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Positive Affect and Well-Being in Huntington's Disease Moderates the Association Between Functional Impairment and HRQOL Outcomes

Rebecca E. Ready^a, Nicholas R. Boileau^b, Stacey K. Barton^c, Jin-Shei Lai^d, Michael K. McCormack^{e,f}, David Cella^d, Nora E. Fritz^g, Jane S. Paulsen^h, Noelle E. Carlozzi^{b,*}

^aDepartment of Psychological and Brain Sciences, University of Massachusetts, Amherst, MA, USA

^bDepartment of Physical Medicine and Rehabilitation, University of Michigan, Ann Arbor, MI, USA

^cDepartment of Neurology, Washington University School of Medicine, St. Louis, MO, USA

^dDepartment of Medical Social Sciences, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

^eDepartment of Psychiatry, Rutgers-Robert Wood Johnson Medical School, Piscataway, NJ, USA

^fDepartment of Pathology, Rowan-SOM, Stratford, NJ

^gPhysical Therapy Program, Wayne State University, Detroit, MI, USA

^hDepartments of Neurology, Psychiatry, and Psychological and Brain Sciences, University of Iowa, Iowa City, IA, USA

Abstract

Background: Positive affect is associated with resiliency and beneficial health outcomes, but little is known about associations between positive affect and health-related quality of life (HRQOL) in Huntington's disease (HD).

Objective: This longitudinal study determined the association between positive affect and several HRQOL outcomes in persons with HD. Functional status was examined as a moderator of the association between positive affect and HRQOL.

Methods: Participants, with premanifest (i.e., genetically at risk but no clinical diagnosis, $n = 50$) and manifest HD (early-stage $n = 171$; late-stage $n = 101$), completed a measure of positive affect

*Correspondence to: Noelle E. Carlozzi, PhD, University of Michigan, Department of Physical Medicine and Rehabilitation, North Campus Research Complex, 2800 Plymouth Road, Building NCRC B14, Room G216, Ann Arbor, MI 48109-2800, USA. Tel.: +1 734 763 8917; Fax: +1 734 763 7186; carlozzi@med.umich.edu.

CONFLICT OF INTEREST

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and well-being and several HRQOL measures at baseline, 12-, and 24-month follow-ups. UHDRS Functional Assessment scale indicated functional status.

Results: Positive affect was associated with better HRQOL for persons with premanifest and manifest HD over the 24-month time frame. These associations were moderated by functional status. For persons with higher functional status, positive affect was associated with better HRQOL, including less depression, lower anxiety, less anger, better social role satisfaction, better executive functions, greater upper extremity function, less dyscontrol, and less concern with death and dying. For persons with lower functional status, positive affect was not associated with HRQOL.

Conclusions: Positive affect predicted better self-reported HRQOL over a 24-month period in persons with premanifest and manifest HD, particularly when participants had better functional status. Interventions to enhance positive affect in HD may have beneficial effects on HRQOL.

Keywords

Quality of life; positive affect; functional assessment; Huntington's disease; longitudinal

INTRODUCTION

Positive affect is defined by pleasant feelings, such as happiness, contentment, and interest [1, 2]. Positive affect is associated with resiliency and beneficial health outcomes [3]. Greater positive affect predicts viral suppression in women with HIV [4], lower risk for the common cold [5], decreased stroke incidence in older adults [6], and lower risk of mortality [7, 8]. Frederickson's broaden-and-build theory of positive emotions suggests that positive affect achieves these beneficial outcomes via two pathways: 1) serving to buffer the harmful effects of stress, and 2) promoting the accumulation and availability of psychosocial resources that foster healthy behaviors [9].

Positive affect might be an area of preserved function in some persons with Huntington's disease (HD) and could serve as a psychological resource and/or a target for therapeutic intervention. The benefits of positive affect in persons with HD, however, are not known. Greater attention to positive affect is warranted because HD is a progressive, debilitating, and ultimately fatal genetic disorder with onset in midlife [10]. Age of symptom onset is partially determined by genetic factors, but also likely influenced by environmental, emotional, and/or behavioral factors [11]. HD is characterized by a triad of psychiatric, motor, and cognitive symptoms that—cumulatively and over time—have profound and detrimental impacts on daily functioning. Indeed, in online support groups, persons with HD and those in their social networks report considerable stress and anxiety [12]. Neuropsychiatric features characterized by depressive symptoms, apathy, and irritability are common at all stages of the HD disease continuum, from premanifest (i.e., genetically at risk but showing no or only mild symptoms) through late stage HD [13, 14].

Positive affect and health outcomes

Positive affect is associated with indicators of good health, as well as adaptive coping with adverse conditions [15, 16]. However, the links between positive affect and health outcomes

can be complex. In a prospective study of women with HIV, high positive affect was associated with a greater likelihood of undetectable viral load at follow-up [4]. The association between positive affect and reduced viral load, however, diminished in the context of stress. That is, the benefits of positive affect were limited by the presence of a negative affect state.

In HD, a greater understanding of positive affect and its associations with health-related quality of life (HRQOL) outcomes (i.e., mental, physical and social well-being [17]) could be useful in maximizing HRQOL and quality living. If positive affect, in the context of participants with different disease burden, is associated with better HRQOL, there may be a number of ways to preserve or enhance HRQOL in HD by increasing positive affect. For example, evidence-based interventions to strengthen positive affect (e.g., acceptance-based therapies, meditation, positive affect skill intervention [18-21]) might be useful for persons with HD to promote better HRQOL.

