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The Patient Education Program for Huntington's Disease

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Submitted

Abstract

Aim: The Patient Education Program for Huntington's disease is aimed to improve quality of life of patients and partners by education and training of coping strategies to deal with psychosocial stressors. It was derived from a standardized evidence-based program for Parkinson's disease. This pilot study assessed the feasibility of the program Huntington's disease.

Methods: Forty manifest patients with 28 caregivers and 19 premanifest carriers with 14 partners participated. Assessments were performed on depression and anxiety, psychosocial burden and need for help, quality of life, and coping at 1) two months before, 2) one week before and 3) within two weeks after participation in the program. Behavioral, motor and cognitive assessments were performed.

Results: After participation, significant improvement was found for patients on behavioral symptoms and anxiety, and they used a less passive coping style and more seeking social support. The caregivers reported less psychosocial burden. Premanifest carriers and their partners improved their coping by seeking social support more often.

Conclusion: This pilot study demonstrated the feasibility of the program in Huntington's disease, especially in manifest stages. Further research to assess the effectiveness of the program is the next step.

Introduction

Huntington's disease (HD) is an autosomal dominant inherited neurodegenerative disorder with mean age of onset in middle age. The disease is characterized by progressive motor, psychiatric and cognitive symptoms, causing functional decline.[1] Among the psychiatric symptoms, depression, anxiety, apathy and irritability have a prevalence rate varying across studies from 33% to 69%.[2] Psychosocial stressors may include feelings like sadness and anxiety about the cognitive and physical decline, changes in social role, and children at risk. Loss of social support is a risk factor for depression.[3] The most important source of social support and provider of informal daily care is often provided by family members, like the spouse. The complexity of the symptoms, the psychosocial aspects and the fear that children develop HD often cause a huge caregiver burden.[4-6] Psychosocial challenges not only exist in the period of manifest symptoms and signs. With the discovery of the HD gene, premanifest testing became available creating a stage before onset of apparent symptoms with the knowledge to become ill. This may lead to anticipatory stress, anxiety, preoccupation with impending symptoms, suicidal ideation and feelings of hopelessness.[7,8] It also may influence important future planning issues, like reproductive decisions. Despite many recommendations for future research about the need for studies on psychological interventions in HD,[4,5,9,10] no such study was performed thus far. Therefore, we adapted an available standardized program from another neurodegenerative disease: the Patient Education Program for Parkinson's disease' (PEPP). In a recent randomized controlled trial, benefits for this program were found regarding PD patients' Qol and caregivers' psychosocial problems and need for help.[11] The aim of the program is to empower them in dealing with psychosocial stressors caused by the disease. Techniques from the cognitive behavioural therapy (CBT)[12] were implemented like cognitive restructuring, systematic relaxation training, situational behavioural analysis and training in social skills. The program was adjusted for use in HD and named: the Patient Education for Huntington's disease (PEP-HD). The aim of the present pilot study is to evaluate the feasibility of the PEP-HD program in Huntington's disease.

Methods

Participants

HD mutation carriers without manifest symptoms (PM carriers) and with known HD symptoms (HD patients) attending the outpatient neurological department of the Leiden

University Medical Center (LUMC) or the outpatient department for Huntington's disease Nij Friesma Hiem (NFH) in Grou, were selected from a database. An invitation letter was sent to 106 HD patients and 54 PM carriers to participate in the study with their partner (Figure 1). Participation without partner was also possible, but participation of both was encouraged. Inclusion criteria were the following: 1) DNA confirmed diagnosis by expanded trinucleotide (CAG) repeat in the HD (*HTT*) gene; 2) a total functional score (TFC) $\geq$ 5); 2) a Mini Mental State Examination score (MMSE) $\geq$ 23); and 3) no current psychotic symptoms or severe behavioral problems. Inclusion criteria were carried out by means of the documentation in the medical file from the last visit at the hospital. If no recent data (last year) were available, then data were obtained at the initial patient screening. Patients who were not able or willing to participate, were considered as non-participants, and participants who stopped during the study or missed more than two sessions were considered as drop-out. The study was approved by the Medical Ethical Committee and all participants gave informed consent.

