

Psychological functioning before predictive testing for Huntington's disease: the role of the parental disease, risk perception, and subjective proximity of the disease

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Abstract

Background—Psychometric testing of participants in predictive DNA testing for Huntington's disease (HD) has shown that 15% of the subjects at risk for HD had at least mild depression or a high score for general anxiety or both in the pre-test period. The main aim of the study was the delineation of variables associated with pre-test distress of applicants for predictive testing for HD. Based on theoretical considerations, four specific hypotheses were tested regarding the role of (1) the test participant's age at the (perceived) parental onset of HD, (2) the affected parent's sex, (3) the perception of the risk for HD, and (4) the subjective proximity of the disease. Secondly, these four variables were used in multiple regression analyses to select the best predictors of pre- and post-test psychological functioning (one year after the test). Increasing the understanding of pre- and post-test distress is important for developing better counselling and support strategies for test applicants.

Methods—Data were collected by means of clinical interviews and psychometric questionnaires during the pre- and post-test (one year after the test) counselling sessions for predictive testing for HD.

Results—We found significant associations of the participant's age at the parental onset, the subjective proximity of the disease onset, and the perceived risk with pre-test psychometric measures of psychological functioning. Multiple regression analyses showed that the best predictors of pre-test functioning were the perceived proximity of the disease onset and its interaction with risk perception. Regarding post-test functioning, none of the proposed variables had a unique contribution beyond that accounted for by pre-test psychological functioning.

Conclusions—Test participants who are close to the perceived age of onset of HD and who have a pessimistic risk perception should be given special attention during pre-test counselling because of their possible negative affective condition at that time. Pre-test psychological measures were the best predictors of post-test distress, irrespective of the test result. **Suggestions for future longitudinal re-**

search are formulated. This kind of research should enable clinical geneticists and mental health professionals to refine the pre- and post-test counselling strategies for predictive DNA testing, not only for HD, but also for other incurable late onset disorders.

(*J Med Genet* 1999;36:897-905)

Keywords: Huntington's disease; predictive DNA testing; psychological distress

More than 10 years of experience with predictive testing for Huntington's disease (HD) all over the world has shown that the predictive test result has a mixture of positive and negative consequences, which vary over time, but that severe psychiatric reactions are rare.¹⁻⁷ This low incidence of psychiatric reactions after a test result has been attributed to the careful pre- and post-test counselling for predictive testing and to the robustness of the people who chose to be tested.⁸⁻¹³ Psychometric testing in the pre-test period¹⁰ indicated that test participants are a self-selected group with a significantly higher mean ego strength and with significantly better coping strategies than the general population; test participants react more with active problem solving, with comforting and optimistic thoughts, and with social support seeking. The impact of testing on post-test psychological well being and on reproductive decisions has been reviewed by Evers-Kiebooms and Decruyenaere.¹⁴ Several studies^{5, 15-18} trying to predict post-disclosure distress (anxiety, hopelessness, depression) showed that measures of pre-test distress were the best predictors, irrespective of the test result.

The factors that explain the distress in the pre-test period have received little attention until now. However, psychometric testing of Flemish test participants^{10, 17} showed that 15% of the test applicants had at least a mild depression level on the Beck Depression Inventory and/or a high score for general anxiety on Spielberger's anxiety scale during the pre-test period. This could not be explained by the carrier status of the test applicants; mean pre-test scores of carriers and non-carriers were not significantly different. DudokdeWit *et al*¹⁹ assessed pre-test distress with the Impact of Event Scale in a sample of predictive test applicants for HD, cerebral haemorrhage, heredi-

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Revised version received 7 July 1999
Accepted for publication 5 August 1999

tary breast and ovarian cancer, and familial polyposis coli. They found that pre-test intrusive and/or avoiding thoughts about the disease were associated with more experiences with the disease in close relatives, with the emotional impact of the disease on the applicant's life, and with the anticipation of adverse effects of the test result. Pre-test distress may be caused by aspects associated with the genetic nature of the disease, such as the perceived genetic risk, the expected impact of the test outcome and the perceived proximity of the disease onset. Moreover, it may be influenced by environmental factors, such as past and/or current negative experiences with HD in the family. Increasing the understanding of pre-test distress should lead to better counselling and support strategies before and after the predictive test.

Aim of the study

In the present study we endeavour to gain more insight into pre-test psychological functioning of subjects who applied for predictive testing for HD. Psychological functioning was conceptualised as ego strength, general anxiety, and depression level. Hypotheses were tested regarding the role of the following variables: (1) the test participant's age at the (perceived) parental onset of HD, (2) the sex of the affected parent, (3) the perception of the risk for HD, and (4) the subjective proximity of the disease. Moreover, we investigated whether these four variables were associated with post-test psychological functioning (one year after the test).

