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Perceived stress in prodromal Huntington disease

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Abstract

This study examines perceived stress and its relationship to depressive symptoms, life changes and functional capacity in a large sample of individuals who are positive for the Huntington disease (HD) gene expansion but not yet diagnosed. Participants were classified by estimated proximity to HD diagnosis (far, mid, near) and compared with a non gene-expanded comparison group. Persons in the mid group had the highest stress scores. A significant interaction between age and time since HD genetic testing was also found. Secondary analyses using data from a different data collection point and including a diagnosed group showed the highest stress scores in the diagnosed group. Possible explanations and implications are discussed.

Keywords

Huntington disease; perceived stress; depression

Introduction

Huntington disease (HD) is a progressive neurological disease that leads to significant impairments in cognition, behavior and motor function as well as premature death (Walker, 2007). The disease is caused by a trinucleotide (CAG) repeat expansion on the huntingtin

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gene on chromosome 4 (Myers, 2004). Formal diagnosis is usually made when a person develops distinctive motor signs (Hogarth, 2003). People who test positive for the HD gene expansion but who show no manifest motor symptoms are considered to have prodromal HD, meaning that they will develop HD symptoms in the future, given a normal life span (Nance, Myers, Wexler, & Zanko, 2003). The average age of diagnosis is 40 (Walker, 2007). Therefore, people could live for over 20 years with the knowledge that they will develop HD. However, while aspects of the psychological effects of HD gene testing have been explored, little is known regarding the perception of daily stress by persons who have been identified as having the HD gene expansion.

The Perceived Stress Scale (PSS) was developed for use in health research to measure participants' perceptions of whether or not daily life is "unpredictable, uncontrollable and overloading" (Cohen & Williamson, 1988). Though the PSS has been used extensively in health research, we are not aware of any studies examining this measure in a prodromal HD population. In a study using the PSS in a small sample of participants with diagnosed HD, 85% endorsed stress, although mean PSS scores were not reported (McGarva, 2001). Perceived daily stress may be influenced by other factors, including depression, life experiences and functional and cognitive decline. The purpose of this study is to explore perceived daily stress in persons with prodromal HD and the relationships between perceived stress and other related factors.

Perceived stress may be influenced by depressive symptoms (Farabaugh et al., 2004; Ghorbani, Krauss, Watson, & LeBreton, 2008). Depression rates are high in manifest HD; indeed, in one study, over 40% of participants endorsed sad mood using the Unified Huntington's Disease Rating Scale (UHDRS; Paulsen et al., 2005). However, in general, persons with prodromal HD report less severe depressive symptoms than one might expect given they have a fatal degenerative disease. In a cross-sectional study, persons who tested positive for the HD gene expansion but were not yet diagnosed averaged scores on the Beck Depression Inventory-II (BDI-II; Beck, Steer, Ball, & Ranieri, 1996) indicative of minimal depressive symptoms, although their BDI-II scores were on average 4 points higher than for persons who tested negative; those who were diagnosed averaged scores indicative of mild depression (Lickleder, Wolff, & Barth, 2008). However, not stratifying a sample by proximity to diagnosis can obscure differences. For example, Julien et al. (2007) retrospectively classified participants by proximity to diagnosis after they were diagnosed and then reviewed psychological assessments conducted at the time of HD gene testing. Over 60% of persons less than one year from diagnosis met criteria for Major Depressive Disorder using the Composite International Diagnostic Interview, but only 5% of persons 6–9 years from diagnosis met criteria for Major Depressive Disorder, suggesting that examinations of psychiatric symptoms in this population should use a stratified approach.

Due to the complex relationship between depression and stress, it can be difficult to distinguish between them. The authors of the PSS address this issue by including positively-worded items that allow participants to endorse perceived control over stressors regardless of their perception of stress in order to differentiate the scale from measures of depression (Cohen & Williamson, 1988). An exploratory factor analysis of the PSS conducted by the scale authors revealed two factors—one comprised of the seven negatively-worded items and the second comprised of the seven positively-worded items. The authors labeled these factors "distress" and "control," respectively. In addition, the authors demonstrated that the PSS maintains predictive value even when depressive symptoms (as measured by the Center for Epidemiologic Studies Depression Scale) are partialled out in the prediction of physical illness symptoms. Thus, the PSS appears to measure a construct distinct from depressive symptoms.