Procedure

A two-period single group pre-post study, in which participants served as their own control, was used because of statistical efficiency considering the relatively small Dutch HD population. Groups of four to seven PM carriers or HD patients and groups of their partners subsequently entered the study. The first group started in month 0, the second group in month 1, and etcetera. They first received baseline assessment at the hospital two months prior to the program, then served as a control during two months, and then received second assessment one week before participation in the program. After eight weeks of PEP-HD intervention, they received post-assessment within two weeks afterwards.

Intervention

Carriers/patients and partners participated in separate, but parallel groups of 4-7 members. The program consists of eight two-weekly sessions of 90 minutes duration: session 1) taking a (pro) active role in treatment, seeking information about the disease; session 2) self-monitoring of body, behavior, cognitions, and mood; session 3) performing pleasant activities and relaxation; session 4) stress management by replacing unhelpful and unrealistic thoughts into helpful and realistic thoughts; session 5) dealing with or preventing depression and anxiety; session 6) social competence like communication and standing up for yourself; session 7) asking for social support. Session 8 is an overall

rehearsal and program evaluation session. The program's content is standardized across groups; it is adapted from the detailed manual for Parkinson's disease.[13;14] In the training, examples specifically for Parkinson's disease were transformed into examples specifically directed at HD. Video materials were made HD-specific. The PEP-HD groups were trained by healthcare professionals who followed two days of training for this intervention.

Assessment

To assess disease signs, the Unified Huntington's Disease Rating Scale (UHDRS)[15] was administered at the first and third measurement. The UHDRS provides a motor, functional and cognitive score. A neurologist performed motor (a higher score indicating more motor symptoms) and functional assessment (Total Functional Capacity (TFC), higher score indicating better functioning in daily life). Cognitive functioning was measured by the sum of raw scores (a higher score indicating better cognitive functioning) of three neuropsychological tests: Symbol Digit Modalities Test (SDMT),[16], Stroop color-word test,[17] and Controlled Oral Word Association Test (FAS).[18] Additionally, general cognitive functioning was assessed with the Mini Mental Status Examination (MMSE)[19] (a higher score indicating better general cognitive functioning). Finally, the UHDRS provides a behavioral score by the sum of the product of severity and frequency per behavioral problem (a higher score indicating more behavioral problems). Cognitive and behavioral assessments were performed by a neuropsychologist. Medication was recorded by means of self-report and at every measurement, participants were asked if medication had changed.

The following self-report questionnaires were administered. The Hospital Anxiety and Depression Scale (HADS) provides an anxiety and depression score (a higher score indicating more depression/anxiety).[20;21] Quality of life (divided into mental and physical) was measured with the generic 36-item Short Form health survey questionnaire (SF-36) (a higher score indicating better quality of life).[22;23] Psychosocial burden and need for help were assessed by an adapted version of the 'Belastungsfragebogen Parkinson kurzversion' (BELA-P-k).[24] This questionnaire has a partner version, the 'Belastungsfragebogen Parkinson Angehörigen kurzversion' (BELA-A-k)[25] (a higher score indicating more psychosocial burden or need for help) . Coping strategies were measured with the Utrecht Coping List (UCL).[26,27] Before and after each session of the PEP-HD, participants were asked to rate their present mood on a 100-point Visual Analogue Scale (Mood-VAS) (a

higher score indicating better mood).[28] At the third measurement, participants filled out an evaluation questionnaire.