The current study

In the current longitudinal study, positive affect and a number of dimensions of HRQOL were measured in persons with HD over a 24-month period. Participants ranged from premanifest to late-stage HD. Disease severity was indicated by functional impairment, which is a good marker of HD severity and is associated with poorer HRQOL in other neurodegenerative diseases [22, 23]. The primary aims were to determine (1) if positive affect was associated with HRQOL in HD [24] and (2) if these associations were moderated by functional status (Fig. 1).

MATERIALS AND METHODS

Participants

Data for the current analyses included a subset of participants from the HDQLIFE study [25]; participants were included in this study if they had a Unified Huntington Disease Rating Scale (UHDRS) Functional Assessment (FA) score. The HDQLIFE study aimed to examine HRQOL across three time points (baseline, 12-, and 24-months). Recruitment included established HD clinics, existing research HD research studies, HD support groups, HD specialized nursing home units, the National Research Roster for Huntington's Disease, online medical record data capture systems [26], and articles/advertisements in HD-specific newsletters and websites. To be eligible for the study, participants were required to have a positive gene mutation test and/or a clinical diagnosis of HD [25], be at least 18 years of age, and able to read and comprehend English, and be capable of providing written informed consent. Informed consent was obtained from all individual participants included in the study. The study was approved by the Institutional Review Boards at all participating institutions. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Self-reported health-related quality of life measures

Several HRQOL measures from the Patient Reported Outcomes Measurement Information System (PROMIS; [27]) and the Quality of Life in Neurological Disorders (Neuro-QoL; [28]) were administered as part of the larger study protocol [25]. This included the PROMIS measures of Depression, Anxiety and Anger, and the Neuro-QoL measures of Positive Affect and Well-being (PAW), Satisfaction with the Ability to Participate in Social Roles and Activities (Satisfaction with Roles and Activities), Ability to Participate in Social Roles and Activities (Participate in Roles and Activities), Upper Extremity Function, Lower Extremity Function, Stigma, Emotional/Behavioral Dyscontrol, and Applied Cognition-Executive Function. All PROMIS and Neuro-QoL measures are reported on a T-score metric with a mean of 50 (SD = 10) where higher scores indicate more of that domain being measured (i.e., higher Stigma scores indicate more stigma, higher PAW scores mean more positive affect and well-being).

In addition, several HD-specific HRQOL measures were administered from the Huntington Disease Quality of Life (HDQLIFE) measurement system [25, 29, 30]. Specifically, we administered HDQLIFE Chorea, Speech Difficulties, Swallowing Difficulties, Concern with Death and Dying, and Meaning and Purpose. Again, these measures are scored on a T-score metric with a mean of 50 (SD = 10), with higher scores indicating more of that domain being measured (i.e., higher Meaning and Purpose scores indicate better sense of purpose).

Clinician-administered measure of functioning

The UHDRS is a clinician-rated tool used to measure motor functioning, cognition, overall functioning, and independence [31]. For the purposes of analyzing the interaction between PAW and functional status on health-related life quality, the UHDRS FA scale was used to measure functional status. The FA scale is a 25-item clinician rated measure of participant's ability to perform daily activities (e.g., dressing themselves, operating a motor vehicle, managing finances without help). Higher scores reflect better capabilities.

The UHDRS Motor Scale evaluates multiple aspects of motor abnormality and requires the rater to indicate their overall level of confidence for whether or not the participant has unequivocal signs of HD; participants with a confidence rating of 99% were required for inclusion in the manifest HD group.

The Total Functional Capacity (TFC), which assesses a participant's ability to work, manage finances, do chores, live independently, and perform activities of daily living, was used to determine *HD stage* for those with manifest HD. TFC scores range from 0 to 13, with higher scores indicating better ability. For manifest participants, early-stage was defined as TFC scores of 7–13 and late-stage was defined as TFC scores of 0–6 [32].

Statistical analyses

Analyses for the current study were conducted using SAS 9.4. A one-way analysis of variance (ANOVA) was used to assess whether our three staging groups differed in levels of PAW at baseline. In addition, Pearson correlations were calculated at baseline to determine the association between PAW and HRQOL outcome measures (PROMIS Depression,

Anxiety, and Anger; Neuro-QoL Satisfaction with Roles and Activities, Ability to Participate in Roles and Activities, Upper Extremity Function, Lower Extremity Function, Stigma, Emotional/Behavioral Dyscontrol, and Executive Function; HDQLIFE Chorea, Speech Difficulties, Swallowing Difficulties, Concern with Death and Dying, and Meaning and Purpose). Next, fifteen linear mixed models (LMM) with time points nested within each participant were used to determine if FA moderated the association between PAW and the HRQOL outcomes over time. Each LMM was conducted using restricted maximum likelihood (REML) estimation method with a compound symmetry covariance structure and Kenward-Roger degrees of freedom method. Each model contained two main fixed effects, PAW and FA, and an interaction term between them, to examine the significance of the slope change between the two continuous variables. Simple (conditional) slope estimates were tested for significance at varying levels of FA to determine at which point the slope of PAW became insignificant [33]. In addition, each LMM included time as a covariate and controlled for disease stage, gender and race. The maximum likelihood method allows for participants with missing assessments to be utilized to determine means for a single time-point. Since change over time was not the primary focus of the current study, participants were included in the analyses so long as they had complete baseline data. Type III partial eta-squared (η^2) effect sizes were calculated to estimate the amount of variance accounted for by the predictor variables; effect sizes for η^2 are classified as small ($\eta^2 = 0.01$), moderate ($\eta^2 = 0.06$), and large ($\eta^2 = 0.14$) [34].

