were blinded to HD gene status [11]. Participants were followed-up for several years after the initial evaluation; thus, the date of HD motor onset

was available for 51 of the 89 subjects, allowing characterization of psychiatric symptoms by time to HD diagnosis. At baseline, 20% of the gene-positive prodromal group had a lifetime history of major depression, compared with 12% of the gene-negative group. The prevalence of depression was higher in individuals who were closer to motor onset; however, the difference compared with noncarriers was only significant among those who were evaluated 1 year prior to diagnosis. For comparison, the lifetime prevalence of depression in the general population has been measured between 15 and 16% [12,13]. van Duijn *et al.* evaluated 55 presymptomatic individuals (using the Unified Huntington disease Rating Scale [UHDRS] Diagnostic Confidence Level [DCL] 0 or 1) and 85 with motor symptoms (UHDRS DCL 2–4) using the CIDI to diagnose psychiatric illnesses over the previous 12 months [9]. A total of 20% of prodromal and 16.5% of symptomatic individuals met the criteria for a depressive disorder, compared with 7.1% of 56 noncarriers. The rate of depression was only significantly different when compared with the general population (5.8%). This sample was also evaluated using the Problem Behavior Assessment (PBA). Compared with noncarriers, all HD groups reported significantly higher depressive symptoms. The early symptomatic HD group had the highest level of symptoms, but this was not significantly different from advanced symptomatic or prodromal subjects [14].

Two ongoing prospective HD studies have published baseline reports that measure depressive symptomatology. In the PREDICT-HD study, we use the Symptom Checklist-90 Revised to measure the spectrum of psychopathology. Comparing baseline data from 553 individuals with prodromal HD and 92 gene-negative individuals, the HD-positive group reported more symptoms of depression that were statistically significant, however, the difference in symptoms was not clinically significant [6]. We have also found that gene-positive subjects have increased symptoms measured by the Beck Depression Inventory (BDI)-II compared with gene-negatives, with average scores for both groups in the mild range [15]. More detailed analyses of depression in the PREDICT-HD sample are in progress. TRACK-HD is another prospective longitudinal HD study that includes 120 premanifest subjects (UHDRS Motor Score <5), 123 individuals with early symptomatic HD, and 123 gene-negative controls. Mood symptoms noted from the PBA were found to be significantly increased in the early symptomatic HD group compared with controls. The premanifest group also had increased depressive symptoms, but this was not significantly different from controls [16].

From these results, individuals appear to report depression very close to onset of motor symptoms and during the earlier stages with motor symptoms. These are critical periods to monitor for depression when caring for patients with the HD mutation. Although most do not meet the criteria for major depressive disorder, the presence of a mood disturbance in a significant number warrants careful screening. As previously noted by our group and others, factors in the later stages of HD such as communication difficulties and cognitive changes may make it more difficult to recognize and report depressive symptoms [10,17]. Longitudinal studies such as the PREDICT-HD and TRACK-HD studies will continue to provide additional information regarding the prevalence of depression over time in this population.

What is the relationship of biological & social factors with depression in HD?

Many studies have also investigated whether specific biological and/or social factors contribute to depression in early-stage HD. This information provides some insight into the causes of depression and is also informative to the clinician treating patients with the HD mutation. Some questions in this area, which are addressed in the proceeding sections, include:

- Are there any specific symptoms or markers that correlate with depression?
- Are there individuals or families who may have a biological predisposition to depression?
- Are there environmental factors unique to individuals with the HD mutation, specifically life events or stressors that contribute to the development of depression?

Correlations with other symptoms & biomarkers

Depression in HD has been associated with other psychiatric symptoms and in some studies with other HD phenotypes, but not with variables related to disease progression. A principal component analysis of the PBA identified a factor encompassing depression, depressive cognitions, anxiety, tension and suicidal ideation [14]; the last of these is discussed later. In the HSG sample, those with obsessive–compulsive symptoms reported significantly higher depressive symptoms [18]. Sleep disturbances are common in HD, and Aziz *et al.* found that depression measured by the BDI (without sleep questions) was the only clinical variable that significantly correlated with sleep impairment [19]. Jurgens *et al.* found no correlation between basal ganglia volumes and BDI scores in HD subjects [20]; however, a PET study by Paradiso *et al.* identified decreased activity in the frontal and parietal lobes, thalamus and cerebellum of HD patients with dysphoric mood induced by viewing negative images [21].