Statistical analysis

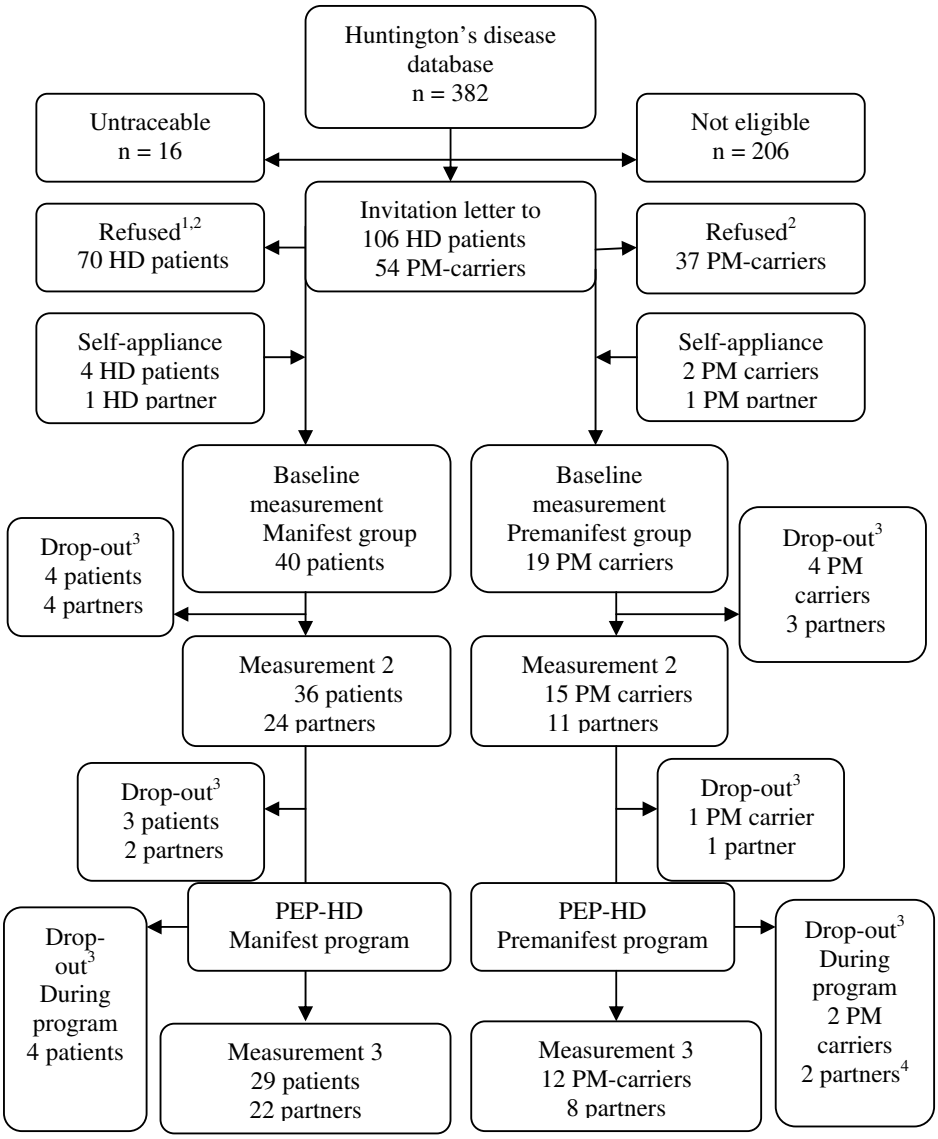
The data were analyzed with the Statistical Package for the Social Sciences (SPSS 16.0). The significance level used was $p \leq 0.05$. Estimated age of symptom onset was calculated according to the equation of Langbehn [29]. Comparisons between participants versus non-participants were made (independent t-tests or Pearson Chi-Square). Participants were compared with drop-outs (Mann-Whitney U Tests or Pearson Chi-Square). Changes (Δ) in the control period (measurement 1-2) were assessed to explore if scores within the same group changed without any intervention. If no important changes will occur, then the means of scores of measurement 1 and 2 will be used as baseline scores to assess the changes from pre- to post-intervention (dependent t-tests or Wilcoxon Rank tests). Premanifest and manifest participants' scores will be analyzed together and separately. Patients/carriers and partners scores will be analyzed separately. To compare pre/post – session Mood-VAS ratings, a linear mixed model with random participant effect, fixed time, fixed before-after session effect and fixed manifest-premanifest and fixed carrier/patient-partner effect was performed.

