Impact of Presymptomatic Genetic Testing for Hereditary Ataxia and Neuromuscular Disorders

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Background: With the exception of Huntington disease, the psychological and psychosocial impact of DNA testing for neurogenetic disorders has not been well studied.

Objective: To evaluate the psychosocial impact of genetic testing for autosomal dominant forms of hereditary ataxia and neuromuscular disorders.

Patients: Fifty subjects at risk for autosomal dominant forms of spinocerebellar ataxia (n=11), muscular dystrophy (n=28), and hereditary neuropathy (n=12).

Design and Setting: A prospective, descriptive, observational study in a university setting of individuals who underwent genetic counseling and DNA testing. Participants completed 3 questionnaires before testing and at regular intervals after testing. The questionnaire set included the Revised Impact of Event Scale, the Hospital Anxiety and Depression Scale, demographic information, and an assessment of attitudes and feelings about genetic testing.

Results: Thirty-nine subjects (78%) completed 6 months to 5 years of posttest follow-up. Common reasons for pursuing genetic testing were to provide an explanation for symptoms, emotional relief, and information for future planning. Thirty-four (68%) had positive and 16 (32%) had negative genetic results. In those with a positive result, 26 (76%) had nonspecific signs or symptoms of the relevant disorder. Forty-two participants (84%) felt genetic testing was beneficial. Groups with positive and negative test results coped well with results. However, 13 subjects (10 with positive and 3 with negative results) reported elevated anxiety levels, and 3 (1 with positive and 2 with negative results) expressed feelings of depression during the follow-up period. The test result was not predictive of anxiety or depression.

Conclusions: Most individuals find neurogenetic testing to be beneficial, regardless of the result. Anxiety or depression may persist in some persons with positive or negative test results. Testing can have a demonstrable impact on family planning and interpersonal relationships. Further studies are needed to assess the long-term impact of such testing.

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DIRECT DNA testing is available for an ever-increasing number of genetic disorders. The ability to test for genetic conditions has outpaced our knowledge of the psychological and societal impact of this testing. Risks associated with genetic testing include emotional distress, psychological harm, and insurance and employment discrimination. Perceived benefits include relief of stress and uncertainty and improved ability for future and, in particular, family planning. Most studies concerning the social and emotional impact of genetic testing have focused on hereditary forms of cancer and Huntington disease (HD). A single systematic study has examined genetic testing in autosomal dominant forms of dementia.

Numerous DNA-based tests for autosomal dominant forms of ataxia and neuromuscular disorders exist. These disorders have many characteristics that distinguish them from HD and familial dementias, such as usual absence of cognitive impairment, absence of adventitious movements, often normal life span, frequent presence of progressive weakness, gait disability, and sometimes sensory loss. For these reasons it is important to understand the motivation for and impact of genetic testing in the lives of persons at risk for these diseases. Especially important is...
Avoidance. Intrusion refers to constantly experienced ideas, and the Depression Scale (HADS) were also administered. The testing was performed according to established methods at Athena Diagnostics, Worcester, Mass, for CMT, DM2, HNPP, and OPMD; the University of Washington Genetics Laboratory for DM1 and SCA; and the Department of Pathology, The University of Iowa, Des Moines for FSHD. A positive test result indicated a disease-causing gene alteration.

**METHODS**

Subjects came from the neurogenetics clinics at the University of Washington and the Veterans Affairs Medical Center, Seattle. The autosomal dominant neurogenetic disorders included in this study were hereditary neuropathy (Charcot-Marie-Tooth disease [CMT]), hereditary neuropathy with liability to pressure palsy [HNPP]), muscular dystrophy (facioscapulohumeral dystrophy [FSHD], myotonic dystrophy [DM], oculopharyngeal muscular dystrophy [OPMD]), and spino-cerebellar ataxia (SCA).

The study was approved by the University of Washington Human Subjects Research Committee. Thirty-eight subjects (76%) were at 50% genetic risk. Pretest genetic counseling and informed consent were required in the testing process. However, 2 participants were referred to our center after a positive predictive test result and did not receive genetic counseling before testing. A neurologic examination of all subjects was performed by one of us (T.D.B.).