RESULTS

We examined data for 322 participants with HD ($n = 50$ premanifest, $n = 171$ early-stage manifest, $n = 101$ late-stage manifest). For the longitudinal analyses, 322 (100%) participants had data for their baseline visit, 221 (68.6%; $n = 30$ premanifest, $n = 121$ early-stage HD, $n = 70$ late-stage HD) provided 12-month data, and 177 (55.0%; $n = 25$ premanifest, $n = 75$ early-stage HD, $n = 77$ late-stage HD) provided 24-month data. Thus, there were 720 observations available for the LMMs.

Premanifest participants were significantly younger than the two manifest groups, $F[2,319] = 16.8$, $p < 0.0001$ (Table 1). Premanifest participants also had more years of education than either of the two manifest groups, $F[2,309] = 5.31$, $p < 0.0001$. Overall, the sample majority was female, white, and married. There were significant group differences in race (Fisher's Exact = 0.0032); the late-stage participants included more African Americans than the other two groups. There were no significant differences between the three HD groups with regard to gender, race, or marital status.

Average PAW score was 54.8 (SD = 8.5) at baseline, which is half a standard deviation better than individuals in the normative population. The three HD groups did not significantly differ in PAW, $F[2,319] = 0.26$, $p = 0.76$. Pearson correlations indicated that higher PAW was associated with better HRQOL on all measures at baseline (Table 2).

Figure 1 illustrates the path diagram for the moderation analyses. There were significant interactions between FA and PAW for PROMIS Depression ($t[532] = -2.99$; $p = 0.003$), PROMIS Anxiety ($t[550] = -1.99$; $p = 0.047$), and PROMIS Anger ($t[666] = -2.55$; $p =$

0.01) (Table 3). Additionally, FA moderated the effect of PAW on Neuro-QoL Satisfaction with Roles and Activities ($t[645] = 2.22$; $p = 0.03$), Neuro-QoL Executive Function ($t[546] = 2.02$; $p = 0.04$), Neuro-QoL Upper Extremities Functioning ($t[671] = 3.05$; $p = 0.002$), Neuro-QoL Lower Extremities Functioning ($t[676] = 2.06$; $p = 0.04$), Neuro-QoL Emotional/Behavioral Dyscontrol ($t[662] = -2.21$; $p = 0.03$), and HDQLIFE Concern with Death and Dying ($t[658] = -2.9$; $p = 0.01$). For each of the significant interactions, the effect size was small. These interactions indicate that for individuals with higher functioning, greater PAW is significantly associated with better HRQOL. However, participants with lower functional status showed a weaker association between PAW and HRQOL (Fig. 2).

For models with significant interaction effects between PAW and FA, cut-points were identified for FA to determine when PAW no longer exhibited a potentially protective association with HRQOL (i.e., when the slope of PAW was no longer significant, Table 4). For example, when FA is below 2, the association between PAW and depression becomes insignificant; thus, having high PAW is not associated with less depression when functioning drops to 1 or less.

DISCUSSION

Positive affect, as defined by pleasant feelings, predicted better self-reported HRQOL over a 24-month period in a large sample of persons with premanifest and manifest HD. The associations between positive affect and HRQOL often depended on participant's functional status. For persons with higher functional status, positive affect was strongly associated with better HRQOL along a number of dimensions, including less depression, lower anxiety, less anger, better social role satisfaction, better executive functions, greater upper extremity function, less emotional/behavioral dyscontrol, and less concern with death and dying. Our longitudinal data give some confidence that, although the effect sizes were small, positive affect may be predictive of future HRQOL in persons with HD, particularly for persons with HD that have higher level functioning. For persons with lower functional status, positive affect was not associated with HRQOL.

Our results are similar to studies in other populations. For example, as mentioned earlier, in women with HIV, Wilson et al. (2017) found that high positive affect was prospectively associated with greater health outcomes (e.g., undetectable viral load). However, the association between positive affect and reduced viral load diminished in the context of a liability (e.g., high negative affect). That is, the benefits of positive affect were limited by greater negative affect. Likewise, our data suggest that the potentially adaptive links between positive affect and HRQOL in HD could be limited by functional status. There may be limitations on the beneficial mental health effects of positive affect. When persons are faced with a certain intensity of stressor (e.g., more severe functional limitations), positive affect confers diminishing returns and/or is a less potent protective factor. If so, theoretical models about the protective effects of PA should be modified to account for boundary effects of its protective actions. Our data suggest the limitations of PA to be associated with positive outcomes may vary by domain (Table 4).

Positive affect had associations with a broad range of HRQOL outcomes. Positive affect was associated with less depression, anxiety, and anger. These findings are consistent with data suggesting that strong negative affect states are inversely associated with positive affect [35-37]. Indeed, there were inverse links between positive affect and other adverse outcomes, including behavioral dyscontrol and concern with death the dying. Positive affect also was associated with the adaptive outcome of better upper extremity function, which also is consistent with a large corpus of data [38].