Apathy may be part of a depressive disorder, but it can occur as a separate syndrome, with symptoms of decreased initiative, activity and self-care. Research demonstrates that distinct syndromes of depression and apathy exist in HD and should be examined and treated independently [22]. Apathy is common in HD, developing as early as in the prodromal period [23], and it is more prevalent than depression in HD [24,25]. Unlike depression, apathy has been shown to increase with disease progression and to correlate with motor symptoms and cognitive dysfunction [25]. Antidepressants are often prescribed to treat apathy, but the effectiveness of this treatment or any other is entirely unknown [24].

Familial predisposition to depression

Clustering of neuropsychiatric phenotypes such as depression in some HD families may indicate a biological predisposition to the disorder. These families may have a genetic background that increases the risk of developing depression in conjunction with the HD mutation. While several studies have identified families with increased prevalence of psychosis, only one study published many years ago by Folstein *et al.* compared the presence of affective disorders between families [26]. The authors found that some families had an increased prevalence of affective disorders, and the rate of affective disorders was significantly higher in HD individuals compared with nonaffected relatives. These results are consistent with the idea that genetic modifiers may be present in individuals with the HD mutation that increases the risk of depression, although these results still require confirmation. Shared environmental factors may also contribute.

Relationship between environmental factors and depression

Life events and stressors are important contributors to the etiology of depression, and HD has its own specific stressors due to individuals struggling with relatives affected by the illness and the issues related to presymptomatic genetic testing [27,28]. Some groups over the years have reported increases in depression following a positive test result, including recent studies from Gargiulo *et al.* [29] and Almqvist *et al.* [30]. With a mean follow-up of 3.7 years after testing, they found that 58% of prodromal gene-positive individuals reported depression and 24% of the gene-negatives were also depressed. The strongest predictor of post-testing depression was a prior episode of depression. In PREDICT-HD, we measured

life stresses using the Perceived Stress Scale and found a positive correlation between levels of stress and depression measured by the BDI-II [15]. We also found an interesting relationship between perceived stress, age and time since genetic testing. In those under 34 years of age, stress levels increased with longer time since genetic testing, while stress levels decreased in those over 34 years of age as time since testing increased.

A critical issue related to depression is the attribution of a patient's symptoms to either biological or psychological factors. This is an artificial distinction that needs to be avoided in making any diagnostic or treatment decisions, as minimization of depression only due to psychological stress of having HD may lead to underdiagnosis and inadequate treatment [31]. Both factors interact to contribute to the development of depression, with the presence and severity of clinical symptoms the primary determinants of diagnosis and treatment.

Suicide in HD

Suicide is a significant cause of mortality in individuals with HD, with rates estimated between 5–10% [2]. It is therefore critical to monitor for suicidal ideation in all HD patients; there are also specific time periods where the risk is highest. Additional analysis of the HSG sample, including 1483 who were at risk for HD with a family history but not diagnosed, in addition to 2688 diagnosed, found that suicidal ideation doubled between the group at risk and without neurologic symptoms compared with those who had soft neurological signs (9.1–19.8%), and increased to 23.5% in the group with possible HD [32]. The diagnosed cohort, stage 2, which also had the most depressive symptoms, also had the highest level of suicidal ideation (21.6 vs 16.7% in stage 1). These results indicate that receiving a diagnosis of HD does not increase the risk of suicidal ideation, but that the risk is highest during the period prior to diagnosis and during a specific period following diagnosis. Monitoring for suicide risk at the time of genetic testing is also critical [27].

One recent study examined possible risk factors for suicidal ideation in a large HD cohort [33]. Results demonstrated that depression/anxiety, aggression/irritability and substance/drug abuse were significant predictors of increased suicidal ideation, with depression/anxiety having the highest risk. This suggests that vigilant psychiatric treatment may assist with suicide prevention in HD. In PREDICT-HD, less than 2% of 719 subjects attempted suicide, and factors contributing to the risk of suicide attempts were comparable with the general population [34]. The low prevalence of suicide attempts in PREDICT-HD may be due to selection bias or unique factors related to the study population, although the inclusion of attempts made by participants before entry into the PREDICT-HD study increased the proportion to 7.2%, which is higher than the general population. Other factors, such as past experience with an HD-affected relative, the presence of a terminal illness, personality changes or impulsivity may also contribute to the risk of suicide, although more research is needed to verify these possibilities [33]. One treatment for HD warrants mention owing to its side-effect profile: tetrabenazine, a dopamine-depleting agent, is the only US FDA-approved medication to treat the chorea of HD; however, an increased risk of depression and suicidal ideation have been reported [35,36]. Based on the current data, the strongest factors contributing to suicide risk in HD are similar to other populations.

