Task-Specific Training in Huntington Disease: A Randomized Controlled Feasibility Trial

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Background. Task-specific training may be a suitable intervention to address mobility limitations in people with Huntington disease (HD).

Objective. The aim of this study was to assess the feasibility and safety of goal-directed, task-specific mobility training for individuals with mid-stage HD.

Design. This study was a randomized, blinded, feasibility trial; participants were randomly assigned to control (usual care) and intervention groups.

Setting. This multisite study was conducted in 6 sites in the United Kingdom.

Patients. Thirty individuals with mid-stage HD (13 men, 17 women; mean age=57.0 years, SD=10.1) were enrolled and randomly assigned to study groups.

Intervention. Task-specific training was conducted by physical therapists in participants' homes, focusing on walking, sit-to-stand transfers, and standing, twice a week for 8 weeks. Goal attainment scaling was used to individualize the intervention and monitor achievement of personal goals.

Measurements. Adherence and adverse events were recorded. Adjusted between-group comparisons on standardized outcome measures were conducted at 8 and 16 weeks to determine effect sizes.

Results. Loss to follow-up was minimal (n=2); adherence in the intervention group was excellent (96.9%). Ninety-two percent of goals were achieved at the end of the intervention; 46% of the participants achieved much better than expected outcomes. Effect sizes on all measures were small.

Limitations. Measurements of walking endurance were lacking.

Conclusions. The safety of and excellent adherence to a home-based, task-specific training program, in which most participants exceeded goal expectations, are encouraging given the range of motivational, behavioral, and mobility issues in people with HD. The design of the intervention in terms of frequency (dose), intensity (aerobic versus anaerobic), and specificity (focused training on individual tasks) may not have been sufficient to elicit any systematic effects. Thus, a larger-scale trial of this specific intervention does not seem warranted.

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[Quinn L, Debono K, Dawes H, et al; for the members of the TRAIN-HD project group. Task-specific training in Huntington disease: a randomized controlled feasibility trial. *Phys Ther.* 2014;94:1555–1568.]

Published Ahead of Print: July 10, 2014
Accepted: June 28, 2014
Submitted: March 23, 2014

Huntington disease (HD) is an autosomal dominant, neurodegenerative disease, predominantly affecting the medium spiny neurons of the striatum and resulting in a triad of mobility, cognitive, and behavioral symptoms. Onset is frequently in midlife, with gradual progression of mobility problems over a period of 15 to 20 years, leading eventually to people with HD requiring assistance with activities of daily living. Specific impairments in planning and sequencing of complex tasks, secondary to degeneration within the basal ganglia and damage to corticostriatal pathways, result in difficulties with specific functional skills, such as walking,[1–3] sit-to-stand transfers,[4] and standing balance activities,[5–7] which can contribute to deterioration in quality of life.

Treatment for HD is purely symptomatic, with no disease-modifying therapies available at present. The potential benefits of physical activity and environmental enrichment, including motor training, have been subject to increasing attention, both in animal models (with and without striatal transplantation)[8–12] and in small-scale human studies in early to mid-stage HD, with promising results.[13–16] One recent study focused on aerobic exercise delivered in community gyms alongside an independent walking program with some indication of benefit.[14] Two home-based intervention studies specifically using DVD[13] and videogame technology[16] provide further support for the potential impact of physical therapy interventions. However, no controlled studies to date have evaluated home-based physical interventions specifically in people with mid-stage HD, who have more significant balance and walking problems and hence may need support to adhere to the required intervention. Several studies over the past few years have focused on the benefits of inpatient, multidisciplinary rehabilitation in people with HD,[17–20] with very promising results; however, such programs have significant limitations for widespread implication based on cost and service provision in both the United States and the United Kingdom.

In designing a structured physical therapy program for people with HD, the nature of the complex movement disorder, which includes abnormal timing and sequencing of integrated motor tasks, must be considered. Indeed, motor skill learning is thought to be mediated by corticostriatal pathways, and impairments in motor learning have been demonstrated in both people with Parkinson disease (PD) and those with HD.[21,22] Current research has suggested that optimal training to enhance motor skill learning occurs through repetition and task-specific practice,[23] although it is becoming increasingly evident that motor and cognitive functioning, with respect to motor skills, are in many ways inseparable both functionally and anatomically.

The benefits of a physical therapy program based on task-specific practice as a means to improve functional abilities and performance of specific skills have been documented in individuals with neurological conditions such as stroke and PD.[24,25] Task-specific practice involves repetitive practice of a task (eg, walking, rising from a chair, or reaching) using repetitions, alterations of the environment, and modification of the conditions of the task as a means of progressing task difficulty.[26,27] In addition to functional improvements, task-specific practice has been associated with neuroplastic changes within the cortical and subcortical areas of the brain,[28,29] indicating that motor learning has occured. This type of program, in which extensive practice and repetition of tasks facilitate automaticity of

movements that are lost during the disease process, may be particularly suitable for individuals with HD. However, to date, there has been no evaluation of such a focused program in this population.

The purposes of this trial were: (1) to evaluate the feasibility and safety of a task-specific physical therapy program designed to address limitations in functional mobility commonly seen in people with HD and (2) to determine effect sizes to inform future trials. A key component of this approach was that it was individualized, providing one-to-one therapy with tailored progression specific to a person's individual mobility goals.

Method

Design Overview

We conducted a randomized feasibility trial (ISCTRN94284668) of a task-specific physical therapy intervention over 8 weeks. Estimates of effect size were calculated.