Positive affect is conceptualized as (1) a buffer against stress and (2) a means by which psychosocial resources are accrued [39]. Positive affect in persons with HD, operating via one or both of these pathways, may improve or maintain HRQOL over time. The association between positive affect and social role satisfaction is particularly pertinent to Frederickson's Broaden and Build model of positive affect, confirming important links between positive affect and social role fulfillment and better function. Social partners are a major psychological resource by which the benefits of positive affect are accrued.

Implications

Interventions to enhance positive affect in HD may benefit HRQOL, at least when patients are higher functioning. Acceptance and meditation therapies hold promise to enhance positive emotions in HD and may have beneficial outcomes [4-8, 40]. Indeed, data suggest that persons with HD who are more accepting of their disorder also have greater well-being [41]. Whereas knowledge about non-pharmacologic therapies for persons with HD is limited [42, 43], persons with HD could respond positively to these interventions. Persons with HD have rich emotional experiences in laboratory paradigms that include positive as well as negative emotions [44], and there may be potential to capitalize on and enhance their positive emotions. Further, persons with cognitive impairments associated with other neurologic disorders have successfully engaged in psychotherapy [45]. Our data indicate that there were no significant differences in positive affect and well-being based on HD disease stage (i.e., premanifest, early-stage, late-stage). Thus, positive affect may not necessarily align with disease stage and may be a preserved resource for some persons that can be targeted in therapies.

Limitations

Our sample was primarily female, highly educated, and white, which may limit the generalizability of our findings. Individuals with lower education and of other races may experience different associations between positive affect, functional status, and HRQOL. We did not have cognitive status measures, which likely are an important predictor of life quality in persons with HD, and could not address their association with HRQOL. Additionally, the protocol for the study allowed for the participant to answer self-report measures up to two weeks following the functional status measure (i.e., functional assessment). Therefore, correlations between our measures may be less robust when broken down between those who completed self-report measures at the time of their in-person assessment and those who completed the measures afterward, though a change in functional status over two weeks would not be expected.

As noted earlier, for persons with lower functional status, positive affect was not associated with HRQOL. It is possible that the lack of significant association between positive affect and HRQOL was due, in part, to the fact that more severely impaired persons with HD provide self-report data of lesser reliability than persons who are higher functioning [46]. Thus, research that relies less exclusively on self-report will be an important step in this line of work.

Future directions

Future research should include a broader assessment of positive and negative affect in persons with HD, to provide a more comprehensive assessment of current affective state. Methods should capitalize on multiple assessments of affect and emotion that include self-report, observational, and physiological data. Further research on how affect predicts coping with functional status in HD could lead to preventative and therapeutic interventions to enhance HRQOL. Essential to this effort would be identification of the mechanisms that drive the associations between positive affect and HRQOL in higher functioning persons with HD, how negative affect may interfere with this association, and how this protective mechanism may fail in individuals with lower functioning.

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REFERENCES

- [1]. Isen AM. Positive affect In: Dalgleish T, Power MJ, Dalgleish T, Power MJ, editors. Handbook of cognition and emotion. New York, NY: John Wiley & Sons Ltd.; 1999 p. 521–39.
- [2]. Watson D, Clark LA. The PANAS-X: Manual For The Positive And Negative Affect Schedule - Expanded Form. Iowa City, IA: The University Of Iowa; 1999.
- [3]. Frederickson B The role of positive emotions in positive psychology. The Broaden-And-Build Theory of positive emotions. Am Psychol. 2001;56:218–26. [PubMed: 11315248]