Hypotheses

The possible role of the test participant's age at the (perceived) parental onset of HD and of the affected parent's sex is based on publications on child psychiatry. Several studies have shown that traumatic events and negative, enduring circumstances during childhood, such as parental loss or parental mental illness, are associated with adult affective symptoms like depression or anxiety.²⁰⁻²⁴ A crucial aspect of the childhood condition that makes it liable to provoke adult symptoms is the child's age; distress is more marked the younger the child. Age below 5 years is critical²⁵ because attachments are first becoming established at this age and because cognitive skills are lacking at this time. The role of the sex of the parent proved to be less clear. Given the mothers' greater concern and feelings of responsibility for child rearing in our society, one might expect that more adult problems would occur if the negative event concerns the mother of the child rather than the father, but the evidence is not straightforward.²¹⁻²⁶ In HD, patients often have young children when the symptoms become manifest. Folstein *et al*²⁷ stated that patients quickly become handicapped in their role as parents because of the illness. The increasing irritability, emotional lability, and lack of judgement of the HD patient interfere with adequate parental behaviour. Moreover, psychotic symptoms, such as major affective disorders, may be present. The partner of the affected person plays a major role in managing the care of the patient, often at an enormous

personal price. Many spouses suffer from anxiety disorders, depression, and psychosomatic complaints.²⁸⁻³¹ They have the responsibility for taking care of the children, while struggling with their own feelings of sadness, guilt, hostility, or social isolation. Children of an affected parent are not only at genetic risk, but also at psychological risk. Folstein *et al*²⁷ have described conduct disorders in the offspring of patients with HD that were related to the instability of the parent, the lack of discipline and structure in the family, and marital conflict.

The first hypothesis states that the younger the test participants were at the onset of HD in their parent, the more vulnerable they are to adult adverse reactions, like depression or anxiety, and the less ego strength they have. The adult distress will be especially marked in those who were in early childhood when the disease started in their parent.

The second hypothesis states that adverse adult reactions are more pronounced when the mother is affected than when the father is affected. Kessler³² also drew attention to the possible role of gender as a major factor in disorganising the family: "when the mother is affected it appears to have a greater impact on effective family functioning than when the father is affected". Moreover, we would expect an interaction of the child's age at parental onset of HD and the sex of the affected parent. We predict that the effect of the parental disease on adult psychological functioning is larger if the mother becomes affected in the offspring's early childhood than if the father becomes affected, while we would expect no such difference if the parent becomes ill beyond the offspring's childhood.

Hypothesis 3 concerns the relationship between the subjective proximity of the disease and the level of anxiety and depression. The impact of temporally distant events on present behaviour and affect depends on their distance; proximity increases and distance diminishes the influence of the event.³³ We predict that the nearer the perceived onset of HD, the higher the pre-test anxiety and depression will be in the test participants. Moreover, this association will still be significant after controlling for the subject's age at the parental onset of the disease. Regarding the post-test period we would expect a negative relationship between the subjective proximity of the disease and the level of anxiety and depression in carriers, while in non-carriers we would expect no relationship.

The fourth hypothesis concerns the relationship between the subjectively perceived risk for HD and the level of anxiety and depression. Major cognitive theories of depression (Beck's cognitive model,³⁴ the learned helplessness theory³⁵) emphasise the role of hopelessness about the future in the aetiology and maintenance of depression. Hopelessness is defined as the belief that desirable outcomes are highly improbable, that adverse outcomes are highly probable, and that one is helpless to change these outcomes. Empirical research³⁶⁻³⁷ has moreover shown that depressed or anxious

subjects make more negative predictions of future adverse events than normal subjects. We predict that a high perceived risk in the pre-test period (predictive pessimism) is associated with higher pre-test anxiety and depression than a low perceived risk (predictive optimism) or an "accurate" risk perception. Moreover, we expect an interaction effect of the subjective proximity of HD and the perceived risk on psychological well being; persons with predictive pessimism will be more vulnerable to anxiety and depression as the disease comes closer than persons with a more accurate risk perception or with predictive optimism.

The second part of hypothesis 4 concerns the post-test period. The Vancouver group^{1, 3, 38, 39} found that post-test symptoms of depression and anxiety were more likely in those who received a test result contradictory to the expected outcome. Subjects with pre-test predictive optimism (low perceived risk for HD) who received a bad result and those with pre-test predictive pessimism (high perceived risk for HD) who received a good result are expected to be more depressed and anxious after the test than participants who received a test result that corresponded to their pre-test expectations.