Treatment of depression in HD

No randomized controlled trials have been conducted to evaluate the treatment of depression in HD, but there are several individual case reports and series examining different treatment modalities [31,37]. An examination of medication logs in an observational study demonstrated that at least 20% of persons at risk for HD took antidepressants. Of those, the majority took serotonergic antidepressants (selective serotonin reuptake inhibitors [SSRIs] or serotonin-norepinepherine reuptake inhibitors [SNRIs]), which was significantly higher

than a healthy comparison group. Moreover, findings suggest that antidepressant usage increased as proximity to estimated motor manifestations increased [38]. A case series using the SNRI antidepressant venlafaxine XR for 4 weeks in a sample of 26 individuals with HD and depression reported a significant reduction in depressive symptoms [39]. SSRIs, typically the first-line medication for treatment of depression, have only case reports of efficacy in depressed HD patients [37]. Antidepressants may also treat executive dysfunction, irritability and obsessive–compulsive symptoms. Our institution, in collaboration with other sites, is currently conducting a double-blind, pilot, randomized controlled trial with the SSRI citalopram to determine the effect of the medication on executive function and other symptoms in early HD (CIT-HD) [102].

Owing to the lack of HD-specific data, it is recommended that standard clinical guidelines for the treatment of depression should also apply to patients with HD who are depressed. Treatment of identifiable causal factors, such as other medical conditions or substance misuse is essential. Psychotherapy for depression has not been formally studied in HD, but the extensive evidence of its benefit in other populations warrants its recommendation as a treatment option. If medication is prescribed, SSRIs are usually prescribed first, with other antidepressants including the SNRI venlafaxine also an option. The presence of psychotic symptoms with depression may require the addition of an antipsychotic, and those who are treatment resistant with medications are candidates for electroconvulsive therapy [31,37]. Individuals with active suicidal ideation and a plan warrant immediate psychiatric evaluation and possibly hospitalization.

Conclusion & future perspective

Depression is a common symptom in HD and can appear at any stage, in many cases before the onset of motor or cognitive symptoms. Current evidence indicates that it is most prevalent when very near to the onset of motor symptoms and in stage 2 following diagnosis. Evaluation of depression includes a complete evaluation of all possible contributing biological and psychological factors, then tailoring treatment based on this information. Patients also need to be screened regularly for suicidal ideation. All individuals at risk for HD should be regularly screened for depression. Standard treatments for depression are applicable to the treatment of depression in HD; however, controlled clinical trials are needed in order to determine the optimal treatment of depression in this population. Current longitudinal studies following the progression of symptoms in HD mutation carriers will soon reveal new information on the presentation and course of depression in this population and further advance understanding of the full spectrum of the neuropsychiatric manifestations in this devastating illness.

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Bibliography

Papers of special note have been highlighted as:

- ■ of interest
- ■■ of considerable interest

1. Ross CA, Tabrizi SJ. Huntington's disease from molecular pathogenesis to clinical treatment. Lancet Neurol. 2011; 10(1):83–98. [PubMed: 21163446]
2. Walker FO. Huntington's disease. Lancet. 2007; 369(9557):218–228. [PubMed: 17240289]
3. Beglinger LJ, O'Rourke JJ, Wang C, et al. Earliest functional declines in Huntington's disease. Psychiatry Res. 2010; 178(2):414–418. [PubMed: 20471695]
4■. van Duijn E, Kingma EM, Van Der Mast RC, et al. Psychopathology in verified Huntington's disease gene carriers. J Neuropsychiatry Clin Neurosci. 2007; 19(4):441–448. Excellent review of psychiatric syndromes from several Huntington disease (HD) studies. [PubMed: 18070848]
5. Ho AK, Gilbert AS, Mason SL. Health-related quality of life in Huntington's disease Which factors matter most? Mov Disord. 2009; 24(4):574–578. [PubMed: 19097181]
6■. Duff K, Paulsen JS, Beglinger LJ, et al. Psychiatric symptoms in Huntington's disease before diagnosis: the Predict-HD study. Biol Psychiatry. 2007; 62(12):1341–1346. Baseline results of psychiatric symptoms from the largest cohort of prodromal HD subjects. [PubMed: 17481592]
7. Paulsen JS, Langbehn DR, Stout JC, et al. Detection of Huntington's disease decades before diagnosis: the Predict-HD study. J Neurol Neurosurg Psychiatry. 2008; 79(8):874–880. [PubMed: 18096682]
8. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4th. American Psychiatric Association; Washington, DC, USA: 2000. Task Force on DSM-IV. DSM-IV-TR
9. van Duijn E, Kingma EM, Timman R, et al. Cross-sectional study on prevalences of psychiatric disorders in mutation carriers of Huntington's disease compared with mutation-negative first-degree relatives. J Clin Psychiatry. 2008; 69(11):1804–1810. [PubMed: 19026253]
10■■. Paulsen JS, Nehl C, Hoth KF, et al. Depression and stages of Huntington's disease. J Neuropsychiatry Clin Neurosci. 2005; 17(4):496–502. Analysis of depression in a large cohort of individuals diagnosed with HD. [PubMed: 16387989]
11■. Julien CL, Thompson JC, Wild S, et al. Psychiatric disorders in preclinical Huntington's disease. J Neurol Neurosurg Psychiatry. 2007; 78(9):939–943. Retrospectively evaluated prevalence of depression based on years before HD onset. [PubMed: 17178819]
12. Bijl R, Ravelli A, Van Zessen G. Prevalence of psychiatric disorder in the general population. results of The Netherlands Mental Health Survey and Incidence Study (NEMESIS). Soc Psych Psych Epid. 1998; 33(12):587–595.
13. Kessler RC, Berglund P, Demler O, et al. The epidemiology of major depressive disorder results from the National Comorbidity Survey Replication (NCS-R). JAMA. 2003; 289(23):3095–3105. [PubMed: 12813115]
14. Kingma EM, van Duijn E, Timman R, et al. Behavioural problems in Huntington's disease using the Problem Behaviours Assessment. Gen Hosp Psychiatry. 2008; 30(2):155–161. [PubMed: 18291297]
15. Downing N, Smith M, Beglinger L, et al. Perceived stress in prodromal Huntington's disease. Psychol Health. 2011 Epub ahead of print. 10.1080/08870446.2010.529141
16■■. Tabrizi SJ, Langbehn DR, Leavitt BR, et al. Biological and clinical manifestations of Huntington's disease in the longitudinal TRACK-HD study. Cross-sectional analysis of baseline data. Lancet Neurol. 2009; 8(9):791–801. Baseline data from a comprehensive prospective study of HD pathology. [PubMed: 19646924]
17. Craufurd D, Thompson JC, Snowden JS. Behavioural changes in Huntington's disease. Neuropsychiatry Neuropsychol Behav Neurol. 2001; 14:219–226. [PubMed: 11725215]
18. Anderson KE, Gehl CR, Marder KS, et al. Comorbidities of obsessive and compulsive symptoms in Huntington's disease. J Nerv Ment Dis. 2010; 198(5):334–338. [PubMed: 20458194]
19. Aziz NA, Anguelova GV, Marinus J, et al. Sleep and circadian rhythm alterations correlate with depression and cognitive impairment in Huntington's disease. Parkinsonism Relat Disord. 2010; 16(5):345–350. [PubMed: 20236854]
20. Jurgens CK, Van De Wiel L, Van Es AC, et al. Basal ganglia volume and clinical correlates in ‘preclinical’ Huntington's disease. J Neurol. 2008; 255(11):1785–1791. [PubMed: 19156490]
21. Paradiso S, Turner BM, Paulsen JS, Jorge R, Ponto LL, Robinson RG. Neural bases of dysphoria in early Huntington's disease. Psychiatry Res. 2008; 162(1):73–87. [PubMed: 18068955]