Setting and Participants

Thirty sequential eligible people with HD were recruited from 6 HD centers in the United Kingdom* between July 1, 2012, and July 31, 2013. Inclusion criteria were: (1) diagnosis of manifest HD (confirmed by genetic testing); (2) self-reported or physician-reported difficulties with walking or balance; (3) at least 18 years of age; (4) capacity to give informed consent; (5) total functional capacity (TFC) of at least 4; (6) on stable medication regimen for 4 weeks prior to initiation of trial and able to maintain a stable regime for the course of trial; and (7) enrolled in the European Huntington's Disease Network (EHDN) Registry study.† Exclusion criteria were: (1) history of other prior neurological condition; (2) inability to understand or communicate in spoken English; (3) any orthopedic condition limiting walking ability; (4) cardiac precautions that would prevent the participant from completing intervention or full battery of outcomes; (5) currently in receipt of active physical therapy input; (6) current involvement in, or within 2 months of completing, an interventional trial; and (7) uncontrolled psychiatric symptoms.

The trial was conducted in accordance with the recommendations for physicians involved in research on human participants adopted by the 18th World Medical Assembly General Assembly, Helsinki, Finland, 1964 and later revisions, and was approved by the South East Wales National Health Service Research Ethics Committee (NHS REC 12/WA/0151). All participant identification and referral procedures as well as procedures for data storage, processing, and management complied with the Data Protection Act 1998.

The research team at each site was responsible for recruiting participants and conducting the assessments in accordance with trial protocol. Standard operating procedures were utilized for conducting all outcome assessments and for the intervention protocol. Routine monitoring was conducted at each of the sites with respect to both assessment procedures and intervention delivery.

Randomization and Intervention

Participants were randomly assigned to either a control (usual care) group or an intervention group. Independent random allocation to treatment group was performed centrally to ensure allocation concealment. A minimization program for randomization (MINIM)[30] was used to balance the groups with regard to sex, disease burden score, and site.

For those participants allocated to the intervention group, a task-specific intervention program, based on those effectively utilized in other neurological conditions,[31] was delivered by a physical therapist twice a week for 8 weeks in each participant's home, up to a maximum of 15 sessions.‡ Each session was planned to last approximately 1 hour, and participants wore a heart rate monitor during each session. The programs were individually tailored to participants' specific activity limitations related to the areas of walking, sit-to-stand transfers, and standing ability and modified to their home environments (Appendix).

An important component of the intervention was setting individualized goals using the Goal Attainment Scale (GAS).[32,33] The goals were set by the intervention therapist in collaboration with the participant and were discussed with and approved by the lead intervention therapist, who coordinated interventions and supervised therapists across all sites. Goals were set within the first 3 sessions and were scored based on assessment by the intervention therapist at the last session.

Goals focused on specific mobility-related or activity-level skills that the participant wanted to achieve at the

* Cardiff and Vale University Health Board–7 participants; University College London Hospitals National Health Service (NHS) Foundation Trust–5 participants; Oxford University Hospitals NHS Trust–5 participants; Birmingham and Solihull Mental Health Foundation NHS Trust–4 participants; Sheffield Children's NHS Trust Hospital–4 participants; and Central Manchester University Hospitals NHS Foundation Trust–5 participants.

† The EHDN Registry study is a full clinical data set, including full medical history and medication history, sponsored by the European Huntington's Disease Network (04//WSE05/89).

‡ We chose a maximum of 15 sessions, allowing for one missed session over the course of the intervention. In the event that no sessions were missed, there was only one intervention session in the last week.

end of the 8-week training. These goals were in accordance with the 3 activities that were the focus of the overall intervention (ie, sit-to-stand, standing, and walking tasks). The goals were used to provide focus for both the therapist and the participant for the sessions. For example, if a participant set a goal related to increasing the distance that he or she could walk outside, the intervention trainer would focus the walking program in line with that goal.

The goals were scored by the intervention therapist. The current level of skill attainment (determined within the first 3 intervention sessions) was set at a score of −1. The expected outcome at the end of the intervention was set at a score of 0. A somewhat better outcome than expected was set at a score of +1. A much better outcome than expected was set at a score of +2. A worse outcome than expected was set at −2. The scores at the end of the intervention (last intervention session) were determined by the intervention therapist. Some goals relied on participant report, whereas others required reassessment by the therapist.

Therapists recorded the length of each session as well as breakouts of time spent specifically on sit-to-stand, standing, and walking activities to confirm intervention fidelity. Each participant's response to the intervention was monitored by recording resting, maximum, and average heart rate using a heart rate monitor (Polar monitor, Polar Electro [UK] Ltd, Warwick, United Kingdom).

In addition to the one-to-one sessions, participants in the intervention group were requested to practice activities independently at least once a week between visits. These activities were from the same range of activities that were performed during the training sessions (ie, sit-to-stand, walking, and standing activities) and were designed so that the participants could practice them safely on their own.

Therapists completed session notes following each session, which included a description of tasks practiced, amount of time spent on various tasks, heart rate responses, and subjective reports. Upon completion of the intervention, participants were encouraged to continue with their independent activities and were given exercise diaries to complete and return at the final assessment.

Participants assigned to the control group received usual care and were requested to continue as normal between assessments. They were specifically asked to not begin any new medication or physical activity regimens. At the end of the study, the participants in the control group were offered the intervention.

Outcomes and Follow-up

Feasibility was determined by retention and adherence rates. *Retention rate* was defined as the percentage of individuals who completed the intervention. *Adherence rate* was defined as the percentage of intervention sessions completed by those in the intervention group. Adherence to the home-based exercise program was documented using participant-recorded exercise diaries, which were completed weekly.