Although some of the four predictor variables may be correlated, we predict that each will have an independent contribution to the participant's pre-test well being. In other words, we expect that it will be possible to identify the proportion of the variance in the participant's pre-test functioning that can be attributed uniquely to each of the four variables.

Methods

PARTICIPANTS

Before March 1997, 94 subjects with an affected parent received a predictive test result in Flanders (35 carriers and 59 non-carriers). For 34 persons, the test result was obtained by linkage analysis. Immediately after the identification of the gene in 1993, they were informed by letter about the possibility of direct testing. Only three of them (two carriers and one non-carrier) asked for a confirmation of the initial result. This low number may be explained by the fact that in our centre linkage testing was only performed if a preceding DNA analysis in the family had shown that a high level of informativeness could be expected. Otherwise, the testees did not proceed in the test programme and no blood sample was taken for analysis. Moreover, the age adjusted risk after testing was very close to 99% or 1% except in a few cases. For the latter, much more attention was given to the nature of the risk modification after the disclosure of the test result. All test applicants were very well informed about the small level of residual uncertainty, but they subjectively evaluated their result in a binary way "carrier" or "non-carrier".

During pre-test counselling, test applicants were informed about the longitudinal study aimed at evaluating the impact of the predictive test on people's life. They agreed that their psychometric tests and interview data would be

used for research purposes. For 69 tested persons, complete psychometric data were available one year after the test (40 with a favourable and 29 with an unfavourable result). Data were missing for the following reasons: eight persons had a follow up in another genetic centre (no psychometric testing); five persons (three with a favourable and two with an unfavourable result) were not interested in follow up counselling; one person with a favourable result was in a psychiatric clinic; seven French or German speaking testees were not included since no appropriate psychometric norms were available; four persons received their test result less than one year ago.

MEASURES

To assess pre- and post-test psychological functioning, psychometric questionnaires were administered during the pre-test and post-test (one year after the test) counselling sessions.

General anxiety

The STAI (Spielberger's State Trait Anxiety Inventory^{40, 41}) was used to measure the general anxiety (STAI trait) in the pre-test period and one year after the test.

Level of depression

We used the BDI (Beck Depression Inventory^{42, 43}) to assess the depression level of the person in the pre-test period and one year after the predictive test.

Ego strength

The ego strength scale of the MMPI (Minnesota Multiphasic Personality Inventory⁴⁴⁻⁴⁶) was used to assess ego strength in the pre-test period and one year after the test. Ego strength is conceptualised as the general capacity for personality integration. Subjects with high ego strength tend to have good coping strategies to deal with stress. For people with low ego strength, problems are likely to be long standing in nature because their coping resources are limited. High scorers on the ego strength scale are expected to respond better to psychotherapy than low scorers.

Data on the predictor variables were assessed during the counselling sessions before the test.

(1) THE TEST PARTICIPANT'S AGE AT THE PERCEIVED ONSET OF THE DISEASE IN THE PARENT (TAPO)

During the pre-test counselling, we asked the test participants about their earliest memory of problems in their affected parent. Some participants gave very vague indications ("there were problems", "there was something odd about my mother"), while some others had a clear memory of symptoms or situations (uncontrollable movements, disorganised housekeeping, frequent quarrelling between the parents). We then asked how old they were when they became aware of these problems for the first time (=TAPO). If the test participants answered that the parent had already had symptoms when they were born (n=5), the variable TAPO was given the value 0.

Table 1 Sociodemographic characteristics of the people who received a predictive test result more than one year ago

| | Carriers (n=29) | Non-carriers (n=40) |
|--------------------------------------|--------------------|------------------------|
| Sex | | |
| Men | 16 (55%) | 16 (40%) |
| Women | 13 (45%) | 24 (60%) |
| Age (mean (SD)) | 31.9 (8.0) | 33.7 (9.2) |
| Education | | |
| <High school | — | 3 (7.5%) |
| High school | 17 (58.6%) | 22 (55%) |
| >High school | 12 (41.4%) | 15 (37.5%) |
| Marital status | | |
| Stable relationship | 28 (96.6%) | 32 (80%) |
| Single | 1 (3.4%) | 8 (20%) |
| Children | | |
| No | 18 (62.1%) | 17 (42.5%) |
| Yes | 11 (37.9%) | 23 (57.5%) |
| Parental age at onset (mean (SD)) | 43.9 (8.0) | 43.5 (10.4) |

(2) SUBJECTIVE PROXIMITY OF THE ONSET OF HD (SP)

This variable was estimated by subtracting the test participant's age at the time of the test from the perceived age at onset of HD in the parent. Three test participants of respectively 40, 49, and 51 years of age had passed the critical age of onset (33, 32, and 30 years respectively) which resulted in a negative SP score. All three persons received a negative test result.