Perceived daily stress may also be influenced by temporal factors. Several studies have indicated that persons who test positive for the HD gene expansion experience increased depression, anxiety and hopelessness immediately after testing, but these symptoms decline in the year following test results (Decruyenaere et al., 1996; Tibben, Timman, Bannink, & Duivenvoorden, 1997; Timman, Roos, Maat-Kievit, & Tibben, 2004). For some, psychiatric symptoms increased again 3+ years after testing (Timman et al., 2004) and were associated in one study with impending diagnosis (Gargiulo et al., 2009). Thus, time since HD genetic testing might also impact perceived stress in prodromal HD.

In addition to genetic testing, life events in general influence perceived stress. Pbert, Doefler and DeCosimo (1992) reported that PSS scores were positively correlated with negative perceptions of life changes using the Life Experiences Survey (Sarason, Johnson, & Siegel, 1978). The creators of the PSS also recognized the possible contribution of significant life events on the perception of stress (Cohen, Kermarck, & Mermelstein, 1983). Using a version of the Life Events Scale (which measures both number of events and perception of events as negative or positive), they found a small but significant correlation between PSS scores and number of significant life events in college students. In addition, the correlation between PSS scores and *perception* of events was higher, indicating that it is important to assess not only number of life events, but the perception of them as negative or positive.

Perceived stress may also be associated with decreased functional capacity. Although this relationship has not previously been explored, depression has been associated with decreased functional capacity in HD (Helder, Kaptein, van Kempen, van Houwelingen, & Roos, 2001; Ho, Gilbert, Mason, Goodman, & Barker, 2009), indicating a possible relationship between distress and functional capacity. Curiously, when functional capacity based on Total Functional Capacity Scale scores was stratified into five stages in a sample of persons with diagnosed HD, persons in stage two had the highest rates of depressive symptoms (sadness, low self-esteem and anxiety) using the UHDRS (Paulsen et al., 2005). Persons in stage two are beginning to show enough functional impairment that loss of employment and cessation of driving occur. The authors speculate that beyond stage two people may become acclimated to their disease and/or have impaired insight which might contribute to decreased negative appraisal of their condition. Cognitive functioning has also been found to be impaired in prodromal HD (Stout et al., 2007). It may be that cognitive changes contribute to perceived stress in prodromal HD if participants are aware of cognitive loss or if cognitive changes contribute to feelings of loss of control, unpredictability or overload.

Further exploration of the relationships between depression, life events, functional capacity and cognitive changes to perceived stress is important in order to anticipate issues and plan interventions to mitigate stress in persons with prodromal HD. The purpose of this study is to characterize perceived stress in prodromal HD by describing the relationship between perceived stress and depression, functional capacity, cognitive function and life events. The following hypotheses were tested: (1) perceived stress is higher in prodromal HD than in healthy comparisons; (2) perceived stress is related to proximity to diagnosis (i.e., perceived stress is lowest in HC and increases in each prodromal HD group as estimated time to diagnosis decreases); (3) perceived stress is positively correlated with depression and life changes, and negatively correlated with functional capacity and cognitive function; (4) there is an interaction between age and time since HD genetic testing in predicting PSS scores in persons with prodromal HD. Secondary analyses were conducted to further explore the relationships discovered in the primary analyses and allow for the inclusion of a group diagnosed with HD to explore whether patterns found in the primary analyses would remain the same.

Methods

Participants

Participants included 1020 individuals enrolled in the PREDICT-HD study. PREDICT-HD is a multi-site longitudinal study designed to identify and track markers of HD prior to diagnosis (Paulsen et al., 2006). Individuals in PREDICT-HD have independently undergone genetic testing prior to and separate from their participation in PREDICT-HD. Individuals with the CAG repeat expansion (CAG ≥ 36) serve as cases. Those at risk for HD who test negative for the gene expansion (CAG < 36) are invited to participate as healthy comparisons (HC). All participants were ≥ 18 years of age. Exclusion criteria include: unstable medical or psychiatric illness, use of an antipsychotic medication in the past 6 months, CNS disorder, active substance abuse and/or history of significant head trauma.