- [4]. Wilson T, Weedon J, Golub E, Young M, Cohen J, Cohen M, et al. Positive affect and its association with viral control among women with HIV infection. *Health Psychol.* 2017;36(1):91–100. [PubMed: 27685456]
- [5]. Cohen SA, Doyle W, Turner R, Alper C, Skoner DP. Emotional style and susceptibility to the common cold. *Psychosom Med.* 2003;65:652–7. [PubMed: 12883117]
- [6]. Oster G, Markides KS, Peek M, Goodwin J. The association between emotional well-being and the incidence of stroke in older adults. *Psychosom Med.* 2001;63:210–5. [PubMed: 11292267]
- [7]. Moskowitz J. Positive affect predicts lower risk of AIDS mortality. *Psychosom Med.* 2003;65:620–6. [PubMed: 12883113]
- [8]. Steptoe A, Wardle J. Positive affect measured using ecological momentary assessment and survival in older men and women. *Proc Natl Acad Sci U S A.* 2011;108:18244–8. [PubMed: 22042845]
- [9]. Frederickson BL. Positive emotions broaden and build In: Devine P, Plant A, Editors. *Advances in experimental social psychology*, Vol 47 Burlington, VT: Academic Press; 2013 p. 1–53.
- [10]. Roos RA. Huntington's disease: a clinical review. *Orphanet J Rare Dis.* 2010;5(1):40. [PubMed: 21171977]
- [11]. Lee J, Ramos EM, Lee J, Gillis T, Mysore JS, Hayden MR, et al. CAG repeat expansion in Huntington disease determines age at onset in a fully dominant fashion. *Neurology.* 2012;78:690–5. [PubMed: 22323755]
- [12]. Coulson NS, Buchanan H, Aubeeluck A. Social support in cyberspace: a content analysis of communication within a Huntington's disease online support group. *Patient Educ Couns.* 2007;68(2):173–8. [PubMed: 17629440]
- [13]. Martinez-Horta S, Perez-Perez J, Van Duijn E, Fernandez-Bobadilla R, Carceller M, Pagonabarraga J, et al. Neuropsychiatric symptoms are very common in premanifest and early stage Huntington's disease. *Parkinsonism Relat Disord.* 2016;25:58–64. [PubMed: 26898966]
- [14]. Paulsen JS, Ready RE, Hamilton JM, Mega MS, Cummings JL. Neuropsychiatric aspects of Huntington's disease. *J Neurol Neurosurg Psychiatry.* 2001 9;71(3):310–4. [PubMed: 11511702]
- [15]. Greenglass ER, Fiskensbaum L. Proactive coping, positive affect, and well-being: testing for meditation using path analysis. *Eur Psychol.* 2009;14(1):29–39.
- [16]. Park SH, Sonty N. Positive affect mediates the relationship between pain-related coping efficacy and interference in social functioning. *J Pain.* 2010;11(12):1267–73. [PubMed: 20418176]
- [17]. Cella DF. Measuring quality of life in palliative care. *Semin Oncol.* 1995 04;22(2 Suppl 3):73–81. [PubMed: 7537908]
- [18]. Sears S, Kraus S. I think therefore i am: cognitive distortions and coping style as mediators for the effects of mindfulness meditation on anxiety, positive and negative affect, and hope. *J Clin Psychol.* 2009;65(6):561–73. [PubMed: 19241400]
- [19]. Frederickson B, Cohn M, Coffey K, Pek J, Finkel S. Open hearts build lives: positive emotions, induced through loving-kindness meditation, build consequential personal resources. *J Pers Soc Psychol.* 2008;95(5):1045–62. [PubMed: 18954193]
- [20]. Cheung EO, Cohn MA, Dunn LB, Melisko ME, Morgan S, Penedo FJ, et al. A randomized pilot trial of a positive affect skill intervention (lessons in linking affect and coping) for women with metastatic breast cancer. *Psychooncology.* 2017;26(12):2101–8. [PubMed: 27862646]
- [21]. Moskowitz JT. Coping interventions and the regulation of positive affect In: Folkman S, Editor. *The Oxford Handbook Of Stress, Health, And Coping.* Oxford; New York: Oxford University Press; 2011.
- [22]. Giovannetti AM, Schiavolin S, Brenna G, Brambilla L, Confalonieri P, Cortese F, et al. Cognitive function alone is a poor predictor of health-related quality of life in employed patients with MS: results from a cross-sectional study. *Clin Neuropsychol.* 2016;30(2):201–15. [PubMed: 26930374]
- [23]. Logsdon RG, Gibbons LE, McCurry SM, Teri L. Quality of life in Alzheimer's disease: patient and caregiver reports. *J Mental Health Aging.* 1999;5(1):21–32.
- [24]. Carlozzi NE, Tulskey DS. Identification Of health-related quality of life (HRQOL) issues relevant to individuals with Huntington disease. *J Health Psychol.* 2013;18:212–25. [PubMed: 22427174]

- [25]. Carlozzi NE, Schilling SG, Lai JS, Paulsen JS, Hahn EA, Perlmuter JS, et al. HDQLIFE: development and assessment of health-related quality of life in Huntington disease (HD). *Qual Life Res.* 2016 8 13;25(10):2441–55. [PubMed: 27522213]
- [26]. Hanauer DA, Mei Q, Law J, Khanna R, Zheng K. Supporting information retrieval from electronic health records: a report of University Of Michigan's nine-year experience in developing and using the Electronic Medical Record Search Engine (EMERSE). *J Biomed Inform.* 2015 6;55:290–300. [PubMed: 25979153]
- [27]. Cella D, Riley W, Stone A, Rothrock N, Reeve B, Yount S, et al. The Patient-Reported Outcomes Measurement Information System (PROMIS) developed and tested in its first wave of adult self-reported health outcome item banks: 2005-2008. *J Clin Epidemiol.* 2010;63:1179–94. [PubMed: 20685078]
- [28]. Cella D, Nowinski C, Peterman A, Victorson D, Miller D, Lai J-S, et al. The Neurology Quality Of Life Measurement (Neuro-QOL) Initiative. *Arch Phys Med Rehabil.* 2011 10;92(10 Suppl):S28–36. [PubMed: 21958920]
- [29]. Carlozzi NE, Downing NR, McCormack MK, Schilling SG, Perlmuter JS, Hahn EA, et al. New measures to capture end of life concerns in Huntington disease: meaning and purpose and concern with death and dying from HDQLIFE (a patient-reported outcomes measurement system). *Qual Life Res.* 25(10):2403–15.
- [30]. Carlozzi NE, Schilling SG, Lai JS, Perlmuter JS, Nance MA, Waljee JF, et al. HDQLIFE: the development of two new computer adaptive tests for use in Huntington disease, speech difficulties, and swallowing difficulties. *Qual Life Res.* 25:2417–27.
- [31]. Unified Huntington's Disease Rating Scale: reliability and consistency. Huntington Study Group. *Mov Disord.* 1996;11:136–42. [PubMed: 8684382]
- [32]. Shoulson I, Kurlan R, Rubin A, Goldblatt D, Behr J, Miller C, et al. Assessment of functional capacity in neurodegenerative movement disorders: Huntington's disease as a prototype, quantification of neurologic deficit. In: Munsat T, Editor. Stoneham, MA: Butterworths; 1989 p. 271–83.
- [33]. Aiken LS, West SG, Reno RR. Multiple regression: testing and interpreting interactions. Newbury Park, CA: Sage Publications; 1991.
- [34]. Cohen J Statistical power analysis for the behavioral sciences (2nd Edition). Hillsdale, NJ: L. Erlbaum; 1988.
- [35]. Saboonchi F, Lundh L-G. Perfectionism, anger, somatic health, and positive affect. *Pers Individ Dif.* 2003;35:1585–99.
- [36]. Cohen JN, Dryman MT, Morrison AS, Gilbert KE, Heimberg RG, Gruber J. Positive and negative affect as links between social anxiety and depression: predicting concurrent and prospective mood symptoms in unipolar and bipolar mood disorders. *Behav Ther.* 2017;48:820–33. [PubMed: 29029678]
- [37]. Eisner LR, Johnson SL, Carver CS. Positive affect regulation in anxiety disorders. *J Anxiety Disord.* 2009;23:645–9. [PubMed: 19278820]
- [38]. Cameron DS, Bertenshaw EJ, Sheeran P. The impact of positive affect on health cognitions and behaviours: a meta-analysis of the experimental evidence. *Health Psychol Rev* 2015;9:345–65. [PubMed: 27028049]
- [39]. Frederickson B Positive emotions broaden and build. *Adv Exp Soc Psychol.* 2013a;47:1–53.
- [40]. Frederickson B The role of positive emotions in positive psychology. The broaden-and-build theory of positive emotions. *Am Psychol.* 2001;56:218–26. [PubMed: 11315248]
- [41]. Helder DI, Kaptein AA, Van Kempen GM, Weinman J, Van Houwelingen JC, Roos R. Living with Huntington's disease: illness perceptions, coping mechanisms, and patients' well-being. *J Health Psychol.* 2002;7(Part 4):449–32.
- [42]. Silver A Cognitive-behavioural therapy with a Huntington's gene positive patient. *Patient Educ Couns.* 2003; 49(2):133–8. [PubMed: 12566207]
- [43]. Van Bruggen-Rufi M, Vink A, Achterberg W, Roos R. Music therapy in Huntington's disease: a protocol for a multi-centre randomized controlled trial. *BMC Psychol.* 2016;4:38. [PubMed: 27457568]

