Emotional and functional impact of DNA testing on patients with symptoms of Huntington's disease

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Abstract

The potential impact of DNA testing on asymptomatic subjects at risk for Huntington's disease (HD) has been addressed by numerous studies, but the effect of revealing the genetic results to patients with a clinically established diagnosis of HD has not been previously evaluated. We studied 36 patients, with equal distribution of men and women, mean age 53.9 (SD 12.3) years (range 25-76) and mean duration of symptoms of 11.2 (SD 7.7) years (range 2-33), whose clinical diagnosis of HD was confirmed by expanded CAG repeats (>40). Coping strategies and depression levels were assessed before the results of DNA testing were imparted. The assessments were repeated two weeks and three months after the results were explained to the patients and their relatives and were compared to the baseline assessments. This group of HD patients was compared with 10 patients who had similar symptoms but the diagnosis of HD was excluded by normal CAG repeats (<30). Although some patients with HD expressed a subjective reaction to the positive result (four were "surprised", one was "frustrated", and one "devastated"), there were no differences in any psychological scores including Beck Depression Inventory, functional capacity, symptom interference, independence scale, and other measures of mood and behaviour two weeks and three months later. Similarly, no change was noted in any of these measures in the non-HD group. These results suggest that mood and coping strategies are unaffected by DNA confirmation of diagnosis in symptomatic patients with HD.

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Huntington's disease (HD) is an incurable hereditary neurological disorder affecting about 10 000 to 25 000 people in the United States.¹ With the increasing availability of DNA diagnostic testing, questions about coping strategies in response to diagnosis of a terminal illness are being addressed by a growing number of investigators.²⁻⁵ While the potential impact of DNA testing on asymptomatic subjects at risk for HD has been addressed by numerous reports,⁶⁻¹² the effect of communicating the genetic results to patients with a previous clinical

diagnosis of HD has not been evaluated before. This study was designed to address the question of whether genetic confirmation of a clinical diagnosis of HD will have an adverse impact on mood and coping strategies in these patients.

Methods

Thirty six patients with the clinical diagnosis of HD participated in this study after signing a consent form approved by the Institutional Review Board for Human Research at Baylor College of Medicine. The patients in the HD group had already been told that they most probably had HD, based on typical clinical presentation and family history of HD (present in at least one first degree relative of 30 of the 36 patients). This group of patients with HD was compared with a group of 10 patients in whom HD was initially suspected, but it was excluded by genetic testing. In this latter group there were three patients with neuroacanthocytosis, two with idiopathic chorea, and one each with Sydenham's chorea, hereditary ataxia, chorea associated with exposure to vinyl chloride, tardive dyskinesia, and Hallervorden-Spatz disease. Three of 10 patients in this non-HD group had a family history of a movement disorder among their first degree relatives. The diagnosis of HD was confirmed if the blood DNA analysis, performed by a previously described method⁶ using primers that exclude the adjacent polymorphic CCG repeats, indicated >40 CAG repeats, and it was excluded if the number of CAG repeats was <30.

The subjects were asked to complete questionnaires designed to measure mood and to assess patient's functional capacity. Depression was measured with the Beck Depression Inventory,¹³ functional capacity was assessed with staging of functional capacities,¹⁴ degree of functional impairment was rated on modified Physical Disability/Independence Rating Scale,¹⁵ and modified Behavioral and Functional Assessment measures from the Unified Huntington's Disease Rating Scale were used to evaluate mood, self-esteem, guilt, anxiety, suicidal thoughts, aggressive behaviour, and functional capacity.¹⁵

Statistical analysis was performed using the Wilcoxon rank sum test to compare non-parametric measures in the positive versus negative group. The non-parametric signed rank test for paired comparisons was used to analyse changes in each group from baseline to first

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Table 1 Assessment of impact of communicating the results of DNA testing on patients with known Huntington's disease

Variable	Baseline	Follow up at 2 weeks	Follow up at 3 months
Number	36	31	28
Age (mean (SD))	53.9 (12.3) (25–76)	53.1 (13.8) (25–76)	53.6 (11.7) (25–76)
Duration of symptoms (y)	11.2 (7.7) (2–33)	11.2 (7.8) (2–33)	11.5 (7.9) (2–33)
Female/male	18/18	14/17	14/14
Beck Depression Scale	14.6 (9.9) (0–41)	14.5 (9.1) (1–35)	14.1 (10.8) (0–41)
Functional capacity	6.4 (3.5) (0–13)	6.3 (3.5) (0–13)	6.4 (3.4) (1–13)
Functional assessment	605 (62%) Y	505 (60%) Y	452 (60%) Y
Symptom interference	4.3 (2.2) (0–8)	4.3 (2.2) (0–8)	4.3 (2.4) (0–8)
Independence scale	70.4 (25.6) (10–100)	72.9 (23.2) (10–100)	73.4 (22.6) (10–100)
Sad mood	1.2 (1.2) (0–4)	1.3 (1.3) (0–4)	1.5 (1.5) (0–4)
Low self-esteem/guilt	1.1 (1.3) (0–4)	0.8 (1.1) (0–3)	1.0 (1.3) (0–4)
Anxiety	1.3 (1.4) (0–4)	1.1 (1.2) (0–4)	1.3 (1.2) (0–4)
Suicidal ideation	0.3 (0.7) (0–3)	0.3 (0.5) (0–2)	0.3 (0.7) (0–3)
Aggressive behaviour	0.6 (0.9) (0–3)	0.3 (0.6) (0–3)	0.4 (0.8) (0–3)