(3) RISK PERCEPTION (RP)

During the pre-test counselling sessions, it was clear that all the testees knew their genetic risk. The subjective perception of this risk was assessed by means of an open question. The answers were categorised as follows: thinking that one will be a non-carrier/probably a non-carrier/"accurate" perception/probably a carrier/a carrier. For the statistical analyses, the categories were labelled on an ordinal scale, varying from 1 (thinking that one will be a non-carrier) to 5 (thinking that one will be a carrier).

Statistical analyses

The four hypotheses were tested using correlation analyses (Pearson), *t* tests, analysis of variance (ANOVA) for categorical independent

variables, and multiple linear regression analyses (MR). Given the intercorrelations between the independent variables, MRs were also used to calculate the unique contribution of each variable to explain the variance in pre- and post-test psychological functioning. The type III SS (sum of square) of the MR are model order independent and give information about the unique contribution of each variable (each effect is adjusted for all other effects in the equation). The type I SS are dependent on the order in which the variables are entered in the equation; each effect is only adjusted for the preceding effects in the model. The coefficient of determination or R^2 is the proportion of the variance in the dependent variable that is accounted for by the independent variables of the equation; the larger the R^2 , the better the fit of the model with the data. R^2 is independent of the order in which the variables are entered. The F value with the associated significance probability reflects how well the model as a whole accounts for the dependent's variability.

With regard to post-test psychological adjustment, we first included the four proposed variables in the regression model. Secondly, we investigated whether the combination of these four variables with the pre-test psychometric tests significantly improved the proportion of explained variance of the post-test psychological adjustment. And thirdly, we added the test result to the equation.

Results

Table 1 presents some sociodemographic data for carriers and non-carriers. The differences between the groups were not statistically significant (chi-square and Kolmogorov-Smirnov test for independent samples and two tailed *t* test⁴⁷). Table 2 summarises the data for the dependent and the independent variables. The differences between carriers and non-carriers were not significant (chi-square and Kolmogorov-Smirnov test for independent samples and two tailed *t* test). The direct testing group did not significantly differ from the linkage group. The means of the pre- and post-

Table 2 Frequency distribution, mean scores, and standard deviations (SD) of predictor variables and of pre- and post-test psychometric tests

| | Carriers (n=29) | | Non-carriers (n=40) | |
|---|-----------------|-------------|---------------------|-------------|
| | Frequency (%) | Mean (SD) | Frequency (%) | Mean (SD) |
| Affected parent | | | | |
| Father | 15 (51.7%) | | 15 (37.5%) | |
| Mother | 14 (48.3%) | | 25 (62.5%) | |
| Participant's age at parental onset of HD | | 14.7 (8.0) | | 14.8 (11.0) |
| Subjective proximity of the onset | | 12.0 (7.4) | | 9.8 (12.0) |
| Risk perception | | 2.4 (0.9) | | 2.3 (0.9) |
| I think that I will be... | | | | |
| A carrier | 3 (10.3%) | | 9 (22.5%) | |
| Probably a carrier | 11 (37.9%) | | 10 (25.0%) | |
| "Accurate perception" | 9 (31.0%) | | 14 (35.0%) | |
| Probably not a carrier | 0 | | 3 (7.5%) | |
| Not a carrier | 1 (3.4%) | | 0 | |
| (Vague or evasive answer) | 5 (17.2%) | | 4 (10.0%) | |
| Pre-test | | | | |
| Ego strength (MMPI scale) | | 59.8 (7.9) | | 56.6 (11.9) |
| Anxiety (STAI-trait) | | 36.1 (7.3) | | 38.5 (11.1) |
| Depression (BDI) | | 3.8 (3.7) | | 6.4 (7.7) |
| Post-test (one year after the test) | | | | |
| Ego strength (MMPI scale) | | 60.4 (8.6) | | 57.3 (12.7) |
| Anxiety (STAI-trait) | | 35.3 (10.6) | | 35.6 (8.9) |
| Depression (BDI) | | 3.4 (3.9) | | 4.1 (6.5) |

Table 3 Intercorrelations (Pearson coefficients) of the predictor variables with the pre- and post-test psychological functioning

| | Sex of affected parent | Participant's age at parental onset | Subjective proximity of the onset | | Risk perception | |
|--------------------------------|------------------------|-------------------------------------|-----------------------------------|--------|-----------------|--------|
| Sex of affected parent | – | | | | | |
| Partic's age at parent's onset | –0.28* | – | | | | |
| Subjective proximity | –0.13 | 0.53*** | – | | | |
| Risk perception | –0.19 | –0.08 | –0.16 | | | |
| Pre-Ego S | –0.09 | 0.24* | 0.42*** | | –0.17 | |
| Pre-STAI | 0.03 | –0.25* | –0.41*** | | 0.14 | |
| Pre-BDI | 0.16 | –0.28* | –0.56*** | | 0.33* | |
| Post-Ego S | –0.02 | 0.08 | 0.26† | 0.14‡ | –0.18‡ | –0.21‡ |
| Post-STAI | 0.09 | –0.06 | –0.23† | –0.13‡ | 0.06† | 0.16‡ |
| Post-BDI | 0.02 | –0.12 | –0.32*† | –0.18‡ | 0.11† | 0.36*‡ |

*p<0.05. **p<0.01. ***p<0.001.