22. Levy ML, Cummings JL, Fairbanks LA, et al. Apathy is not depression. J Neuropsychiatry Clin Neurosci. 1998; 10(3):314–319. [PubMed: 9706539]

23. Duff K, Paulsen JS, Beglinger LJ, et al. “Frontal” behaviors before the diagnosis of Huntington's disease and their relationship to markers of disease progression evidence of early lack of awareness. J Neuropsychiatry Clin Neurosci. 2010; 22(2):196–207. [PubMed: 20463114]

24. Naarding P, Janzing JG, Eling P, et al. Apathy is not depression in Huntington's disease. J Neuropsychiatry Clin Neurosci. 2009; 21(3):266–270. [PubMed: 19776305]

25. Van Duijn E, Reedeker N, Giltay EJ, et al. Correlates of apathy in Huntington's disease. J Neuropsychiatry Clin Neurosci. 2010; 22(3):287–294. [PubMed: 20686135]

26. Folstein S, Abbott MH, Chase GA, et al. The association of affective disorder with Huntington's disease in a case series and in families. Psychol Med. 1983; 13(3):537–542. [PubMed: 6226055]

27. Robins Wahlin TB. To know or not to know a review of behaviour and suicidal ideation in preclinical Huntington's disease. Patient Educ Couns. 2007; 65(3):279–287. [PubMed: 17000074]

28. Lickleder C, Wolff G, Barth J. Mental health and quality of life after genetic testing for Huntington's disease. a long-term effect study in Germany. Am J Med Genet A. 2008; 146A(16): 2078–2085. [PubMed: 18627060]

29. Gargiulo M, Lejeune S, Tanguy ML, et al. Long-term outcome of presymptomatic testing in Huntington's disease. Eur J Hum Genet. 2009; 17(2):165–171. [PubMed: 18716614]

30. Almqvist EW, Brinkman RR, Wiggins S, Hayden MR. the Canadian Collaborative Study of Predictive Testing. Psychological consequences and predictors of adverse events in the first 5 years after predictive testing for Huntington's disease. Clin Genet. 2003; 64:300–309. [PubMed: 12974735]

31. Rosenblatt A. Neuropsychiatry of Huntington's disease. Dialogues Clin Neurosci. 2007; 9(2):191–197. [PubMed: 17726917]

32. Paulsen JS, Hoth KF, Nehl C, Stierman L. Critical periods of suicide risk in Huntington's disease. Am J Psychiatry. 2005; 162(4):725–731. [PubMed: 15800145]

33. Wetzel H, Gehl C, Dellefave L, et al. Suicidal ideation in Huntington's disease. The role of comorbidity. Psychiatry Res. 2011; 188(3):372–376. [PubMed: 21605914]

34. Fiedorowicz J, Ruggle A, Mills J, et al. Suicidal behavior in Huntington's disease. Neurodegener Dis. 2011; 69(11):1758–1765.

35. Kenney C, Hunter C, Jankovic J. Long-term tolerability of tetrabenazine in the treatment of hyperkinetic movement disorders. Mov Disord. 2007; 22(2):193–197. [PubMed: 17133512]

36. Jankovic J. Treatment of hyperkinetic movement disorders. Lancet Neurol. 2009; 8(9):844–856. [PubMed: 19679276]

37■■. Phillips W, Shannon KM, Barker RA. The current clinical management of Huntington's disease. Mov Disord. 2008; 23(11):1491–1504. Thorough review of treatments for all domains of HD symptoms. [PubMed: 18581443]

38. Rowe K, Paulsen JS, Langbehn DR, et al. Patterns of serotonergic antidepressant usage in prodromal Huntington's disease. Psychiatry Res. In Press.

39. Holl AK, Wilkinson L, Painold A, Holl, et al. Combating depression in Huntington's disease. effective antidepressive treatment with venlafaxine XR. Int Clin Psychopharmacol. 2010; 25(1): 46–50. [PubMed: 19996754]

40. Marshall J, White K, Weaver M, et al. Specific psychiatric manifestations among preclinical Huntington's disease mutation carriers. Arch Neurol. 2007; 64(1):116–121. [PubMed: 17210818]

Websites

101. PREDICT-HD. http://predict-hd.net

102. CIT- HD Study. ClinicalTrials.gov www.clinicaltrials.gov/ct2/show/NCT00271596?term=cit-hd&rank=1

Box 1

Symptoms and diagnosis of mood disorders[†]