- [44]. Ille R, Holl A, Kapfhammer H, Reisinger K, Schafer A, Schienle A. Emotion recognition and experience in Huntington's disease: is there a differential impairment? *Psychiatry Res.* 2011;188(3):377–82. [PubMed: 21550669]
- [45]. Gottberg K, Chruzander C, Backenroth G, Johansson S, Ahlstrom G, Ytterberg C. Individual face-to-face cognitive behavioural therapy in multiple sclerosis: a qualitative study. *J Clin Psychol.* 2016;72(7):651–62. [PubMed: 26991065]
- [46]. Carlozzi NE, Schilling S, Kratz AL, Paulsen JS, Frank S, Stout JC. Understanding patient-reported outcome measures in Huntington disease: at what point is cognitive impairment related to poor measurement reliability? *Qual Life Res.* 2018;27(10):2541–55. [PubMed: 29909483]

Fig. 1. Moderation Diagram. *Displays the moderation diagram of the primary analyses. Positive Affect and Well-Being is moderated by Functional Assessment; greater impairment weakens the relationship between Positive Affect and HRQOL.*

Fig. 2.

Interactions between Functional Assessment and Positive Affect on HRQOL. Scores *shows the slope of Positive Affect and Well-Being at various levels of functioning. Refer to Table 4 for the value of functioning where the slope of Positive Affect and Well-Being becomes insignificant.*

Table 1

Baseline descriptive statistics for demographic, disease, and HRQOL variables

Variable	Premantifest-HD (N = 50)	Early-HD (N = 171)	Late-HD (N = 101)	Combined Sample (N = 322)
Age at Baseline (Years) *				
M (SD)	43.4 (11.3)	51.6 (12.6)	55.5 (11.7)	51.6 (12.7)
Gender (%)				
Female	54.0	52.0	58.4	54.4
Male	46.0	48.0	41.6	45.6
Race (%) *				
White	96.0	95.9	92.1	94.7
African American	0.0	1.2	7.9	3.1
Other	2.0	2.9	0.0	1.9
Unknown	2.0	0.0	0.0	0.3
Ethnicity (%)				
Not Hispanic or Latino	96.0	93.0	97.0	94.7
Hispanic or Latino	2.0	4.1	1.0	2.8
Not Provided	2.0	2.9	2.0	2.5
Education (# of years) *				
M (SD)	15.7 (2.9)	14.6 (2.7)	14.2 (2.5)	14.7 (2.7)
Marital Status (%)				
Single, Never Married	10.0	16.4	10.9	13.7
Married	72.0	51.5	62.4	58.1
Separated/Divorced	16.0	24.6	22.8	22.7
Widowed	0.0	3.5	4.0	3.1
Living with Partner	2.0	4.1	0.0	2.5
CAG Repeats *				
M (SD)	41.9 (2.3)	43.2 (4.0)	44.8 (7.2)	43.3 (4.7)
UHDRS Functional Assessment *				
M(SD)	24.5 (1.1)	22.0 (2.6)	11.8 (5.5)	19.2 (6.3)
Neuro-QoL Positive Affect and Well-Being				