†Carriers.

‡Non carriers.

test ego strength, anxiety, and depression scores were in the normal range. Individual psychometric scores showed that the number of test applicants with at least a mild level of depression (BDI >10, corresponding with approximately the 80th centile in the general population)⁴³ was 11 (16%) in the pre-test period and 6 (9%) in the post-test period (one year after the test). The number of participants with a high score for anxiety (STAI trait >80th centile)⁴¹ was 8 (12%) in the pre-test period and 7 (10%) in the post-test period.

Table 3 displays the intercorrelations of the variables in this study (Pearson correlation coefficient). The correlations of the perceived proximity of the disease onset and of perceived risk with post-test psychometric scores were presented separately for carriers and non-carriers because different predictions were made for the two groups.

HYPOTHESIS 1

We found low but significant correlations between the test participant's age at parental onset of the disease (TAPO) and pre-test psychological functioning (table 3); only 5.8% of the variance of ego strength, 6.2% of the variance of anxiety, and 7.8% of the variance of depression level in the pre-test period was explained by the test participant's age at parental onset of HD. We found no significant correlations of TAPO with post-test psychological functioning. We specified in the first hypothesis that adult distress is most marked if the adverse condition starts in the early childhood of the test participant. To test this hypothesis, two groups of test participants were identified, those who were in early childhood when the disease started in their parent (TAPO ≤5) and those who were older at the parental onset of HD (TAPO >5). One tailed *t* tests were

conducted to compare the means on the psychometric tests for the two groups. The results are in line with the interaction hypothesis for pre-test psychological functioning (table 4), but not for post-test functioning.

HYPOTHESIS 2

The sex of the affected parent was not significantly associated with pre- and post-test psychological functioning in the test participant (table 3). To test the interaction hypothesis, an analysis of variance was performed with pre- and post-test ego strength, general anxiety, and depression level as dependent variables and with the child's age at parental onset of HD (TAPO), sex of the affected parent, and their product term as independent (categorical) variables (not in table). The variable TAPO was reduced to two levels (TAPO ≤5 and TAPO >5). The main effect of TAPO was significant (p<0.01) for pre-test functioning. The interaction effect of TAPO and the sex of the affected parent on psychological functioning was not statistically significant. Moreover, we investigated whether there was an interaction effect of the sex of the test participant with the sex of the affected parent, but this was not found in our data.

HYPOTHESIS 3

Table 3 shows that the subjective proximity of the disease onset (SP) is significantly correlated with pre-test level of anxiety (r=–0.41) and depression (r=–0.56). It is also significantly correlated with the carriers' post-test depression level (r=–0.32), but not with their anxiety level (r=–0.23, p=0.10). This means that carriers are more depressed when the onset of the disease comes closer. As expected, the correlation was not significant for non-carriers. To test the interaction between the subjective proximity and test result, we performed two hierarchical multiple regression analyses with post-test anxiety and depression as dependent variables and with subjective proximity, test result, and their product as independent variables. However, the interaction term was not significant. These results did not change after elimination of the three participants with a negative SP score. After adjustment for the test participant's age at the parental onset of the disease, the contribution of SP remained significant for pre-test anxiety (p<0.05) and

Table 4 Mean scores on the pre- and the post-test psychometric tests for the group with the Test participant's Age at the Parental Onset of HD (TAPO) ≤5 years versus TAPO >5 years and statistical significance of the differences between the two groups (one tailed *t* test)

| Tests | TAPO ≤5 years (n=16) Mean (SD) | TAPO >5 years (n=53) Mean (SD) | p value |
|-----------------|-----------------------------------|-----------------------------------|---------|
| Pre-test | | | |
| Ego strength | 51.9 (12.7) | 59.8 (9.1) | <0.01 |
| General anxiety | 42.2 (13.1) | 36.0 (7.9) | <0.05 |
| Depression | 9.4 (10.4) | 4.1 (4.0) | <0.05 |
| Post-test | | | |
| Ego strength | 55.4 (10.4) | 59.5 (11.4) | 0.10 |
| General anxiety | 37.7 (13.4) | 34.8 (8.1) | 0.21 |
| Depression | 5.3 (7.4) | 3.4 (4.9) | 0.17 |