Symptoms of depression

- Depressed mood
- Loss of interest
- Insomnia or hypersomnia
- Weight gain or loss
- Decreased energy
- Psychomotor agitation or retardation
- Worthlessness/guilt
- Poor concentration
- Suicidal ideation or attempt
- Psychotic symptoms in severe depression (hallucinations and delusions)

Symptoms of mania

- Elevated or irritable mood
- Racing thoughts
- Grandiose thoughts/plans
- Hypertalkative
- Decreased sleep owing to feeling it is not necessary
- Distractable
- Increased social, work, school or sexual activities
- Excessive spending
- Psychomotor agitation

[†]For complete information regarding diagnostic criteria, see the Diagnostic and Statistical Manual of Mental Disorders, Volume IV, Text Revision [8].

Practice Points

- Depression is common in Huntington disease (HD) and can develop in the prodromal or manifest stages of the illness.
- In manifest disease, earlier stages have the highest prevalence of depression.
- In the disease prodrome, depression can develop many years before motor symptoms and the highest prevalence of depression during this period may be within 1 year of clinical diagnosis.
- Depression in HD is not associated with other measures of illness progression.
- Suicide risk screening is critical in this population due to increased risk of suicidal ideation and attempts.
- Standard depression treatments are advised for HD patients with depression, as there is minimal research available specific to HD.

Table 1

Recent studies on the prevalence of depression and suicide in Huntington's disease.

Study (year)	Sample	Measures used	Results	Ref.
Paulsen (2005)	2835 manifest Stratified by functional capacity stages 1–5	UHDRS sad mood, low self-esteem, anxiety	Sad mood >30% in all stages, highest in stage 2 (45%)	[10]
Paulsen (2005)	2688 manifest, 1483 at risk, stratified by motor symptoms	UHDRS suicidal ideation and severity	Suicidal ideation increased in at risk group with increasing motor symptoms (up to 23.5%). In manifest group, highest suicidal ideation in stage 2 (21.6%)	[32]
Julien (2007)	89 gene-positive 115 gene-negative	CIDI	Higher history of major depression in gene positive (20 vs 12%), significant depression 1 year before motor diagnosis	[11]
van Duijn (2008)	55 presymptomatic† 85 symptomatic‡ 56 gene-negative	CIDI	20% early symptomatic and 16.5% late symptomatic with depression in previous 12 months vs 7.1% in gene-negatives	[9]
Kingma (2008)	55 presymptomatic† 97 symptomatic‡ 56 gene-negative	PBA	Gene-positive groups with more depression than gene-negatives	[14]
Duf (2007)	553 prodromal§ 92 gene-negative	SCL-90R	Significantly higher mean symptoms of depression in prodromal group	[6]
Marshall (2007)	29 minimal symptoms† 20 some symptoms¶ 34 manifest# 171 gene-negative	SCL-90R	Group with some motor symptoms but not yet manifest had highest symptoms of depression; no significant differences between groups	[40]
Tabrizi (2009)	120 premanifest†† 123 early-stage†† 123 gene-negative	PBA	Early-stage group with significantly increased affective symptoms compared with gene-negatives	[16]
Aziz (2010)	21 prodromal‡‡ 63 manifest 63 gene-negative	BDI-II	Manifest group with highest level of symptoms, followed by prodromal group, then gene-negatives, significant difference across groups	[19]
Lickleder er (2008)	54 prodromal§§ 15 manifest§§ 52 gene-negative	BDI-II	Manifest with significantly more symptoms compared with other groups	[28]

†UHDRS Diagnostic Confidence Level (DCL) = 0 or 1.

‡UHDRS DCL = 2–4.

§UHDRS DCL = 0–3.

¶UHDRS DCL = 2–3.

#UHDRS DCL = 4.

††All gene-positives with burden of pathology score >250 (age × [CAG−(35 × 5)]), Premanifest have UHDRS motor score <5.

‡‡UHDRS motor score <5.

§§Subject self-report.

BDI-II: Beck Depression Inventory-II; CIDI: Composite International Diagnostic Interview; PBA: Problem Behaviors Assessment; SCL-90R: Symptom Checklist 90 Revised; UHDRS: Unified Huntington's Disease Rating Scale.