Prodromal HD participants included 508 females (64%) and 290 males (36%) (total = 798). HC participants included 143 females (64%) and 79 males (36%) (total = 222). Prodromal HD participants were subdivided by estimated proximity to HD diagnosis based on current age and CAG repeat number: far (>15 years; $n = 309$), mid (9–15 years; $n = 295$), and near (<9 years; $n = 194$) (Langbehn, Brinkman, Falush, Paulsen, & Hayden, 2004). Recent studies indicate subtle changes in cognitive, behavioral and motor function occur several years prior to HD diagnosis (Biglan et al., 2009; Duff et al., 2010; Marshall et al., 2007; Paulsen et al., 2008); therefore, stratification allows for the detection of subtle differences that might not be detectable if prodromal HD participants are combined in a single group. There were 222 HC subjects. Complete data were available for 753 prodromal HD participants in the analysis testing the relationships between age and time since HD genetic testing and PSS scores in prodromal HD participants.

In secondary analyses (described below), participants were persons completing measures at Visit 3 in their annual PREDICT-HD study participation. Therefore, all of the participants included in this analysis were represented in the baseline analysis; however, their diagnostic category might have changed. At this sampling point, there were 145 in the HC group, 189 in the far group, 198 in the mid group, 171 in the near group and 60 in the group who had been diagnosed with HD since their baseline visit. A diagnosis of HD was made based on receiving a motor score of 4 on the UHDRS (Huntington Study Group, 1996).

Procedures

This study was approved by The University of Iowa Institutional Review Board, as well as by the Institutional Review Boards at each site where participants were recruited. All aspects of the study are in compliance with national legislation and the Declaration of Helsinki. Written informed consent was obtained from all participants prior to participation for both participation and to allow de-identified research data to be sent to collaborative institutions for analysis. The data reported represent measures collected during in-person baseline visits; secondary analyses data are from Visit 3.

Measures

Demographic variables—Age, gender and years of education were assessed via self report on a demographic form at each visit. In addition, on their initial visit, PREDICT-HD participants report the date they underwent HD genetic testing.

Perceived stress—The Perceived Stress Scale (PSS; Cohen et al., 1983) is a 14-item, self-rated measure of perceived global stress designed to assess participants' perceptions of the predictability, manageability and controllability (e.g., "How often have you felt that you were unable to control the important things in your life?") of their daily lives over the past

month. Participants rate each item on a 5-point scale according to its frequency of occurrence, from “never” to “very often.” A higher total score indicates greater perceived stress. Total scores range from 0–56.

Life changes and perception of life changes—The Life Experiences Survey (LES; Sarason et al., 1978) assesses both number of life changes in the past 12 months (LES Count), as well as the perception of these changes as positive or negative (LES Sum). The LES includes 48 life events and three blanks to write in events not listed. Items include major and minor life events related to work, relationships, family, social life and health. LES Sum is calculated using a 7-point Likert-type scale ranging from “extremely negative” (–3) to “extremely positive” (+3). The version of the LES included in this study was modified with permission from the authors to include a place to indicate whether any deaths of family members were related to HD or whether participants were providing care for an HD-affected family member.

Depression—The Beck Depression Inventory (BDI-II) is a widely-used, 21-item self-rated measure of mood, cognitive, motivational and somatic symptoms of depression in the past 2 weeks (Beck et al., 1996). Each item is rated on a scale of 0–3 (total range 0–63), with higher scores indicating more severe depressive symptoms.

Functional capacity—Global functional capacity was measured using the Total Functional Capacity (TFC) scale (Shoulson & Fahn, 1979). The TFC is a 5-item scale scored following a brief interview. Assessed items include ability to function at work and at home, manage finances, and perform other activities of daily living. Scores range from 0–13, with higher scores indicating greater functional capacity. The TFC is frequently used as an outcome measure in HD clinical trials (Beglinger, Adams, et al., 2008; Landwehrmeyer et al., 2007).