The impact of DNA testing was evaluated by means of a pretest questionnaire, including demographic information and questions regarding attitudes toward and reasons for pursuing genetic testing. Subjects also completed a questionnaire administered immediately, 6 months, and annually after testing. A neurologic examination of all subjects was performed by one of us (T.D.B.).

The number of participants in this study and the subjectivity and nonparametric nature of the data did not allow statistical analysis. The DNA testing was performed according to established methods at Athena Diagnostics, Worcester, Mass, for CMT, DM2, HNPP, and OPMD; the University of Washington Genetics Laboratory for DM1 and SCA; and the Department of Pathology, The University of Iowa, Des Moines for FSHD. A positive test result indicated a disease-causing gene alteration.

**RESULTS**

We included 50 study participants. Thirty-three participants were women and 17 were men, with an average age of 44.7 years (range, 21.5-74.0 years) and an average 15.2 years of education. Additional demographic data are provided in the Table. Eleven participants underwent genetic testing for SCA (SCA1 [n = 1], SCA2 [n = 2], SCA3 [n = 3], and SCA6 [n = 3]), 10 for CMT (CMT1A [n = 3], CMT1B [n = 6], and CMTX [n = 1]), 2 for HNPP, 17 for DM (DM1 [n = 16] and DM2 [n = 1]), 10 for FSHD, and 1 for OPMD. One participant at 50% risk for DM1 and SCA6 completed questionnaires for both disorders. Another participant with positive test results for CMT died of liver disease during the course of the study. One subject with negative test results for DM1 was unavailable for follow-up. Thirty-nine participants (78%) completed 6 months or more of follow-up, with a maximum follow-up time of 5 years (3 subjects). Thirty-four subjects (68%) had positive test results and 16 (32%) had negative results. Of those with positive test results, 26 (76%) had mild signs of a neuromuscular disorder on results of neurologic examination. They considered themselves asymptomatic, and the mild signs were nonspecific and usually not diagnostic. Two individuals who experienced symptoms and assumed that they were affected with the neurogenetic disorder present in their family had negative DNA results. One participant was pregnant and not interested in prenatal testing. Thirteen participants enrolled in the study after receiving test results and did not complete pretest questionnaires.

**MOTIVATIONS FOR TESTING**

The most commonly cited reasons for pursuing genetic testing included that it “might explain symptoms I’m hav-
ing” (26 [52%]), that the “result might be a relief” (22 [44%]), and that results “might affect insurance, family planning, or travel/retirement planning” (16 each [32% each]). Twelve participants (24%) indicated that preventing disability, career planning, cost, stress, and financial planning were also important issues.

PERCEPTION OF DISEASE SEVERITY

When asked how they would rate the severity of the disease in themselves or their family members, the range of responses varied with the disease type. Of those answering the question, the distribution of responses was as follows: For the 9 participants who answered the question about SCA, 4 rated the disease as severe, 4 as moderate, and 1 as mild. For the 9 participants who answered the question about CMT, 3 rated the disease as severe, and 6 as moderate. For the 2 participants who answered the question about HNPP, both rated it as mild. For the 14 participants who answered the question about DM, 5 rated the disease as severe and 9 as moderate. For the 9 participants who answered the question about FSHD, 3 rated the disease as severe, 4 as moderate, and 2 as mild. The 1 participant who answered the question about OPMD rated the disease as severe. For all ratings, 16 (36%) of 44 rated their disease as severe; 23 (52%) as moderate; and 5 (11%) as mild.

FAMILY PLANNING

Eight individuals with positive test results stated that they were not planning to have biological children or another child. Four individuals with negative test results reported they felt comfortable or confident about having children. One woman expressed gratitude that she could now have a grandchild through her son who had negative test results for FSHD (both participated in this study). One man stated that he did not want more children and that if he remarried a younger woman who wanted children, this could represent a serious conflict.