Results

Of the 106 HD patients and 54 PM carriers who were invited to participate with their partner, eventually, 40 HD patients and 19 PM carriers were willing to participate in the study (Figure 1). In Table 1, demographics and clinical characteristics of all participants are presented. Participating HD patients were significantly more often female ($p = 0.03$) and higher educated ($p = 0.04$) as compared to non-participating patients. Arguments for non-participation were: too much travel time ($n = 30$); too time-consuming ($n = 27$); too burdensome ($n = 40$); participation in group uncomfortable ($n = 3$); no need for/no interest ($n = 19$); not without partner ($n = 1$); unknown ($n = 8$). The drop-out rate during various moments in the study was 25% in the HD group (patients n = 11; partners n = 6) and 39% in the PM HD group (carriers n = 7; partners n = 6), of which most dropped out before the start of the program. HD patients who dropped out had significantly worse physical quality of life (SF-36, $p < 0.01$) as compared to completers. PM-carriers who dropped out had significantly less motor symptoms (UHDRS-motor, $p = 0.03$) and better cognitive

functioning (UHDRS-cognitive, $p = 0.03$) than completers. PM-partners who dropped out had significantly more psychosocial need for help (BELA-A-k, $p = 0.04$) as compared to completers. Reasons for drop-out during study were: too burdensome (3 M couples, 3 HD patients); participation in group not comfortable (1 HD patient and 1 PM carrier); personal circumstances (3 M and 3 PM couples, 1 PM carrier, 1 PM caregiver); death (1 HD patient); unknown (1 PM couple).

Figure 1 Flowchart of inclusion of subjects



1 Two partners of manifest patients who refused to participate did participate themselves.

2 Arguments for non-participation: too much travel time (n = 30); too time-consuming (n = 27); too burdensome (n = 40); participation in group uncomfortable (n = 3); no need for/no interest (n = 19); not without partner (n = 1); unknown (n = 8).

3 Reasons for drop-out during study (n =8): too burdensome (3 M couples, 3 HD patients); participation in group not comfortable (1 HD patient and 1 PM carrier); personal circumstances (3 M and 3 PM couples, 1 PM carrier, 1 PM caregiver); death (1 HD patient); unknown (1 PM couple).

4 The two caregivers missed too much sessions due to personal circumstances.

Table 1 Demographics and clinical characteristics of all participants

	HD patients *n* = 40	PM carriers *n* = 19	HD caregivers *n* = 28	PM partners *n* = 14
Women, *n*	14	13 *	16	4
Age, years	53.4 (9.0)	41.3 (10.4)*	55.6 (9.1)	44.9 (14.1)*
Having a partner, *n*	30	16	28	14
Participation in couple	26	15	26	14
Higher education level, *n*	16	3	11	7
Employed, *n*	9	15 *	14	12 *
Normal/Increased CAG, range	15-31/40-53	15-25/38-51	-	-
Years since genetic test	7.0 (6.1)	5.7 (5.5)	-	-
Estimated age of onset	48.6 (8.3)	49.5 (13.1)	-	-
UHDRS			-	-
-Motor	32.8 (17.0)	4.7 (3.5)*	-	-
-Independence scale	85.0 (13.0)	99.4 (1.6)*	-	-
-Total Functioning Capacity	9.2 (2.5)	12.6 (0.8)*	-	-
-Cognitive	210.7 (61.4)	267.4 (64.1)*	-	-
-Behavioral	10.8 (9.1)	9.6 (9.5)		
MMSE, global cognitive functioning	27.8 (2.0)	27.9 (1.3)	28.6 (1.2)	28.9 (1.4)
Medication use†				
- Antidepressants, *n*	18	0	3	0
- Neuroleptics, *n*	9	0	0	0
- Benzodiazepines, *n*	7	0	1	0
- Anti-epileptics, *n*	2	0	0 (	0
- Other, *n*	23	7	15	5
- No medication, *n*	6	12	11	9

Values are mean (SD) unless otherwise indicated. Abbreviations: CAG, Cytosine-Adenine-Guanine repeat lengths; UHDRS, Unified Huntington's Disease Rating Scale; MMSE, Mini Mental State Examination; HD, Huntington's disease; PM, premanifest.