Variable	Premanifest-HD (N = 50)	Early-HD (N = 171)	Late-HD (N = 101)	Combined Sample (N = 322)
M(SD)	55.1 (8.7)	54.9 (8.5)	54.3 (8.5)	54.8 (8.5)
PROMIS Depression				
M(SD)	49.4 (10.0)	51.3 (10.8)	51.3 (11.1)	51.0 (10.8)
PROMIS Anxiety				
M(SD)	52.8 (9.7)	53.4 (10.1)	54.1 (11.4)	53.5 (10.4)
PROMIS Anger				
M(SD)	48.3 (12.1)	48.4 (12.3)	47.1 (12.8)	48.0 (12.4)
Neuro-QoL Satisfaction with Social Roles and Activities *				
M(SD)	50.5 (8.2)	48.3 (7.9)	44.2 (8.1)	47.4 (8.3)
Neuro-QoL Ability to Participate in Social Roles and Activities *				
M(SD)	50.0 (8.3)	47.1 (7.9)	42.8 (8.0)	46.3 (8.3)
Neuro-QoL Executive Function *				
M(SD)	44.4 (10.3)	38.3 (8.9)	28.6 (7.8)	36.3 (10.4)
Neuro-QoL Stigma *				
M(SD)	46.1 (7.7)	51.7 (8.0)	53.3 (9.7)	51.3 (8.8)
Neuro-QoL Upper Extremities Function *				
M(SD)	49.9 (7.7)	43.0 (9.0)	32.4 (7.3)	40.8 (10.3)
Neuro-QoL Lower Extremities Function *				
M(SD)	53.6 (8.3)	46.7 (8.8)	38.0 (8.1)	45.1 (10.0)
Neuro-QoL Emotional/Behavioral Dyscontrol				
M(SD)	46.2 (11.1)	47.4 (10.4)	46.9 (11.6)	47.0 (10.9)
HDQLIFE Chorea *				
M(SD)	42.9 (6.8)	52.9 (7.3)	57.4 (7.3)	52.8 (8.6)
HDQLIFE Speech Difficulties *				
M(SD)	45.3 (6.8)	50.7 (7.6)	55.2 (7.8)	51.3 (8.2)
HDQLIFE Swallowing Difficulties *				
M(SD)	46.1 (7.2)	51.6 (8.1)	56 (7.6)	52.1 (8.5)
HDQLIFE Concern w/ Death and Dying				
M(SD)	50.0 (9.1)	50.6 (9.6)	49.8 (11.0)	50.3 (10.0)

Variable	Prenanifest-HD (N = 50)	Early-HD (N = 171)	Late-HD (N = 101)	Combined Sample (N = 322)
HDQLIFE Meaning and Purpose				
M(SD)	49.0 (10.0)	50.3 (9.7)	48.7 (8.3)	49.6 (9.4)

HD, Huntington's disease.

* Variable differs between the 3 groups ($p < 0.05$).

Table 2

Pearson Correlation (r) between Positive Affect and Well-Being and HRQOL outcomes

	Correlation (r)
PROMIS	
Depression	−0.59
Anxiety	−0.48
Anger	−0.45
Neuro-QoL	
Satisfaction w/ Social Roles and Activities *	0.43
Ability to Participate in Social Roles and Activities *	0.39
Executive Function *	0.30
Stigma	−0.47
Upper Extremities Function *	0.15
Lower Extremities Function *	0.19
Emotional/Behavioral Dyscontrol	−0.45
HDQLIFE	
Chorea	−0.22
Speech Difficulties	−0.15
Swallowing Difficulties	−0.16
Concern w/ Death and Dying	−0.45
Meaning and Purpose *	0.63

All p-values<0.01; correlations calculated at baseline.

* Higher scores indicate better outcomes.

Table 3

Linear regression predicting health related quality of life outcomes

	Functional Assessment			
	Coefficient	SE	η^2	<i>t</i> -value (df) <i>p</i> -value
<i>PROMIS</i>				
Depression				
Assessment (Change per year)	-0.98	0.44	0.01	-2.25 (331) 0.0254
FA	1.22	0.41	0.02	3.00 (534) 0.0029
Positive Affect and Well-being	-0.24	0.15	0.01	-1.65 (527) 0.1001
Interaction (FA * PAW)	-0.02	0.01	0.02	-2.99 (533) 0.0029
Anxiety				
Assessment (Change per year)	-1.45	0.43	0.01	-3.41 (316) 0.0007
FA	0.80	0.42	0.01	1.90 (551) 0.0579
Positive Affect and Well-being	-0.25	0.15	0.00	-1.68 (544) 0.0944
Interaction (FA * PAW)	-0.02	0.01	0.01	-1.99 (550) 0.0472
Anger				
Assessment (Change per year)	0.19	0.40	0.00	0.48 (442) 0.6324
FA	1.09	0.47	0.01	2.34 (668) 0.0194
Positive Affect and Well-being	-0.15	0.17	0.00	-0.92 (665) 0.3571
Interaction (FA * PAW)	-0.02	0.01	0.01	-2.55 (666) 0.0109
<i>Neuro-QoL</i>				
Satisfaction w/ Social Roles and Activities *				
Assessment (Change per year)	0.08	0.26	0.00	0.31 (440) 0.7570
FA	-0.25	0.30	0.00	-0.83 (648) 0.4064
Positive Affect and Well-being	0.11	0.11	0.00	1.05 (643) 0.2947
Interaction (FA * PAW)	0.01	0.01	0.01	2.22 (645) 0.0268
Ability to Participate in Social Roles and Activities *				
Assessment (Change per year)	0.11	0.31	0.00	0.35 (477) 0.7258
FA	-0.05	0.32	0.00	-0.16 (619) 0.8696
Positive Affect and Well-being	0.13	0.11	0.00	1.16 (620) 0.2471
Interaction (FA * PAW)	0.01	0.01	0.00	1.38 (616) 0.1687