Cognitive functioning—Cognitive functioning was evaluated using the Symbol Digit Modalities Test (SDMT; Smith, 1982). The SDMT assesses psychomotor speed and working memory. Participants have 90 seconds to match digits 1 through 9 with unique symbols (e.g., × and =) by writing the digits beneath the symbols presented on a page. The SDMT has been shown to be sensitive to impaired executive function in persons with prodromal HD, especially as they approach diagnosis (Brandt, Shpritz, Codori, Margolis, & Rosenblatt, 2002; Stout et al., 2007).

Data analyses

Means and standard deviations were calculated for demographic variables (age, education and time since HD genetic testing) and measures of interest (PSS, LES Count, LES Sum, BDI-II, TFC, SDMT). Primary data analyses included a one-way ANCOVA to test the contribution of group membership based on estimated proximity to diagnosis or healthy comparison (HC) status to PSS scores. Because age and education have been shown to be negatively correlated with PSS scores, and females have been shown to score higher than males on the PSS (Croghan et al., 2006; Farabaugh et al., 2004; Simpson et al., 2008; Stawski, Sliwinski, Almeida, & Smyth, 2008), these variables were included in the model as control variables. *F* statistics and probabilities were calculated to test for the significance of the contribution of each variable to PSS scores. Effect sizes are reported using η^2 . Planned comparisons of adjusted least square means using *t*-tests were used to examine group differences found on the PSS. Effect sizes were calculated using Cohen's *d*. Pearson correlation coefficients were used to test relationships between the PSS and BDI-II, LES Count, LES sum and TFC. An exploratory principal components analysis (PCA) was conducted on the PSS (with varimax rotation) in order to identify the factor structure in this

sample. Individual PSS items were examined for stressors that might be most problematic for persons with prodromal HD in order to develop appropriate interventions.

A one-way ANOVA using just the prodromal HD participants (without the HC) was conducted to test the contributions of cognitive function and time since HD genetic testing on PSS scores while controlling for age, gender and education. Interaction between age and time since HD genetic testing was also included in the model. F statistics and probabilities were calculated to test for the significance of the contribution of each variable to PSS scores. Effect sizes are reported using η^2 .

Secondary analyses, using Visit 3 data as described previously, were conducted in order to address questions raised by the results of the primary analyses, specifically, whether the same relationships would hold between measures collected at a different data collection point and if a diagnosed group were included. Age, gender and education were again controlled for in the ANCOVA model and planned comparisons of adjusted least square means were used to examine group differences on the PSS. Effect sizes were calculated using Cohen's d .

Results

Preliminary data analyses

Descriptive data analyses are shown in Table 1. There were more females (64%) than males in the sample, but gender difference was not significant between HC, far, mid, and near groups ($X^2 = 4.34$; $p = 0.22$). Mean age between groups differed significantly ($F_{3,1016} = 37.21$; $p < 0.001$). Within the prodromal HD group, the near group was the oldest ($M = 44.9$), the mid group was slightly younger ($M = 42.2$) and the far group was the youngest ($M = 36.7$). The only group that was significantly different in age from the HC group was the far group, who were significantly younger ($t = 8.24$, $p < 0.001$). Demographic data and means and SD for PSS, BDI-II, LES count, LES sum, TFC and time since HD genetic testing are presented in Table 1.

The average time since genetic testing in our sample was 4.1 years. The far group had undergone HD genetic testing more recently ($M = 3.26$, $SD = 3.03$) than the HC or other prodromal HD groups and was the only group that differed significantly from the others with regard to time since HD diagnosis.