INSURANCE

Two participants reported they were not able to obtain a long-term-care policy. One person with life and disability insurance was not able to increase her benefits to the maximum amount after her positive test result and subsequent diagnosis of FSHD. There were no reports of difficulty with obtaining health insurance, at least in part because Washington State law does not allow denial of health insurance based on genetic testing.

SHARING RESULTS

When asked with whom they shared genetic testing results, all 47 participants who responded (94%) said with family. Most also told a limited number of friends. Several said they told results to anyone who asked. Eight individuals disclosed results to their employer and coworkers, whereas 1 subject kept his positive results hidden from these same persons. Those who shared the results did not report lost employment or difficulties with coworkers. No one else stated that they kept results a secret or expressed regret about whom they had told their results. One study participant with an SCA3 mutation shared his results with Newsweek magazine in an issue describing the Human Genome Project. In the article he stated, “knowing I have this has enabled me to take control of my life.”

Participants were also asked whether they would advise others in their situation to undergo genetic testing. Thirty-six individuals responded yes, and several said the testing provided peace of mind. Four said yes but only for family planning purposes; 5 would recommend testing only if a person has symptoms; 2 were unsure about testing; and 1 stated that testing is an individual choice. No subject stated that they would tell others not to undergo genetic testing.

EMOTIONAL IMPACT

Most participants stated that they felt good or glad about having undergone testing. Many expressed relief, regardless of the test result or disease type. Several felt grateful that the result provided them with a definitive answer and an explanation for their symptoms, allowing them to be more accepting of their limitations. Two participants with negative results reported feeling a little guilty that they were spared their family disease. One individual, who underwent predictive testing for SCA and did not have pretest genetic counseling, entered the study immediately after receiving positive results. She reported feeling “numb and confused” immediately after testing, but 1 year later felt better about having had the testing. At 3 years after the test, she stated that, “The testing affected my emotional state severely. I’m having anxiety and depression. I wonder if the testing has made me feel like I have symptoms I normally would not notice.” Several participants were frustrated about a positive result because it confirmed that they were “not normal.” Two persons with positive test results for FSHD who did not receive pretest genetic counseling had a difficult time coping with their results. One stated, “It was hard to see the result on paper. I kept hoping it was wrong. The futility of [the] result was heartbreaking.” The other person was unsure whether the testing was necessary, and would not do it again. One subject expressed “tremendous gratitude, and mind and body relief,” whereas another was “sad, cried a little and scared, but holding to a belief to enjoy life.” One subject with a positive test result said, “Overall, I see more drawbacks than benefits to me.”

The result affected relationships with their spouse or their family for 11 participants. Five stated they had grown closer to certain family members, whereas 5 others experienced strain in their relationships. One participant who had positive test results stated, “Family members remind me of the condition—this does not feel good.” During the course of the study, 1 individual became divorced, indicating that the spouse could not deal with the current and potential medical problems caused by the disease.
ANXIETY

Elevated anxiety levels (a score of ≥10 on the HADS) were reported at some point during the study by 18 participants (35%) (Figure 1A). In this subset of 18 individuals, 7 had negative test results and 11 had positive test results, with every disorder represented. Average anxiety scores for the group with negative results declined slightly in the posttest period, then showed an increase at the 2-year follow-up. Individual anxiety scores were quite variable. The DNA test results were not predictive of anxiety level. One person with a low pretest anxiety score reported an increase in anxiety to moderate levels 1 to 3 years after the test, despite negative test results (Figure 2). This subject attributed the increased anxiety to stress caused by caring for young family members with progressive symptoms of ataxia rather than her own negative test results. In contrast, another participant with the highest pretest anxiety score (19 points) was convinced she had signs of SCA. After the negative test result, her anxiety level dropped dramatically, associated with considerable relief (Figure 2). A third subject with a positive test result maintained a steady level of anxiety throughout a 3-year period (Figure 2). Two partici-
pants, 1 with a positive and 1 with a negative result, reported taking an antianxiety medication during the follow-up period.