Safety of the intervention was assessed from adverse event reports that were conducted in accordance with standard operating procedures. An *adverse event* was defined as any untoward medical occurrence in a participant. Adverse events included falls or any other physical injury that occurred during or outside of performing the intervention. A *serious adverse event* was defined as any untoward and unexpected medical occurrence or effect that results in death, is life-threatening (refers to an event during which the participant was at risk of death at the time of the event), requires hospitalization or prolongation of existing hospitalization, results in persistent or significant disability or incapacity. We did not anticipate any serious adverse events, although it was recognized that participants could require medical care due to unrelated clinical events, such as respiratory problems or injury due to falls, which occur frequently in this population.[7]

Participant demographic data for sex (male/female), age (years), and weight (kilograms) were recorded at baseline. Measurements of TFC[34] and disease burden scores were obtained for purposes of randomization and were obtained from the registry database. The disease burden score is calculated based on an individual's age and the length of the Huntington mutation, where higher scores indicate a greater level of impairment.

Participants were assessed by a blinded rater at baseline (assessment 1) and at 8 weeks (assessment 2) and 16 weeks (assessment 3) later. Assessment 2 provided data on immediate outcomes following the intervention, whereas assessment 3 (follow-up) was intended to inform any sustained outcome. Assessors were physical therapists, nurses, or neurologists and received specific training to conduct all assessments. The following tests were administered in a standardized manner; the same assessor conducted all 3 assessments, and the same order was used for each participant and for repeated testing.

Standard disease-specific clinical measures of disease severity included the Unified Huntington's Disease Rating Scale Total Motor Score (UHDRS-TMS), UHDRS func-

tional assessment, and UHDRS cognitive scales.[35] The cognitive scales included Stroop word reading, color naming, and interference tasks; the Symbol Digit Modalities Test; and verbal fluency tasks. The individual cognitive scores were summed to give a total cognitive score. All assessors had received motor rating certification, via the EHDN, for rating the UHDRS-TMS.

The Physical Performance Test (PPT)[36,37] was used as a measure of physical function. The Timed "Up & Go" Test (TUG)[37,38] was used as a measure of mobility. The 10-Meter Walk Test (10MWT)[37] was used to record both self-selected and fast gait speeds. The 30-Second Chair Stand Test (30CST)[39,40] provided a measure of physical performance to assess mobility and lower extremity function. The Berg Balance Scale (BBS)[37,41] was used to assess balance.

The 7-item Subjective Vitality Scale was used to assess psychological well-being.[42] The Hospital Anxiety and Depression Scale (HADS)[43] was used to determine levels of anxiety and depression. The 5-item EuroQoL (EQ5D) questionnaire was used as a measure of health utility.[44] Quality of life was measured utilizing the Huntington's Disease Health-Related Quality of Life questionnaire (HDQoL).[§,45] Only the summary scale of the HDQoL is reported here.

Participants' subjective reports of tolerability recorded during the individual sessions were reviewed based on therapists' documentation. The Intrinsic Motivation Inventory (IMI)[46] was used as a standardized measure to provide detail relating to acceptability of the intervention. This questionnaire is separated into 5 sections (interest/enjoyment, perceived competence, effort/importance, pressure/tension, and value/usefulness) and was administered to participants at the end of assessment 2.

Table 1.
Mean (SD) [Range] Scores on Disease-Specific Measures for All Participants at Assessment 1 (Baseline), Categorized by Control Group and Intervention Group[a]

Variable	Control Group (n=13)	Intervention Group (n=15)
Sex (men:women)	6:7	7:8
Age (y)	59.4 (10.0) [43–73]	55.0 (10.0) [36–70]
Weight (kg)	69.4 (14.8) [46.0–96.0][b]	68.6 (9.31) [48.6–84.7]
Total functional capacity score	7.7 (2.7) [4–12]	6.7 (1.6) [4–10]
UHDRS Cognitive Score	187.3 (52.1) [115–295]	142.6 (55.2) [41–236]
UHDRS Functional Score	19.7 (3.2) [12–25]	16.8 (3.0) [11–20]
UHDRS Total Motor Score	36.5 (13.6) [12–55]	52.6 (17.3) [23–87]
Disease burden score	405.0 (84.5) [231.0–493.0]	438.1 (87.9) [324.5–569.0]

[a] Total functional capacity: range=0–13, higher is better; Unified Huntington's Disease Rating Scale (UHDRS) Cognitive Score: range=0–no maximum value, higher score is better; UHDRS Functional Score: range=0–25, higher score is better; UHDRS Total Motor Score: range=0–124, lower score is better; disease burden score: lower score is better.
[b] n=12.

Data Analysis

This trial was not powered for efficacy. As a feasibility trial, formal sample size calculations were not made. We aimed to recruit 15 participants per arm of the trial.

All analyses were based on complete cases. Changes in outcomes at the second and third assessments for between-group comparisons were analyzed using analysis of covariance (ANCOVA) and controlling for sex, baseline disease burden, BBS, UHDRS scores, and baseline outcome measures. Results are summarized using regression coefficients, 95% confidence intervals (95% CIs), and effect sizes. Confidence intervals and effect sizes for each outcome were used to provide an indication of benefit.

Role of Funding Source

This study was funded by the Huntington's Disease Association of England and Wales. Professor Dawes is funded by the Elizabeth Casson Trust and the NIHR Oxford BRC.