Primary data analyses

In the one-way ANCOVA analysis group member status predicted PSS scores ($F = 7.15$; $p < 0.001$; $\eta^2 = 0.021$), along with age ($F = 22.23$, $p < 0.001$, $\eta^2 = 0.022$), gender ($F = 10.24$, $p < 0.001$, $\eta^2 = 0.010$) and education ($F = 14.15$, $p < 0.001$, $\eta^2 = 0.014$) (model adjusted $R^2 = 0.066$, $F_{6,1011} = 12.98$, $p < 0.001$). The first hypothesis (perceived stress is higher in persons with the HD gene expansion than in persons who tested negative) was partially supported. Persons in the mid group (9–15 years) had higher PSS scores ($M = 21.33$, $SD = 8.45$) than persons in the HC group ($M = 18.41$, $SD = 6.51$, $p < 0.001$; $t = 3.92$, $d = 0.45$). No other prodromal HD group PSS scores were significantly different from HC. In the prodromal HD participants as a group, females scored higher on the PSS ($M = 20.83$, $SD = 8.28$) than males ($M = 18.95$, $SD = 7.79$; $t = 3.15$, $p < 0.002$). Age also predicted PSS scores in the regression model, with older age associated with lower PSS scores. Greater years of education were also associated with lower PSS scores. However, even after accounting for gender, age and education in the regression model, group member status was retained as a significant predictor of PSS scores.

The second hypothesis (perceived stress is related to proximity to diagnosis) was not supported. PSS scores were highest in the mid group, and the only significant differences between groups were between the mid group and the other groups. The third hypothesis (perceived stress is positively correlated with depressive symptoms and life changes, and negatively correlated with functional capacity) was partially supported. In the sample as a whole, the PSS was significantly correlated with the BDI-II ($r = 0.71$; $p < 0.001$). The correlation between PSS and LES Count for the entire sample was $r = 0.28$ ($p < 0.001$). The only significant difference in number of life experiences in this sample was between the mid ($M = 6.33$, $SD = 4.64$) and near ($M = 5.17$, $SD = 4.32$) groups ($t = -2.71$, $d = -0.24$). The correlation between PSS and LES Sum for the entire sample was $r = -0.34$ ($p < 0.001$). LES Sum was lower in all prodromal HD groups than in the HC group (all $p < 0.05$; d ranged from -0.43 to -0.28). Thus, although number of life experiences was greater only in the mid group when compared with the near group, more participants in the prodromal HD groups reported negative perception of life experiences than in the HC group. As expected, PSS was negatively correlated with TFC in this sample ($r = -0.25$, $p < 0.001$): as function declined, perceived stress increased. The relationship between PSS and TFC was not significant in the HC group ($r = -0.12$). It is important to point out that TFC scores did not differ significantly between groups, with all groups indicating high functional levels on the scale.

The results of the PCA indicated a two-factor structure in this sample, replicating Cohen and Williamson's (1988) findings of positively-worded items loading on one factor and negatively-worded items loading on the second factor. Most individual items on the PSS were scored as 2 or lower by participants in all prodromal HD groups, indicating most items were not problematic for them. Items in which more than 10% of prodromal HD participants marked a 3 or 4 when fewer than 10% of HC marked 3 or 4 included how often they: felt upset when something happened unexpectedly; felt they were unable to control the important things in life; could not cope with all the things they had to do; were angered because of things that happened they couldn't control. On all these items, the mid group scored higher than the far or near groups. In the prodromal HD groups, women were more likely to endorse negatively-worded items on the PSS than men ($t = 5.77$, $p < 0.001$). There was no statistical difference between men and women in the prodromal HD groups for endorsement of positively-worded items.

The results of the ANOVA involving all prodromal HD participants indicated that gender ($F = 8.36$, $p = 0.004$, $\eta^2 = 0.011$), years of education ($F = 5.14$, $p = 0.02$, $\eta^2 = 0.007$), age ($F = 29.66$, $p < 0.001$, $\eta^2 = 0.038$) and SDMT performance ($F = 16.48$, $p < 0.001$, $\eta^2 = 0.022$) contributed to PSS scores. The main effect for time since HD genetic testing was not significant. However, the age and time-since-HD-genetic-testing interaction was significant ($F = 4.60$, $p < 0.05$). In general, persons under age 34 indicated more stress as time since HD genetic testing increased and persons over 34 indicated less stress as time since HD genetic testing increased (see Figure 1).

However, it should be noted that in the under 34 group, PSS scores did not differ by more than 1 point between times since HD genetic testing and the effect size for the age. Also, age and time-since-HD-genetic-testing interaction was very small ($\eta^2 = 0.006$).