* Significantly different from HD patients/HD caregivers.

Missing values: In two HD patients, repeat lengths could not be verified, however DNA tests were performed; Three patients did not complete cognitive assessment because of color blindness (n = 2) and too much burden (n= 1); In one PM carrier, no cognitive, motor and functional assessment was performed because of drop-out.

† Psychotropic medication use during the study changed in 4 HD patients: new antidepressant use (*n* = 1); change of antidepressant (*n* = 1); decrease of antidepressant dose (*n* = 1); new benzodiazepine use (*n* = 1). Neuroleptics included Tiapride, primarily given as treatment for motor symptoms; Anti-epileptics were primarily provided as mood stabilizers; Other medication included all other medication than psychotropic, like medication for coronary, lung or stomach diseases.

No changes were found in HD patients during the control period (from measurement 1 to 2), PM carriers used more comforting cognitions (UCL, $p = 0.02$); HD caregivers experienced a worse physical Qol (SF-36, $p = 0.05$); and PM partners used less passive coping styles (UCL, $p < 0.01$) at measurement 2. Mean scores of measurement 1 and 2 were used as baseline scores (Table 2). Pre- and post-intervention analyses are reported in Table 3. HD patients reported less behavioral problems (UHDRS, $p = 0.05$), less anxiety (HADS, $p = 0.05$), more use of seeking social support (UCL, $p = 0.05$), and less use of passive reaction (UCL, $p = 0.03$) as coping strategies after the program. HD caregivers reported less psychosocial burden (BELA-A-k, $p = 0.02$). More use of seeking social support as coping strategy was found in both PM carriers (UCL, $p = 0.05$) and PM partners (UCL, $p = 0.03$).

Participants' mood ($n = 62$) significantly improved from pre- (M = 74.9) to post-sessions ($\Delta = 5.7$, $p < 0.01$) on the 100-point VAS. Mood also improved from session 1 (M = 76.6) to session 8 ($\Delta = 7.1$, $p = 0.01$), because of significant improvement between session 1 through 7 and 8 ($p < 0.01$). Mood did not improve from session 1 to 7 (all $p > 0.05$). There was no difference in effects between groups (manifest versus premanifest, patient versus caregiver) ($p > 0.05$).

The overall program rating was good, premanifest participants rated the program somewhat higher than manifest participants. Session 4 about stress management was most often reported as the most valuable session. Most participants experienced the program as useful in daily life. Most found the contents of the program not difficult to follow. About one third of the HD patients found it somewhat difficult. Half of the HD patients found the intervention somewhat tiresome. Also, more than one third of the PM carriers experienced it as tiresome. Most premanifest participants found the timing of the intervention right.

Table 2 Baseline scores on questionnaires

	HD patients n = 40	PM carriers n = 19	HD caregivers n = 28	PM partners n = 14
-HADS-Anxiety	6.0 (3.5)	5.9 (3.1)	5.3 (3.9)	4.3 (3.7)
-HADS-Depression	4.4 (3.3)	2.9 (3.2)*	2.5 (3.1)	1.5 (2.5)
BELA-P/A-k				
-Bothered by	19.1 (14.4)†	7.4 (8.0)*	10.1 (7.7)	1.9 (2.2)*
-Need for help	25.5 (18.1)‡	11.5 (13.7)*	14.6 (12.2)[1]	6.4 (7.6)*
SF-36				
-Mental	40.2 (11.5)	43.6 (8.8)	47.7 (8.7)	50.2 (3.7)
-Physical	46.4 (9.6)	52.0 (8.9)*	51.4 (9.3)	53.9 (7.8)
UCL				
-Active coping	16.1 (4.2)	18.4 (4.1)	19.7 (3.6)	21.0 (3.9)
-Palliative reaction	17.5 (4.4)	17.6 (4.1)	17.7 (3.8)	15.7 (2.9)
-Avoidance	16.6 (3.6)	15.5 (3.2)	15.8 (3.5)	14.4 (2.9)
-Seeking social support	13.6 (3.6)	13.1 (2.7)	12.3 (2.7)	13.5 (4.4)
-Passive reaction	12.1 (3.4)	10.2 (2.3)*	10.3 (3.0)	10.2 (2.6)
-Negative emotion expression	5.4 (1.7)	5.7 (1.2)	5.7 (1.0)	5.4 (1.3)
-Comforting cognitions	11.8 (2.2)	11.3 (4.1)	12.2 (2.3)	11.8 (3.7)