Table 5 Multiple regression analyses with pre-test depression and anxiety as dependent variables and with perceived risk, subjective proximity to the disease, and their interaction as independent variables (n=60)

| Variables | Pre-test depression | | | Pre-test anxiety | | |
|---------------------------|---------------------|----------------|----------------|------------------|----------------|---------------|
| | F (type I SS) | R ² | F | F (type I SS) | R ² | F |
| Perceived risk (PR) | 12.53*** | | | 1.52 | | |
| Subjective proximity (SP) | 32.30*** | 0.38*** | F(2, 59)=17.78 | 11.73** | 0.17* | F(2, 59)=6.00 |
| PR × SP (interaction) | 15.85*** | 0.52*** | F(3, 59)=20.23 | 6.96* | 0.27** | F(3, 59)=6.74 |

*p<0.05. **p<0.01. ***p<0.001.

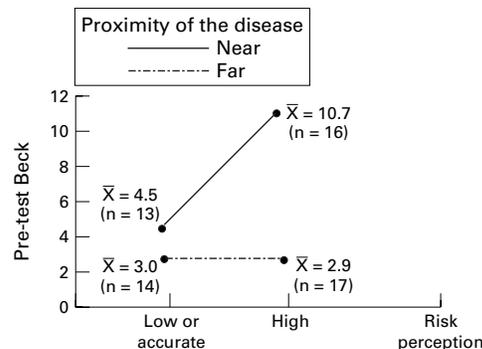


Figure 1 Interaction between risk perception and perceived proximity on depression.

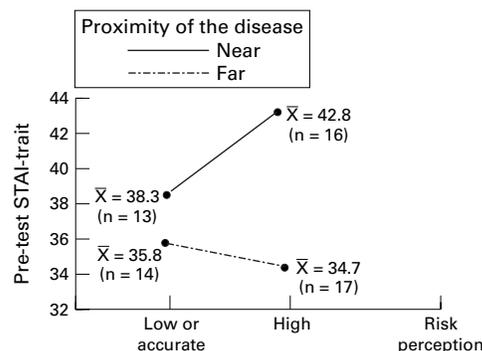


Figure 2 Interaction of risk perception and perceived proximity on anxiety.

depression (p<0.001) but not for post-test depression level in carriers (p>0.05) (not in table).

HYPOTHESIS 4

Table 3 shows that a higher perceived risk for HD in the pre-test period is positively correlated with higher pre-test depression (r=0.33, p<0.01), but not with a higher anxiety level (r=0.14, p>0.05). To test the interaction hypothesis, hierarchical multiple regression analyses were conducted, with the perceived risk, the subjective proximity of the disease, and their product as predictors. The results (table 5) show that the effects of the perceived risk (PR) and the subjective proximity (SP)

were both significant for pre-test depression. For pre-test anxiety, only the subjective proximity had a significant effect. In addition, there was a significant interaction effect of the perceived risk and the subjective proximity on pre-test depression and anxiety. The total variance explained (R²) increased from 0.38 to 0.52 for depression and from 0.17 to 0.27 for anxiety. The interactions remained significant after the elimination of the three participants with a negative proximity score.

In order to understand the nature of the interaction effects, we have illustrated them in figs 1 and 2. Therefore, categorical variables were introduced for PR and SP. For PR we made two categories, high risk perception and accurate or low risk perception. For SP the categories were based on the median SP score (near=smaller than the median SP score (mean SP score=1.9 years, SD=7.3, n=29) and far=larger than the median SP score (mean SP score=19.0, SD=4.1, n=31)).

To test the second part of the hypothesis, we performed hierarchical multiple regression analyses with post-test general anxiety and depression levels as dependent variables and with perceived risk, test result, and their product as independent variables (those with an “accurate” or a “vague” risk perception were not included in the analyses). We did not find a significant interaction effect of perceived risk and test result on post-test depression and anxiety.

The contribution of the combination of the four mentioned variables to predicting pre-test adjustment was investigated by means of multiple regression analyses (table 6). This resulted in an explained variance of 0.20 (F(4,59)=3.35, p<0.05) for pre-test ego strength, 0.41 (F(4,59)=9.54, p<0.001) for depression, and 0.18 (F(4,59)=3.08, p<0.05) for anxiety. The subjective proximity of the onset had a significant unique contribution to predicting the three post-test variables. The perceived risk also explained unique variance of pre-test depression level. Adding the interaction effect between perceived risk and perceived proximity of the disease, in a second step, contributed