Results

One hundred eight individuals with HD were sequentially screened for potential recruitment to the study. Of these individuals, 30 (28%) did not meet the inclusion criteria and 48 (44%) declined participation. Thirty participants (13 men, 17 women; mean age=57.0 years, SD=10.1) (Tab. 1) were recruited into the trial, with a recruitment rate of 28% (recruits from eligible participants). Fifteen participants each were randomly allocated to intervention and control groups. A CONSORT flowchart is provided in the Figure.

Out of the 30 participants who enrolled in the trial, 28 completed all 3 assessments. Two participants in the control group were withdrawn from the trial; 1 was lost to follow-up, and 1 was unable to complete the minimum data set during the first assessment despite meeting the

[§] HDQoL © 2009 The European Huntington's Disease Network Quality of Life Working Group/University of Reading, Reading, Berkshire, United Kingdom/M.B. Hocaoglu/E.A. Gaffan/A.K. Ho. All rights reserved. HDQoL contact information and permission to use: http://www.hdqol.info

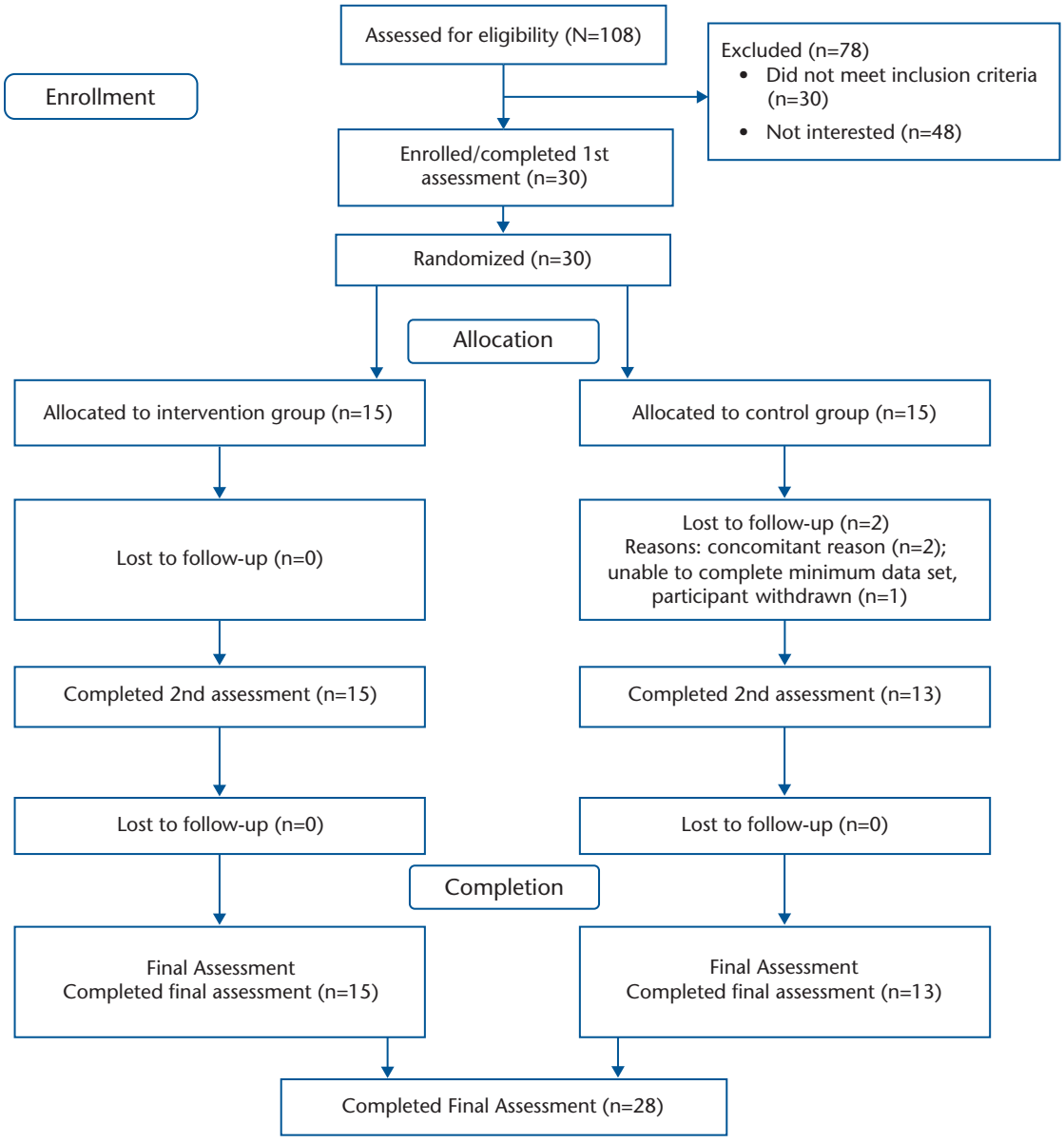

Figure.
Task-Related Training in Huntington's Disease (TRAIN-HD) CONSORT flow diagram.

inclusion criteria. Of the 15 participants who were randomly assigned to the intervention group, there was 100% retention; all 15 participants completed the intervention. The *average adherence rate*, defined as the percentage of completed training sessions out of a maximum of 15, was 96.9%; the mean number of sessions completed over the 8-week period was 14.5 (SD=1.3).

For the independent home activities, 12/15 intervention group participants completed at least some of the recommended activities, as measured by the exercise diaries. The mean number of independent activity sessions completed during the course of the intervention period (between assessments 1 and 2) was 20.3 (SD=12.5), which was, on average, 2.5 sessions per week. Seven of these 12 participants continued with the home activities independently once the intervention finished (between assessments 2 and 3); the mean number of independent sessions completed for these participants was 28.7 (SD=16.2), which was, on average, 3.5 sessions per week.