Values are mean (SD) unless otherwise indicated. Abbreviations: HADS, Hospital Anxiety and Depression Scale; BELA-P/A-k, Belastungsfragebogen Parkinson/Angehörigen kurzversion; SF-36, 36-item Short Form health survey questionnaire; UCL, Utrecht Coping List. HD; Huntington's disease; PM; premanifest. * Significantly different from HD patients/HD caregivers (Mann Whitney U Test or Chi-square). †One missing value; ‡ Two missing values.

Table 3 Change scores from pre- to post intervention for manifest and premanifest participants

	HD patients n = 29 Mean change Δ	PM carriers‡ n = 12 Mean change Δ	HD caregivers n = 22 Mean change Δ	PM partners n = 8‡ Mean change Δ
UHDRS-behavioral	-3.4 (8.8)*	2.1 (6.7)	-	-
HADS-Anxiety	-0.8 (2.2)*	-0.6 (1.4)	-0.4 (3.4)	-1.1 (2.8)
HADS-Depression	-0.6 (2.1)	-0.3 (1.2)	-0.4 (1.9)	-0.6 (1.8)
BELA-P/A-k				
-Bothered by	-1.8 (6.3)	1.11 (4.9)	-1.9 (3.4)*	-0.1 (0.8)
-Need for help	0.2 (11.5)	1.8 (5.5)	-2.1 (5.7)	-0.1 (0.7)
SF-36				
-Mental	2.2 (8.0)	0.4 (3.3)	-1.2 (5.8)	1.8 (5.8)
-Physical	- 0.4 (4.7)	-0.4 (3.7)	0.7 (6.2)	1.0 (2.7)
UCL				
-Active coping	0.5 (2.3)[1]	0.6 (2.3)	0.3 (2.3)	1.6 (2.2)
-Palliative reaction	0.1(2.8)	0.2 (2.7)	0.3 (2.6)	1.5 (2.8)
-Avoidance	-0.6 (2.5)	0.3(2.4)	0.2 (1.9)	-0.3 (1.6)
-Seeking social support	0.6 (1.6)*	0.9 (1.5)*	0.4 (2.1)	1.9 (1.8)*
-Passive reaction	-0.7 (1.6)*	0.2 (1.7)	-0.2 (0.8)	-0.8 (1.4)
-Negative emotion expression	0.1 (1.2)†	-0.1 (1.1)	0.3 (1.8)[1]	-0.1 (0.5)
-Comforting cognitions	-0.1 (1.5)	0.4 (2.1)	-0.2 (2.2)	0.9 (2.5)

Negative change scores reflect improvement on behavioral problems, anxiety, depression, psychosocial burden and need for help and worsening on quality of life; and less use of the particular coping strategy. UHDRS, Unified Huntington's Disease Rating Scale; HADS, Hospital Anxiety and Depression Scale; BELA-P/A-k, Belastungsfragebogen Parkinson/Angehörigen kurzversion; SF-36, 36-item Short Form health survey questionnaire; UCL, Utrecht Coping List.

† A Wilcoxon Rank Test was used. ‡ Wilcoxon Rank Tests were used for all variables. * $p \leq 0.05$.