Table 6 Multiple regression analyses with pre-test ego strength, depression, and anxiety as dependent variables and participant’s age at parental onset, subjective proximity, sex of the affected parent, and perceived risk as independent variables

| Pre-test | Ego strength | | | Depression | | | Anxiety | | |
|-------------------------------------|-----------------|----------------|---------------|-----------------|----------------|---------------|-----------------|----------------|--------------|
| | F (type III SS) | R ² | F | F (type III SS) | R ² | F | F (type III SS) | R ² | F |
| Participant’s age at parental onset | 0.25 | | | 0.04 | | | 0.54 | | |
| Subjective proximity (SP) | 5.53* | | | 17.46*** | | | 5.06* | | |
| Sex of the affected parent | 0.86 | | | 2.37 | | | 0.03 | | |
| Perceived risk (PR) | 1.31 | 0.20* | F(4, 59)=3.53 | 6.19* | 0.41*** | F(4,59)=9.54 | 0.59 | 0.18* | F(4,59)=3.08 |
| SP × PR | 6.17* | 0.29** | F(5, 59)=4.32 | 12.75*** | 0.52*** | F(5,59)=11.82 | 7.05* | 0.28** | F(5,59)=4.15 |

significantly to the explanation of the variance in pre-test ego strength, depression, and anxiety, resulting in $R^2=0.29$ ($F(5,59)=4.32$, $p<0.01$), $R^2=0.52$ ($F(5,59)=11.82$, $p<0.001$), and $R^2=0.28$ ($F(5,59)=4.15$, $p<0.01$).

With regard to post-test psychological functioning (one year after the test), none of the four selected variables had a significant value in the multiple regression equations. In the next step, the pre-test psychometric tests were added first in the regression equation, followed by the four variables mentioned. However, the results of the multiple regression analyses showed that none of the four variables explained unique variance of the post-test psychological measures, beyond that accounted for by the pre-test measures. The pre-test psychometric scores accounted for 54% of the variance of post-test ego strength ($F(1,59)=67.26$, $p<0.001$), 18% of the variance of post-test depression ($F(1,59)=12.62$, $p<0.001$), and 30% of the variance of post-test anxiety ($F(1,59)=25.26$, $p<0.001$). Adding the test result to the previous three models did not significantly improve the R^2 .

Discussion

The present paper aimed to delineate variables associated with pre-test distress of applicants for predictive testing for HD. Based on theoretical considerations, hypotheses were tested regarding the role of (1) the test participant's age at the (perceived) parental onset of HD, (2) the sex of the affected parent, (3) the perception of the risk for HD, and (4) the subjective proximity of the disease. We found low but significant Pearson correlations between the participant's age at the parental onset and pre-test psychometric measures of psychological functioning: the younger the test applicant was at the parental onset of HD, the more likely it was that this person had a lower ego strength, more anxiety, and a higher depression level in the pre-test period. However, this variable did not explain unique variance of pre-test psychological functioning, beyond that accounted for by the other variables in the model. Its effect may be indirect through its influence on subjective proximity of the disease. Moreover, a possible secondary effect of the young age of the proband at the parental onset of the disease may be the length of exposure to the illness in the parent during key developmental stages, particularly in early adolescence, when this would coincide with more severe illness in the parent.

The lack of a unique contribution of the participant's age at parental onset can also be rooted in the self-selection of the sample. As already stated in the introduction, publications on predictive testing for HD have shown that test participants are on average a self-selected group of mentally resourceful people. It cannot be excluded that persons who went through a very traumatic childhood owing to the parental disease do not ask for the test. For these people, having certainty that, one day, the disease in their parent will also happen to them may be unbearable.

Since it was very difficult, if not impossible, to collect reliable information about childhood experiences by means of retrospective reports during the pre-test counselling, we had insufficient data about the early negative experiences of the subject with the affected parent or with a disorganised family. It is plausible that early psychiatric symptoms in the parent are more traumatic for the young child than early cognitive impairment and uncontrollable movements. However, the possible effect of the interaction between the participant's age at the perceived parental onset of HD and the early negative experiences with the disease could not be taken into account in the study. A prospective, longitudinal study of HD families, including (future) test participants and non-participants, might shed more light on these questions.

We found no significant relation between the sex of the affected parent and the test participant's psychological adjustment. One explanation is that the effect of maternal disease in early childhood depends on the extent to which the father or a significant other person can replace the mother figure for the child. Overall, several protective factors in the child and in the environment may compensate for maternal mental illness, and parental mental illness in general, in early childhood. Good intelligence and good scholastic attainments exert a protective effect.²⁵ However, the most important protective factor proved to be the subject's social network; a supportive and understanding relationship in childhood and close personal relations in later life proved to reduce the effect of childhood stressors on later adult psychological functioning.^{23 48 49}

The expected association of the subjective proximity of the disease onset and pre-test depression and anxiety was confirmed; a closer perceived proximity of the onset of HD was uniquely associated with more depression and anxiety in the test participants and this relationship remained significant after adjustment for the participant's age at parental onset.