The mean session length for the participants in the intervention group was 56.3 minutes (SD=11.4). The mean time spent on sit-to-stand, standing balance, and walking activities was 10.4 (SD=4.5), 13.8 (SD=6.6), and 18.0 (SD=8.1) minutes, respectively. Mean resting, average, and maximum heart rates during the training sessions were 79.1 beats per minute (bpm) (SD=11.1), 96.6 bpm (SD=14.7), and 119.6 bpm (SD=19.5), respectively.

A total of 1 serious adverse event (intervention group participant) and 5 adverse events (4 intervention group and 1 control group participant) were reported throughout the duration of the trial. The serious adverse event was a hospitalization due to a fall in the middle of the night; the participant was not found until morning, when she was taken to hospital and subsequently released. Of the 5 adverse events reported, 2 were falls, 2 were slips, and 1 was a change in behavior requiring medication change. For the 3 falls recorded in the intervention group (including the serious adverse event), 1 occurred at the end of an intervention session, when a participant was going to sit down in a chair and fell to the floor. This fall did not result in injury and was categorized as unrelated to the intervention. All other adverse events were categorized by the responsible clinician as unrelated.

Participants' subjective reports of acceptability were recorded during each session. Over the course of the intervention, 7 participants reported nonspecific fatigue. Five participants reported fatigue once, 1 participant reported it 6 times, and 1 participant reported it twice. Two participants reported pain/discomfort during the intervention: 1 during 1 session only and the other over 2 separate sessions. In both cases, the pain resolved without further intervention.

The results from the IMI suggest that the participants highly valued the intervention. Possible IMI scores ranged from 1 to 7, where 1 represents low agreement and 7 represents high agreement. Mean scores (n=11) for the 5 sections of the IMI were: interest/enjoyment: 6.6 (SD=0.4); perceived competence: 6.2 (SD=0.9); effort/importance: 6.7 (SD=0.4); pressure/tension: 2.7 (SD=1.6) (lower values suggest less pressure/tension); and value/usefulness: 6.7 (SD=0.4). Data were missing for 4 participants due to the inventory not being administered by the assessors.

Table 2.
Examples of Goals Set for 3 Different Participants in the Intervention Group Using Goal Attainment Scaling (GAS)[a]

GAS Score	Goals
Participant goal: to be quicker at walking from house around park	
+2	Participant will be able to walk from house, around park, and back with no rests in 23 min
+1	Participant will be able to walk from house, around park, and back with no rests in 27 min
0	Participant will be able to walk from house, around park, and back with no more than 1 rest in 30 min
−1	Participant will be able to walk from house, around park, and back (1.1 miles) with 2 rests in 35 min
−2	Participant will be able to walk from house, around park, and back with up to 4 rests in 40 min
Participant goal: to be able to stand up from sofa without help	
+2	Participant will be able to come from a sitting to a standing position from sofa without use of arms, 10/10 trials
+1	Participant will be able to come from a sitting to a standing position from sofa with use of arms, 5/5 trials
0	Participant will be able to come from a sitting to a standing position from sofa with use of arms, 3/5 trials
−1	Participant requires physical assistance (minimal) to come from a sitting to a standing position from sofa
−2	Participant requires physical assistance (moderate) to come from a sitting to a standing position from sofa
Participant goal: improve standing balance to put on shoes	
+2	Participant will put on slip-on shoes in standing position with no supports and no loss of balance, 3/3 trials
+1	Participant will put on slip-on shoes in standing position without stool, with stand-by supervision for loss of balance, 3/3 trials
0	Participant will put on slip-on shoes in standing position using stool for support, 3/3 trials
−1	Participant will put on slip-on shoes while sitting down without assistance
−2	Participant will need assistance to put on slip-on shoes

[a] The current level of skill attainment (determined within the first 3 intervention sessions) was set at a score of −1; the expected outcome at the end of the intervention was set at a score of 0; a somewhat better outcome than expected was set at 1; a much better outcome than expected was set at a score of 2; a worse outcome than expected was set at a score of −2. The scores at the end of the intervention were determined by the intervention therapist, either based on direct observation (all 3 examples here) or by participant interview (if self-report).

Table 3.
Number of Goals (n=50) Scored on Goal Attainment Scaling and Corresponding Percentages[a]

Score at Assessment 2	No. of Goals	% of Goals
2	23	46%
1	10	20%
0	13	26%
−1	4	8%
−2	0	0%

[a] See Table 2 for Goal Attainment Scaling scoring criteria.

With respect to goal analysis, each participant identified between 2 and 5 goals (median number of goals per participant was 3; total of 50 goals was set across the 15 participants). The most common type of goal was related to walking or stair climbing; all participants chose at least 1 goal related to this functional area. Table 2 presents examples of goals that were set for 3 different participants using GAS. Table 3 presents the number of goals scoring −2, −1, 0, 1, and 2 on the GAS and the corresponding percentage at assessment 2 (postintervention). Ninety-two percent of the goals were achieved at the end of the intervention period, with 46% being achieved at much better than expected outcome.

Effect Sizes

Unadjusted descriptive statistics by treatment group for each outcome at assessments 2 and 3, as well as the adjusted treatment effect from a complete case ANCOVA, are given in Table 4.