Secondary analyses

Secondary data analyses were conducted to test whether the pattern found in the primary analysis (mid group has highest PSS scores) would be reproduced in data collected at a different time point (Visit 3). A diagnosed group was included to explore whether PSS scores remained lower than the mid group after diagnosis. ANCOVA of Visit 3 data show PSS scores were again associated with age, years of education and group membership (model $F = 7.48$, $p < 0.001$). The mid group again had the highest mean PSS scores of the

prodromal HD groups, although the difference between the mid group ($M = 20.37$; $SD = 8.07$) and the near group ($M = 19.82$; $SD = 8.46$) was not statistically significant at Visit 3. The diagnosed group had the highest PSS mean ($M = 21.63$, $SD = 8.91$). While the PSS score was significantly higher in the diagnosed group than the far group ($M = 18.68$, $SD = 7.61$) and the HC group ($M = 17.63$, $SD = 6.12$) was significant ($t = 2.94$, $d = 0.44$, $t = 3.03$, $d = 0.50$, respectively), it was not significantly different from either the mid group or near group. There were no gender differences in PSS scores between men and women in the Visit 3 sample.

Discussion

PSS scores in this study were lower than expected and comparable to Cohen and Williamson's (1988) normative sample of 2376 randomly selected US residents ($M = 19.62$; $SD = 7.49$). PSS scores in our sample were lower than those reported by persons with other chronic health conditions including rheumatoid arthritis ($M = 26.16$, $SD = 8.07$) (Treharne, Lyons, Booth, & Kitas, 2007) and HIV ($M = 24.5$, $SD = 7.4$) (Weaver et al., 2004) and similar to those reported by patients with newly diagnosed atrial fibrillation ($M = 19.3$, $SD = 8.2$) (Lane, Langman, Lip, & Nouwen, 2009). Comparison across health conditions is difficult because each condition is unique. Nevertheless, given the severity of HD, it is surprising that PSS scores were relatively low. On the other hand, prodromal participants in our study were not significantly impaired, as indicated by TFC scores, which might account for the lower than expected PSS scores.

The finding that the mid group scored higher than other prodromal HD groups was unexpected, though the phenomenon of more significant psychiatric burden in the mid group has been demonstrated previously by our group (Beglinger, Paulsen, et al., 2008). Furthermore, the relationships of PSS to BDI-II, LES Count, LES Sum and TFC were in the expected directions, though notably, persons in the mid group scored higher on these measures than persons in other groups. The period of time that constitutes the mid group—9 to 15 years to HD diagnosis—may be the time when ambiguous changes are first evident (Paulsen, 2010), which may contribute to increased distress in this group. Persons in the near group (<9 years to diagnosis) may have had more time to adjust to changes and may receive increased social support, which in turn, may contribute to lower perceived stress. Further exploration using an illness model may provide insight into this phenomenon. Rolland and William's (2005) Family System Genetic Illness model, for example, provides a useful framework for exploring the impact of genetic conditions at various stages of presymptomatic and symptomatic disease, taking into account family life-cycles and development. While the mean age of persons in the mid group (42.2) was similar to that of the near group (44.8), the age and time since HD genetic testing interaction provides a novel way to explore how developmental issues may impact perceived stress in this population. This interaction appeared to be driven by the finding that for persons older than 34, PSS scores were lower as time since genetic testing increased.

From a developmental perspective, persons under age 34 are making decisions regarding career, marriage, and childbearing, while older participants likely have already made these decisions. In addition, persons over 34 may have made these decisions without knowledge of their HD gene status since the direct mutation test for the huntingtin gene was not available until 1993, representing a cohort effect. While linkage analysis was available earlier, it was not definitive and was more complicated because it depended on the participation of different generations of affected individuals.

Another possible explanation for the finding that persons in the mid group endorsed greater distress than other prodromal HD groups in the primary analysis is the potential for impaired

insight and/or apathy in persons who are near HD diagnosis. There is evidence that persons with diagnosed HD have impaired insight and apathy (Duff et al., 2010; Hoth et al., 2007). This may be another explanation for lower than expected endorsement of distress in persons in the near group.