We hypothesised that test participants with predictive pessimism (high risk perception) in the pre-test period would be more anxious and depressed before the test than persons without predictive pessimism. This was confirmed for depression, but not for anxiety. Neither theoretical considerations nor the statistical method allowed the direction of the association between predictive pessimism and pre-test distress to be ascertained. Does a high risk perception cause depression or, conversely, does depression cause a pessimistic risk perception, or is their relationship reciprocal? Another possibility is that both depression and a pessimistic risk perception are the result of the influence of a third set of variables, including the high perceived severity of the disease⁵⁰ or the lack of perceived controllability⁵¹ or both.

The expected interaction effect of subjective proximity of HD and perceived risk on pre-test depression and anxiety was supported; persons with predictive pessimism were more anxious and depressed as the disease came closer than

persons with a more accurate risk perception or with predictive optimism. The mean pre-test depression score of test participants at risk for HD with a high perceived risk for HD who were quite close to the perceived onset of the disease reached a value of 10.7 which corresponds to at least a mild depression level; the variability within this group is however large (SD=9.9). The mean scores of the other three groups were significantly lower and remained at the level of the general population. Test participants at risk for HD who are close to the perceived onset of the disease and who have a pessimistic risk perception should be given special attention during pre-test counselling because of their possible negative affective condition at that time.

One year after the test, about 10% of the tested subjects, carriers as well as non-carriers, had at least a mild depression level or a high score for anxiety or both. Pre-test psychological measures were the best predictors of post-test distress, irrespective of the test result, as shown in previous research.^{5 15-18} In this study we included other variables, such as the participant's age at the parental onset of the disease, the sex of the affected parent, the perceived risk for HD, and the perceived proximity of the disease, but these did not significantly increase the explained variance of post-test functioning, beyond that accounted for by the pre-test psychometric scores. Contrary to Codori *et al*,⁵ who found that the perceived years to disease onset was a significant predictor of the post-test hopelessness of carriers (measured with Beck's Hopelessness Scale³²), we found no significant unique contribution of the subjective proximity of the disease onset to explain the level of anxiety and depression of carriers one year after the test. It is possible that the effect of the perceived proximity of the disease is reflected in more disease specific distress of carriers, such as intrusion/avoidance processes, rather than in more general anxiety and depression.⁵³ Another (associated) explanation is that some carriers use more minimisation and denial as coping mechanisms as the onset of the disease comes closer, which may result in an attenuation of the current level of general anxiety and depression scores.

The expectation that post-test symptoms of depression and anxiety would be higher in those who received a test result contrary to the expected outcome than in those whose result corresponded to their pre-test expectations was not supported by our data. The small number of persons with a low risk perception may have been an obstacle in this context; only four out of 60 participants thought that they were (probably) not a carrier of the HD gene. The hypothesis that, among carriers, those with a low pre-test perceived risk for HD would be more hopeless and depressed than test participants with high perceived risk had also been formulated by Codori *et al*,⁵ but was not confirmed by their data either.

The present study focused on the contribution of environmental influences (such as negative childhood experiences with an affected parent) and of aspects associated with the genetic

nature of the disease (such as perceived genetic risk and perceived proximity of the disease onset) to explain pre- and post-test distress. A large part of the variability in psychological distress remains unexplained. Other variables, such as the condition of affected sibs, the quality of the partner relationship, or the economic resources, may have a considerable impact on the well being of test applicants. The applicant's strategies to cope with a threatening situation can also influence pre- and post-test distress. During counselling, it is important to keep in mind that test participants use psychological defence mechanisms like optimistic thoughts or denial and minimisation to manage strong negative emotions.¹⁵⁻¹⁹ Although the role of social support and family systems has been considered very important in coping with threat,^{3 48 54} it has received little attention until now. Tibben¹⁵ reported that satisfaction with the perceived quality (rather than the number) of supportive other people was associated with low avoidance of HD related situations and with hopeful expectation about the future. Future longitudinal research should more directly investigate the role of negative childhood experiences owing to living in a family with a HD parent and the possible protective effect of social relationships, during childhood and also in later life, in explaining psychological well being. It is also important to address the question whether these aspects are associated with the uptake of predictive testing for HD and with the avoidance attitude and the feelings of hopelessness of non-participants.^{9 55 56} This research should enable clinical geneticists and mental health professionals to refine the pre- and post-test counselling strategies for predictive DNA testing, not only for HD, but also for other serious late onset diseases.

We thank the reviewer for his suggestions.

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