At assessment 2, there was no clear evidence of treatment benefit. At assessment 3, there was some potential indication of treatment benefit in the UHDRS-TMS (95% CI=−1.9, 7.7), 30CST (95% CI=−0.7, 3.3), and vitality score (95% CI=0.1, 1.1).

Discussion

Here we report for the first time data from an 8-week, randomized feasibility trial of a task-specific, home-based training intervention in individuals with mid-stage HD. The results of our study suggest that this intervention was feasible and safe and had high retention rates. Although the program was well received by the participants and facilitated achievement of personal mobility goals, the effect sizes on the standardized outcome measures were small, with wide confidence intervals, suggesting there was little evidence in support of the intervention. Thus, a larger-scale trial utilizing this specific intervention does not seem warranted.

As shown in the CONSORT flowchart (Figure), almost half of the potential participants approached for the study were not interested. Although we did not formally gather information about why participants refused to enroll, we suspect lack of interest in exercise or activity and other time commitments to be the major factors. For those participants in the intervention group, adherence was excellent, and self-reported adherence to the home program was remarkable. This is a very encouraging finding, given the widely reported apathy, motivational, and behavioral issues in people with HD.[47] With respect to safety, falls and slips were documented, which is not unexpected in people with HD,[7,48] and reports of fatigue were noted. The higher number of adverse events in the intervention group was not necessarily unexpected because these participants were seen twice a week, which increased the likelihood of recalling an adverse event such as a fall. Control group participants were not contacted between assessments and thus relied on memory to recall incidents, which we recognize is an inherent limitation. Although the number of falls was not a specific outcome in this study, it would be important to look more specifically at falls using similar diaries in both groups in future studies. Fatigue has not previously been reported in people with HD and warrants further investigation to determine its relationship to exercise and activity.

The design of the intervention, in terms of frequency (dose), intensity (aerobic versus anaerobic), and specificity (focused training on individual tasks), may not have been sufficient to elicit a systematic effect that would be evident across a range of outcome measures. Participants in this study trained twice a week, with one additional independent exercise session recommended. This frequency may not have been sufficient to achieve a training effect over 8 weeks, particularly in individuals with a degenerative condition. Although this intervention was not intended to be aerobic in nature, we utilized heart rate monitors to inform the level of work by the participants and to estimate the intensity of activities. Participants were able to achieve heart rates that were likely in an aerobic zone (as reflected by average heart rates of 96.6 bpm recorded for the entire intervention session, including balance activities and rest times) for a least some portion of the intervention. The home-based nature of the intervention may have been a limiting factor in achieving sufficient aerobic intensity.

Another important consideration for this intervention is specificity of training. The structure of the program was such that while the range of tasks (sit-to-stand, standing balance, and walking) was standardized across participants, the intervention programs were individualized so that specific areas could be addressed. These specific areas were reflected in the goals, which served as both a focus to the intervention and to

Table 4.
Unadjusted Descriptive Statistics Split by Treatment Group for Each Outcome at Assessments 1, 2, and 3[a]

Outcome Measure	Assessment 1 (Baseline) Scores $\bar{X}$ (SD)		Assessment 2 (8-Week) Scores $\bar{X}$ (SD)		Assessment 3 (16-Week) Scores $\bar{X}$ (SD)		Adjusted Estimate of Visit 2 and Effect Sizes From ANCOVA		Adjusted Estimate of Visit 3 and Effect Sizes From ANCOVA	
	Control Group	Intervention Group	Control Group	Intervention Group	Control Group	Intervention Group	Treatment Effect Estimate (95% CI) n=28	Effect Size[b]	Treatment Effect Estimate (95% CI) n=28	Effect Size[b]
9-item Physical Performance Test	24.1 (6.8)	19.1 (5.5)	23.3 (6.9)	19.1 (5.3)	24.6 (6.2)	19.7 (5.6)	0.5 (−2.0, 3.1)	0.08	0.07 (−3.1, 3.2)	0.01
UHDRS Total Motor Score	37.6 (13.8)	52.6 (17.3)	37.3 (10.4)	49 (15.4)	38.0 (12.8)	53.1 (15.3)	0.9 (−4.7, 6.4)[c]	0.06	2.9 (−1.9, 7.7)[c]	0.24
UHDRS Cognitive Scores	181.4 (54.8)	142.6 (55.2)	184.7 (46.3)	148.3 (52.5)	187.9 (54.1)	143.5 (42.5)	0.6 (−14.3, 15.4)[c]	0.02	−5.0 (−25.1, 15.2)[c]	−0.10
Berg Balance Scale scores	47.5 (11.6)	44.3 (8.2)	48.2 (12.4)	44.7 (10.3)	48.5 (10.9)	43.7 (10.5)	−0.009 (−2.9, 2.8)	0	−2.3 (−6.0, 1.4)	−0.24
Self-selected gait speed (m/s)	1.2 (0.5)	1.0 (0.3)	1.2 (0.4)	1.0 (0.4)	1.2 (0.3)	1.0 (0.4)	−0.0004 (−0.2, 0.2)	−0.001	0.03 (−0.12, 0.19)	0.08
Fast gait speed (m/s)	1.4 (0.5)	1.2 (0.4)	1.5 (0.5)	1.3 (0.6)	1.4 (0.3)	1.2 (0.4)	−0.005 (−0.2, 0.2)	−0.01	−0.04 (−0.22, 0.15)	−0.07
30-Second Chair Stand Test	10.2 (4)	7.7 (3)	10.8 (4.8)	9.7 (3.6)	10.5 (4.4)	9.7 (3.5)	0.8 (−1.1, 2.6)	0.16	1.3 (−0.7, 3.3)	0.25
Timed "Up & Go" Test	12.0 (6.7)	14.0 (6.7)	12.1 (9)	14.6 (10.0)	11.3 (6.2)	14.8 (8.9)	0.6 (−2.2, 3.4)	0.08	1.4 (−1.7, 4.4)	0.17
Vitality score	5.5 (1.3)	5.3 (1.4)	5.4 (1.0)	5.3 (1.4)	5.2 (1.1)	5.5 (1.6)	−0.2 (−1.0, 0.6)	−0.10	0.5 (−0.1, 1.1)	0.34
Hospital Anxiety and Depression Scale global score	8.3 (5.7)	6.5 (6.7)	7.5 (6.8)	6.8 (6.8)	6.9 (5.8)	5.8 (6.6)	1.2 (−1.2, 3.7)	0.19	0.8 (−1.9, 3.5)	0.11
HDQoL questionnaire summary scale	84.9 (16.6)	80.5 (23.3)	88.6 (14.3)	80.8 (21.7)	84.9 (19.1)	82.9 (20.3)	−3.7 (−9.0, 1.6)[c]	−0.28	3.9 (−4.1, 11.9)[c]	0.19
EQ5D Health Index	75 (12.6)	75.2 (26.2)	73.1 (16.5)	75.3 (24.5)	68.9 (14.2)	77.6 (25.6)	−0.02 (−0.17, 0.12)	−0.07	−0.02 (−0.12, 0.09)	−0.06