Discussion

Present pilot study is the first to assess the feasibility of a standardized psychosocial Patient Education Program for Huntington's disease (PEP-HD). The program was feasible in premanifest carriers as well as in HD patients and their partners. The assumption was that the program could diminish psychological distress and negative social impact and that it could stimulate the use of helpful coping strategies like active problem solving and seeking social support in order to improve quality of life. Psychosocial wellbeing did improve in HD patients and caregivers: they reported less anxiety, and less behavioral symptoms. Caregivers reported less psychosocial burden as was also found in the PD study.[11] The use of self-management intervention with cognitive behavioral strategies seems to be helpful to improve psychological wellbeing as hypothesized.[12] For example cognitive restructuring may have helped patients to use more helpful and realistic thoughts, which may have reduced anxiety.

We also found improvements in coping strategies. The HD patients used more seeking social support and less use of passive coping. In the program, they learned to actively seek information, to stand up for themselves, use helpful communication skills and to seek social support actively. In premanifest HD, both carriers and partners used more seeking of social support after the program. This may be beneficial for coping with premanifest HD and psychological wellbeing in the future.[3,8] However, this improvement in coping in the premanifest group was not accompanied by improvement on psychological outcome measures directly after the program. Premanifest carriers did have comparable psychological baseline scores regarding behavioral problems, anxiety and mental quality of life. This may indicate that the program is less effective in the premanifest stage of HD. However, we may not have been able to assess the specific premanifest psychosocial problems and possible improvements adequately. The BELA-P/A-k was developed originally for PD patients and caregivers with symptoms. Because some of the items are focused on consequences of disabilities, the questionnaire seems less relevant to the PM group, resulting in floor effects in scores. An outcome measure capturing the specific psychosocial problems in PM HD should be developed. Besides the effects of the program, the drop-out rate was also relatively high in premanifest (39%) compared to the manifest group (25%). Possibly, those premanifest carriers may have feared to be faced with the discussions about HD and its consequences as denial and avoidance are common in

carriers.[8] Participating PM carriers and partners did evaluate their participation in the program as positive and most found timing of the intervention right.

The relatively low baseline scores on psychological self-report questionnaires may be the result of a selection bias of highly motivated and adjusted patients or impaired awareness [30]. Impaired awareness may lead to denial of (psychological) problems and overestimation of competencies, including behavioral and emotional control.[30;31] Both neurological dysfunction and avoidant psychological coping may be causes of impaired awareness. It has been related to deficits in global cognition, memory and executive functioning.[31] Lack of self-awareness may also have contributed to non-participation or drop-out during the study. However, no differences on psychological outcome measures, and coping, were found between participants and drop-outs. Also, completers did not have better scores on cognitive tests as compared to drop-outs or non-participants.

Participants with higher education and female gender were more willing to participate. They may feel more attracted to an education program and to discuss their feelings than lower educated and male patients. HD patients who dropped-out had more physical problems, so the program and/or study may be too burdensome for some patients. Premanifest patients who dropped out had better motor and cognitive scores, but were not further away from disease onset according to our results. The higher psychosocial need for help in premanifest caregivers who dropped out could not be explained.

This study has its limitations as statistical power was reduced because of the small study sample. Because of this small study sample, a single-group design was used. Therefore we are not able to draw firm conclusions about the effectiveness. In follow-up research, an international multicentre randomized controlled trial should be the next step to provide a larger sample and to enable drawing conclusions about the effectiveness. We did explore the changes pre-intervention in a control period of two months in the same group and no improvements were found, indicating that the intervention is likely to cause the improvements found after participation. Follow-up research with follow-up measurements, for example after six months is recommended. For the PM group, follow-up measurements after a longer period of time are of interest because of the possible preventive effects of the program when symptoms and signs will become manifest. Another limitation is that many outcome measures were used, and no statistical corrections for multiple testing were

applied. Psychotropic medication changes were not likely to be of influence on the study results; they were reported only in four out of 29 patients.

In conclusion, this pilot study demonstrated the feasibility of the program in Huntington's disease, especially in manifest stages. Further research to assess the effectiveness is the next step.

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