DEPRESSION

Before genetic testing, no individuals met the criteria for definite depression (HADS score, ≥10), and 5 scored in the borderline range (HADS score, 8-9) (Figure 1B). Overall, depression scores were low (≤5) in the positive and negative groups, with minimal change after provision of test results. In the posttest period, only 1 person with positive test results was in the depressed range, with a score of 10 at the 2-year follow-up. This individual experienced disability from symptoms of CMT and took an antidepressant medication. Of those with negative test results, 2 subjects scored in the depressed range (11-12) after the test. Their depression scores were low in the pretest period and increased at 1 to 2 years after the test. One was the same individual who experienced increased anxiety as a result of caring for family members with SCA6. At 3 years after the test, her depression score decreased to 7. Nine participants reported a history of depression, and 5 stated that they were taking an antidepressant medication during the course of the study.

INTRUSION

On the IES, 8 participants had relatively high intrusion scores (≥9) in the pretest period, indicating frequent thoughts about the disorder (Figure 1C). Of those, 5 persons had positive and 3 had negative test results. In those with positive results, intrusion scores remained high in all but 1 person during the follow-up period. At the time of this report, these individuals are coping with symptoms of the disorder that affect their ability to work and function on a daily basis. Intrusion scores decreased during the posttest period in the 3 persons with negative results.

AVOIDANCE

Pretest scores on the avoidance subscale of the IES were high (≥8) in 4 persons with positive and 4 with negative test results, indicating conscious efforts to avoid thinking about the disorder (Figure 1D). Scores declined after test results in those with negative results, whereas they tended to remain elevated in persons with positive results. Wide individual differences in avoidance between 2 subjects who had positive DNA test results are shown in Figure 3.

Figure 3. Avoidance scores on the Impact of Event Scale (IES) for 2 subjects. Subject 1 had a positive test result for Charcot-Marie-Tooth disease type 1B and subject 2 had a positive test result for myotonic dystrophy type 1. Subject 1 indicated considerably more evidence of avoidance than subject 2 until 2 years after the test, when their scores reversed. This shows the wide and unpredictable differences that can occur between persons with the same test results. The horizontal dotted line indicates the threshold at or above which avoidance scores may be clinically noticeable.

A common motivation for testing is suspicion that one may have early signs of the disease. Indeed, many of the persons with positive test results showed subtle nonspecific signs of the disease on examination. However, some persons who believe they have early symptoms of the disease can be relieved to discover that they have not inherited the genetic condition. Family planning is also an important motivation, and test results may have an impact on decisions about whether to have children.

Overall, most persons coped well with the results of genetic testing. There was a trend for anxiety levels to decrease after testing in persons with both positive and negative results. However, several subjects continued to experience anxiety. Of interest was a subject with a negative genetic test result who continued to experience anxiety and emotional problems related to the need to care for other affected persons in her family. The responses of participants left no doubt that the genetic testing was stressful and had an impact on their feelings and lives, including persons with negative genetic test results. The psychological strengths of such individuals deserve more detailed study.
There is considerable societal concern about potential discrimination by the insurance industry against persons at risk for genetic diseases. None of the subjects in our study were denied health insurance, in part because Washington State law prevents such discrimination. Similar laws are presently under study in other states and at the federal level. Some of our subjects were unable to obtain long-term-care insurance, and we do not have data on the availability of life insurance. These topics require further exploration.

The genetic testing protocol followed in this study was performed in a university setting by persons trained and experienced in genetic counseling. Nongenetic health care providers need to be fully aware of the potential risks and benefits of genetic testing, of the knowledge required, and of the time involved to provide appropriate genetic counseling.1,2

The results of this study should not be overgeneralized to other disease populations because of the relatively small number of subjects in each category, lack of long-term follow-up, and fairly homogeneous socioeconomic strata studied. There were no major differences in the impact of genetic testing among the various disease groups undergoing evaluation in this study.

As part of this study, informational booklets about SCA, DM, and FSHD were written with an emphasis on the issues involved with genetic testing for these disorders. The booklets are available online at http://depts.washington.edu/neurogen/ (accessed 2002) and also in hard copy from the authors.

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