Table 2 Assessment of impact of communicating the results of negative DNA tests on patients with suspected Huntington's disease

Variable	Baseline	Follow up at 2 weeks	Follow up at 3 months
Number	10	8	6
Age (mean (SD))	45.6 (18.9) (13–68)	46.1 (19.3) (13–68)	50.8 (19.9) (13–68)
Duration of symptoms (y)	13.9 (10.5) (1–38)	14.7 (11.2) (1–38)	16.0 (11.4) (8–38)
Female/male	4/6	3/5	3/3
Beck Depression Scale	7.1 (4.8) (0–14)	6.6 (4.1) (0–15)	7.3 (5.1) (0–15)
Functional capacity	6.8 (4.1) (2–13)	6.9 (2.4) (4–12)	6.8 (4.1) (2–13)
Functional assessment	139 (51%) Y	129 (60%) Y	91 (56%) Y
Symptom interference	4.5 (2.3) (0–8)	3.3 (2.2) (0–6)	3.3 (2.3) (0–7)
Independence scale	69.0 (16.4) (50–100)	73.7 (16.5) (50–100)	75.0 (17.1) (50–100)
Sad mood	0.9 (0.9) (0–3)	1.5 (1.3) (0–3)	1.0 (1.1) (0–3)
Low self-esteem/guilt	0.4 (0.5) (0–1)	0.4 (0.7) (0–2)	0.5 (1.1) (0–3)
Anxiety	1.4 (1.0) (0–3)	1.0 (1.1) (0–3)	1.2 (1.2) (0–3)
Suicidal ideation	0	0.4 (1.0) (0–3)	0
Aggressive behaviour	0.2 (0.4) (0–1)	0.2 (0.4) (0–1)	0.2 (0.4) (0–1)

follow up evaluation and from baseline to second follow up evaluation.

Results

All (100%) subjects, “positive” and “negative”, responded to the baseline questionnaire. In the “positive” group, 31/36 (86%) responded at two weeks and 28/36 (78%) responded at three months. In the “negative” group 8/10 (80%) responded at two weeks and 6/10 (60%) responded at three months. Although 29 of 34 patients with clinically diagnosed HD expressed no surprise when the positive DNA results were first communicated to them, four were “surprised”, one was “frustrated”, and one was “devastated”. There was no change in any psychological score including the Beck Depression Inventory, functional capacity, symptom interference, independence scale, and other measures of mood and behaviour two weeks and three months later in the HD group (table 1). Similarly, there was no difference in the respective scores in the non-HD group (table 2).

Discussion

Most studies of the effects of DNA testing on the psychological and functional measures have concentrated on asymptomatic people who carry 25% or 50% risk of inheriting the HD gene. The vast majority of DNA testing, however, involves subjects who are clinically affected and in whom the DNA test provides a definitive confirmation of the diagnosis. Some of these subjects have been previously diagnosed as having HD based on clinical presentation, while others seek the test because they believe that they are asymptomatic although the neurological examination indicates evidence of HD. As many as 15% of those requesting predictive testing for HD have clinical evidence of the disease at the time of the initial examination.^{8,16} DNA testing is also used to exclude the diagnosis of HD in patients whose clinical course resembles that of HD.

Our study shows that communicating a positive result of DNA testing in patients with a clinical diagnosis of HD has not resulted in any detectable change in mood, behaviour, coping strategies, or functional capacity. Similarly, in another group of patients in whom HD was suspected, but, because of lack of family history or atypical findings, the diagnosis was in doubt, there was no change in any of the measured variables after DNA testing for HD was found to be negative.

Although no similar study has been previously performed, the results are not entirely surprising. Psychological and other outcome studies in asymptomatic, at risk subjects have indicated relatively minimal impact of either positive or negative DNA test results. In one study, four of 15 DNA tests on presymptomatic subjects using linkage analysis were positive for the HD gene.¹⁷ While all those with positive results experienced transient symptoms of depression, none reported suicidal ideation. Another study showed that one year after the results of gene testing were disclosed, both increased risk and decreased risk subjects had overall no increase in depression or deterioration in psychological well being.⁷ Despite these findings, the potential risk of catastrophic psychological reaction to positive, and even negative, test results strongly argues in favour of intensive pre- and post-test genetic and psychological counselling in all asymptomatic persons.^{8,9}

Our results suggest that since mood and coping strategies are unaffected by DNA confirmation of the diagnosis in symptomatic patients with HD, extensive psychological testing and counselling do not seem necessary in most such patients. Given the state of denial, however, in some symptomatic patients with clinically diagnosed HD, it is prudent to exercise caution when imparting the results of DNA HD tests in these patients. Although our patients showed no deterioration in mood, none showed evidence of serious depression at the time when the DNA results were communicated. In patients who show evidence of depression, the positive DNA test results may precipitate more profound depression and, therefore, the diagnosis may need to be delayed

until the patient is determined to be "ready". Although appropriate counselling and psychological support should be made available to the patients, rather than insisting on uniform guidelines, we recommend that the approach to DNA test results should be individualised and handled lucidly and compassionately.

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