[a] Assessment 1 was performed at baseline, assessment 2 at week 8, and assessment 3 at week 16. The ANCOVA controlled for sex, disease burden score, Unified Huntington's Disease Rating Scale (UHDRS) Total Motor Score, Berg Balance Scale score, and score of variable in question at assessment 1 (complete case analysis). ANCOVA=analysis of covariance, HDQoL=Huntington's Disease Health-Related Quality of Life.
[b] Effect sizes are calculated from the adjusted treatment effect, and the standard error and sample size are calculated from the ANCOVA.
[c] n=27.

some degree a measure of success of the sessions. This approach may be optimal in complex diseases, such as HD and Alzheimer disease, in which a "one-size-fits-all" approach to management may not be most efficacious.[49] We, therefore, might not expect systematic change in similar outcome measures but rather individualized improvements in targeted activities, as seen in this study.

We can see that of multidisciplinary intervention studies conducted by other researchers in patients with HD, most of the interventions either were more intense or were conducted for longer durations.[18–20] Typically, these rehabilitation interventions have generically addressed impairments in physical fitness, strength, balance, and walking. None of these interventions have been specifically targeted or developed with a view to incorporating striatally directed training activities (in relation to specific deficits seen in HD). It has been suggested that aerobic exercise in combination with goal-directed training in individuals with neurodegenerative diseases, such as PD, has the potential to improve motor functioning through experience-dependent neuroplasticity,[50] which is an important direction for future research in HD.

Despite the small effect sizes seen in the standardized measures, the majority of individuals in the training group were able to achieve their mobility goals, and almost half of the goals achieved a much better than expected outcome. The process of goal setting using GAS was integral to the intervention, and despite a range of cognitive difficulties in this population, they were able to participate in the process of determining appropriate goals. Use of goal attainment is not recommended solely as an outcome measure, particularly when the scoring is not blinded, as was the case in this study.[51] However, goal setting is considered a core component of the rehabilitation process and has been suggested to have a significant impact on the relationship between the participant and the therapist.[52]

Finally, the outcome measures chosen for this study may not have been suitable or sufficiently sensitive to appropriately reflect any improvements in the intervention group. The majority of the interventions were focused on walking ability, as reflected in both time spent on this task and the number of goals set pertaining to walking. Our outcome measures did not encompass the broad spectrum of walking abilities. For example, we did not measure walking endurance or complex walking tasks such as dual-task walking or obstacle negotiation. Outcome measures used in future training studies could be extended to focus on these domains of assessment.

As physical interventions receive more attention in the field of HD, it is critically important to clearly define all of components in order to fully elucidate aspects of the intervention that have the potential to induce the most benefit.[53] The nature of the movement disorder and the cognitive limitations that may have an impact on skill acquisition and motor learning, along with the frequent behavioral issues, mean that developing interventions are all the more challenging. We have now developed and evaluated a well-defined intervention that incorporates a task-oriented approach and focuses on repetitive practice of specific skills. Although the high percentage of goal achievement, high retention and adherence rates, and the value and enjoyment perceived by the participants were encouraging, the lack of any change in standardized outcome measures warrants consideration of whether a larger-scale trial would be prudent. In our view, future studies in HD should incorporate not just greater intensity but also specifically directed activity to facilitate improved brain health (eg, via increased vascularization and neurogenesis) as well as modification of neural circuitry resulting from directed motor activities.

Dr Quinn, Professor Dawes, Professor Rosser, and Dr Busse provided concept/idea/research design. Dr Quinn, Professor Dawes, Dr Kelson, Ms Townson, and Dr Busse provided writing. Ms Debono, Dr Rickards, Professor Tabrizi, Dr Quarrell, Dr Trender-Gerhard, and Dr Busse provided data collection. Dr Quinn, Dr Kelson, and Ms Townson provided data analysis. Dr Quinn, Ms Debono, Ms Townson, and Dr Busse provided project management. Dr Quinn, Professor Dawes, and Dr Busse provided fund procurement. Professor Dawes, Professor Rosser, Dr Nemeth, Dr Rickards, Professor Tabrizi, and Dr Quarrell provided participants. Professor Dawes, Dr Nemeth, Dr Rickards, Professor Tabrizi, and Dr Quarrell provided facilities/equipment. Dr Rickards and Dr Quarrell provided institutional liaisons. Professor Dawes, Professor Rosser, Dr Nemeth, Dr Rickards, Professor Tabrizi, Dr Quarrell, Dr Trender-Gerhard, Ms Debono, and Ms Townson provided consultation (including review of the manuscript before submission).