In addition to the possibility of impaired insight, our findings of highest PSS scores in the mid group support the possibility raised by Beglinger, Paulsen, et al. (2008) that neuroanatomical changes produce varying psychiatric manifestations at different points in prodromal HD. However, our finding that PSS scores increased in the diagnosed group indicate that either progressively impaired insight does not explain the decrease in PSS scores in the near group, or that perceived stress does not follow a linear pattern in HD. Furthermore, the changes that accompany HD diagnosis may be more difficult to ignore even if insight is impaired.

Women with prodromal HD in our Visit 1 sample scored higher on the PSS than men, which is consistent with prior literature that indicates women typically score higher than men on the PSS in a variety of samples. This gender difference was seen only in the negatively-worded, or “distress” items, identified by the factor analysis. Gender differences were not significant in the Visit 3 sample. For all Visit 1 participants, scores were higher in the entire sample on the “distress” items than on the positively-worded “control” items, indicating that while participants may more readily endorse distress, they did not endorse lack of control at the same level.

A possible explanation for the lower than expected PSS scores found in the present study is that participants in this study might not be representative of most people at risk for HD and only represent people who have sought HD genetic testing and volunteer to participate in HD-related research. In addition, PREDICT-HD participants attend annual visits to a PREDICT-HD site which are separate from their regular medical visits. The interactions with HD researchers might provide them with an opportunity to engage with healthcare professionals in a way that other persons from HD-affected families do not. Recent data indicate persons who participate in HD-related research perceive benefits to research participation, including feeling as though they are contributing toward finding a cure and being an advocate for persons with HD (Williams et al., 2010). In addition, there is evidence that persons who undergo genetic testing self-select based on their perceived ability to cope well with the results (Codori & Brandt, 1994) and are less pessimistic and depressed (van der Steenstraten, Tibben, Roos, van de Kamp, & Niermeijer, 1994) than those who decide not to undergo testing. Another author suggests that the rigors of testing protocols and pre-test counseling screen out persons at risk for HD who are more psychologically vulnerable (Meiser & Dunn, 2001).

While participants in this study may not represent most persons at risk for HD, healthcare providers should not assume that persons with prodromal HD are not distressed based on the findings presented here, especially considering the high rates of depression in diagnosed HD. In addition to the possibility that our sample is not representative of most persons at risk for HD, the PSS might not adequately capture the type of stress experienced by persons with prodromal HD. To our knowledge, this is the first time perceived daily stress has been evaluated in relationship to estimated proximity to HD diagnosis. Healthcare providers should be alert for signs of distress in persons who are beginning to notice subtle changes in function. Younger persons and particularly younger women at risk for HD may experience higher rates of stress. Interventions aimed at mitigating stress in this population include counseling to make family planning and career decisions, and family interventions to decrease perceived overload and unpredictability and increase perception of control over stressors.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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The authors report no conflicts of interest.

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Figure 1.
Relationship of age and time since genetic testing

Table 1

Visit 1 data

Variable	Comparison (<i>n</i> = 222)	Far (<i>n</i> = 309)	Mid (<i>n</i> = 295)	Near (<i>n</i> = 194)
Age (M)	43.9	36.8	42.2	44.8
Female	143 (64%)	213 (68%)	187 (63%)	117 (59%)
Male	77 (36%)	100 (32%)	111 (37%)	81 (41%)
Education (mean years)	14.67	14.48	14.33	14.05
PSS M (SD)	18.41(6.51) _a	20.10 (7.92) _a	21.33 (8.45) _b	18.42 (7.73) _a
BDI-II M (SD)	4.47 (5.22)	7.75 (8.4)	9.42 (9.53)	6.71 (8.13)
TFC M (SD)	12.98 (0.13)	12.86 (0.52)	12.8 (0.72)	12.76 (0.79)
LES count M (SD)	5.9 (4.23)	6.45 (4.64)	6.33 (4.64)	5.17 (4.32)
LES sum M (SD)	0.64 (7.65)	−0.88 (9.74)	−2.91 (9.62)	−1.78 (9.63)
Time since HD genetic testing	4.67 (4.66)	3.26 (3.03)	4.22 (3.80)	4.74 (4.25)

Note: Means with different subscripts (a,b) are significantly different in follow-up *t* tests.