Functional Assessment					
	Coefficient	SE	η^2	<i>t-value</i> (df)	<i>p-value</i>
Executive Function *					
Assessment (Change per year)	0.60	0.39	0.00	1.53 (327)	0.1260
FA	-0.05	0.38	0.00	-0.13 (546)	0.8977
Positive Affect and Well-being	-0.02	0.14	0.00	-0.14 (541)	0.8925
Interaction (FA * PAW)	0.01	0.01	0.01	2.02 (546)	0.0440
Stigma					
Assessment (Change per year)	-0.50	0.27	0.00	-1.85 (445)	0.0653
FA	-0.06	0.32	0.00	-0.20 (667)	0.8399
Positive Affect and Well-being	-0.30	0.11	0.01	-2.64 (665)	0.0086
Interaction (FA * PAW)	-0.004	0.01	0.00	-0.64 (666)	0.5201
Upper Extremities *					
Assessment (Change per year)	-0.84	0.24	0.01	-3.53 (428)	0.0005
FA	-0.06	0.30	0.00	-0.21 (670)	0.8323
Positive Affect and Well-being	-0.26	0.11	0.01	-2.33 (701)	0.0201
Interaction (FA * PAW)	0.02	0.01	0.02	3.05 (671)	0.0023
Lower Extremities *					
Assessment (Change per year)	-0.35	0.25	0.00	-1.39 (438)	0.1646
FA	0.12	0.31	0.00	0.38 (675)	0.7068
Positive Affect and Well-being	-0.10	0.11	0.01	-0.90 (677)	0.3694
Interaction (FA * PAW)	0.01	0.01	0.01	2.06 (676)	0.0393
Emotional/Behavioral Dyscontrol					
Assessment (Change per year)	-0.12	0.36	0.00	-0.35 (449)	0.7293
FA	0.78	0.42	0.01	1.87 (663)	0.0623
Positive Affect and Well-being	-0.18	0.15	0.01	-1.22 (660)	0.2243
Interaction (FA * PAW)	-0.02	0.01	0.01	-2.21 (662)	0.0273
<i>HDQLIFE</i>					
Chorea					
Assessment (Change per year)	0.19	0.21	0.00	0.91 (423)	0.3621
FA	-0.24	0.26	0.01	-0.90 (667)	0.3691
Positive Affect and Well-being	-0.04	0.09	0.01	-0.47 (672)	0.6406

Functional Assessment				
	Coefficient	SE	η^2	<i>t-value</i> (df) <i>p-value</i>
Interaction (FA * PAW)	-0.004	0.005	0.00	-0.79 (668) 0.4288
Speech Difficulties				
Assessment (Change per year)	-0.06	0.24	0.00	-0.25 (446) 0.8060
FA	-0.44	0.30	0.00	-1.50 (672) 0.1340
Positive Affect and Well-being	-0.07	0.11	0.00	-0.70 (674) 0.4811
Interaction (FA * PAW)	0.001	0.01	0.00	0.05 (673) 0.9628
Swallowing Difficulties				
Assessment (Change per year)	0.53	0.24	0.00	2.21 (431) 0.0276
FA	-0.39	0.31	0.00	-1.28 (666) 0.2027
Positive Affect and Well-being	-0.06	0.11	0.00	-0.51 (670) 0.6087
Interaction (FA * PAW)	-0.001	0.01	0.00	-0.04 (667) 0.9707
Concern w/ Death and Dying				
Assessment (Change per year)	0.32	0.32	0.00	0.98 (449) 0.3257
FA	1.05	0.38	0.02	2.78 (661) 0.0056
Positive Affect and Well-being	-0.17	0.13	0.00	-1.24 (654) 0.2145
Interaction (FA * PAW)	-0.02	0.01	0.02	-2.49 (658) 0.0129
Meaning and Purpose*				
Assessment (Change per year)	-0.41	0.28	0.00	-1.43 (468) 0.1524
FA	-0.40	0.32	0.01	-1.25 (658) 0.2113
Positive Affect and Well-being	0.47	0.12	0.02	4.05 (652) <0001
Interaction (FA * PAW)	0.01	0.01	0.01	1.69 (653) 0.0922

FA, Functional Assessment; PAW, Positive Affect and Well-Being; (df), degrees of freedom; all models control for gender and race.

* Higher Scores indicate better outcomes.

Table 4

UHDRS values not protected by Positive Affect and Well-Being

Outcome	Functional Assessment Value where Positive Affect no longer provides any benefit
Depression	Below 2
Anxiety	Below 2
Anger	Below 5
Satisfaction with Roles and Activities	Below 5
Executive Function	Below 12
Upper Extremities Function	Below 20
Lower Extremities Function	Below 16
Emotional/Behavioral Dyscontrol	Below 4
Concern with Death and Dying	Below 4

Functional Assessment is scored on a scale of 0 to 25 with higher scores indicating better functioning.