The authors acknowledge all of the participants in the trial and their family members and caregivers. The authors thank all of the site staff who tirelessly worked on this trial. The authors acknowledge the European Huntington's Disease Network (EHDN), NISCHR Clinical Research Centre (NISCHR CRC) in Wales, and Dementias and Neurodegenerative Diseases Research Network (DeNDRoN) for their adoption and support of this trial. The authors also thank the members of the TRAIN-HD Steering Committee for their invaluable guidance and support: Professor Stephen Dunnett (Chair), Mrs Jacqueline Peacock, Mrs Adele Griffiths, Dr Valentina Tomasini, and Mrs Angela Hall.

Research funding for this trial was from the Huntington's Disease Association of England and Wales. Professor Dawes is funded by the Elizabeth Casson Trust and the NIHR Oxford BRC.

The project was approved by the Southeast Wales NHS Research Committee.

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The trial was registered with the International Standard Randomized Controlled Trial (clinical registration number: ISRCTN94284668).

DOI: 10.2522/ptj.20140123

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Appendix.

Intervention Sessions

The intervention was adapted for home use based on task- and context-specific programs. Each session was scheduled to last approximately 1 hour. The key elements of the program were individually tailored to the participants' specific impairments and activity limitations and modified to their home environment. Goal attainment scaling was used by the treating therapists to individually tailor the intervention. All interventions were required to contain the following elements:

A. Walking (suggested time=20 minutes). This task included specific practice of overground ambulation, inside and outside the home, in a variety of contextual environments. Progressions included obstacle walking, dual-task training, tandem walking, and stair climbing.
B. Sit-to-stand transfer (suggested time=10–15 minutes). This task included practice of sit-to-stand and stand-to-sit tasks to improve control of movement and safety as needed. Progression included altering seat height and seat surface, use of hands, use of weighted objects to hold, and altering speed of movement.
C. Standing activities (suggested time=15–20 minutes). Practice of activities in a standing position inside the home. Progression included reaching and lifting of objects of various heights and weights, throwing and catching balls of various sizes, and standing on an altered base of support.

The specific tasks chosen within each of the 3 elements listed above were determined based on the participant's ability as well as his or her specific goals. For example, if a participant had a goal of walking outside (eg, walking around the block), this would be a primary focus of the walking program, but the program also could include indoor walking and stair climbing.

Progression of tasks was generally from easier tasks, within the participant's capabilities, to more challenging tasks. The progression was guided by a taxonomy of tasks, which provides a framework for progressing tasks based on requirements of the performer (eg, use of hands or not), as well as the conditions of the environment (eg, open vs closed).[54]

The focus of the tasks was for participants to complete the tasks independently, with little, if any, manual assistance provided. Therapists utilized appropriate guarding techniques and provided assistance only as needed. Verbal cueing was kept to a minimum, focusing on goal-directed feedback and positive reinforcement of task performance. Specific movement-based information also was kept to a minimum but was provided when deemed essential to task performance (eg, foot positioning during sit-to-stand transfers).

During each session, participants wore a heart rate monitor. The intervention therapists closely monitored participants' heart rate during the intervention. Following each session, therapists completed written documentation outlining the activities performed, including repetitions, equipment used, and participant responses (subjective and objective).

In physical therapy research, it is important to maintain a level of consistency of intervention across participants while allowing for individualization based on each person's specific problems. The interventions outlined above served as a guideline to the development of each individualized program, which was developed in collaboration with the lead intervention therapist. This program was designed to minimize individual variations among therapists working at the 6 different sites. The lead intervention therapist was available on an on-going basis for consultation with the therapists regarding progression and adaptation of the developed program.

In addition to the home-based program, participants in the intervention group were requested to practice some of the exercises independently at least once a week between visits (agreed on in consultation with intervention therapist after first session). These activities were chosen from the same range of activities that were performed during the one-to-one therapy sessions (ie, sit-to-stand, walking, and standing balance activities). They were within the participant's capabilities, and therapists ensured that the participant could safely perform the exercises independently. The independent home program was reviewed each week by the therapist and participant, and modifications, including progressing activities and increasing repetitions, were made. Participants recorded their independent practice sessions in exercise diaries, which were reviewed by the intervention therapist each week. This aspect incorporated specific strategies to facilitate behavioral change in relation to participation in home exercises.

Upon completion of the first 8 weeks of the intervention, participants were encouraged to continue with the recommended independent exercises following completion of the physical therapy intervention. These activities

(*Continued*)

Appendix.
Continued

also were from the same range of activities that were performed during the one-to-one therapy sessions and were within the participant's capabilities to perform safely at home.

A major requirement of this multicenter trial was standardization across sites. As part of the development stage of the trial, the research team produced a training video that was used with the intervention therapists and blinded assessors. The video had 3 parts. The first was an overview of Huntington disease with specific focus on the issues relating to the disease that may affect the physical therapy assessment or treatment process. The second part focused on standardized outcome measures and how these measures should be conducted. The third part addressed the intervention delivery, including specific case demonstrations of intervention sessions. We also produced an associated handbook with summaries of key points for the research team and intervention therapists.