

SHORT COMMUNICATION

The effects of multidisciplinary rehabilitation in patients with early-to-middle-stage Huntington's disease: a pilot study

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Background and purpose: Despite advances in the understanding of Huntington's disease (HD), treatment remains symptomatic. Multidisciplinary rehabilitation, however, appears to impact disease progression. Here we show the feasibility, safety and efficacy of a 9-month multidisciplinary rehabilitation programme in a small cohort of patients with early-to-middle-stage HD.

Methods: Twenty patients with HD were assigned to two groups, equally matched for cognitive and motor scores. One group received the intervention, whilst the other served as control. The Unified-Huntington's-Disease-Rating-Scale-Total-Motor-Score was the primary outcome measure. Neurocognitive/psychological tests, body composition, postural stability, strength and quality of life assessments were secondary outcome measures.

Results: The intervention reduced motor and postural stability deterioration, with minor improvements in depression, cognition and quality of life. Significant gains were observed for fat-free mass and strength.

Conclusion: This pilot study suggests that a prolonged multidisciplinary rehabilitation programme in early-to-middle-stage HD is feasible, well-tolerated and associated with therapeutic benefit. Further explorative, larger studies are warranted.

Introduction

Huntington's disease (HD) is a neurodegenerative disorder characterized by progressive motor, behavioural and cognitive impairments. No cure or disease-modifying therapies exist [1], and treatment remains symptomatic. There is an urgent need, therefore, to identify therapies capable of impacting on the disease.

Multidisciplinary rehabilitation has improved gait, balance, depression, quality of life (QOL) and cognition in people with Alzheimer's and Parkinson's disease [2–4], yet few studies have examined multidisciplinary rehabilitation in HD. The most extensive study to-date examined the effect of an intense, intermittent 2-year programme in 40 patients with early-to-middle-stage HD [5]. The programme was

feasible, well tolerated and associated with positive motor benefits. Similarly, another study in HD demonstrated that 18 months of multidisciplinary care was feasible and perceived as beneficial [6].

We therefore designed and implemented a 9-month multidisciplinary rehabilitation programme, and assessed the effect on motor function, cognition, depression, body composition, postural stability and QOL in a small cohort of patients with early-to-middle-stage HD to evaluate its feasibility, safety and efficacy.

Methods

Design

Twenty patients with early-to-middle-stage HD were assigned to two equal groups based on cognitive and motor scores, with the intervention group randomly assigned. Research was conducted in accordance with the Declaration of Helsinki, with informed consent provided. Ethics approval was granted by the Human

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Research Ethics Committee of Edith Cowan University and the North Metropolitan Area Mental Health Service (NMAMHS). This project was registered with the Australian New Zealand Clinical Trial Registry (ACTRN12610000218099).

Participants

Participants in Perth, Australia were recruited utilizing NMAMHS databases. Inclusion criteria included a positive genetic test, clinical disease diagnosis [Unified-Huntington's-Disease-Rating-Scale-Total-Motor-Score (UHDRS-TMS) ≥ 5], ability to follow verbal instruction and perform sub-maximal exercise. Exclusion criteria included recent substance abuse, an unstable psychiatric or medical condition, or confounding neurological conditions. Medication was adjusted by physicians where necessary. Some individuals in the intervention (I) and control (C) groups commenced new medication: anti-psychotics (I 2; C 2); anti-depressants (I 0; C 1); anxiolytics (I 1; C 2); and anti-dyskinetics (I 0; C 1).

Outcome measures

The primary outcome measure was the UHDRS-TMS, performed by J.L. Secondary outcome measures, assessed over 1 day per time point, are detailed below. All assessors except occupational therapists (OTs) were blinded.

Body composition was quantified using dual-energy X-ray absorptiometry (Hologic Discovery A). Postural stability/balance assessments utilized the Sensory Organization Test (Neurocom SMART Balance Master) and the Activities-Specific Balance Confidence (ABC) Scale. Strength was assessed throughout rehabilitation. Neurocognitive/psychological tests included Symbol Digit Modalities Test (SDMT), Hopkins Verbal Learning Test-Revised (HVLT-R), D-KEFS Colour Word Interference Test and Trail Making Trials, and Beck Depression Inventory-II (BDI-II). The Goal Attainment Scale (GAS) examined achievement of patient-derived goals. QOL perceptions were evaluated using the SF-36v2 Health Questionnaire and Huntington's-Disease-Quality-of-Life-Battery-for-Carers.

Intervention

Following baseline data analysis, exercise physiologists and physiotherapists designed clinical and home-based exercise programmes, and OTs formulated personalized patient-focused programmes targeting deficits detected by psychologists.

The clinical exercise programme comprised supervised group sessions (9 months, once weekly; 5 min warm-up, 10 min aerobic exercise, 40 min resistance exercise, 5 min cool-down) in an exercise clinic. A tailored, self-monitored home-based exercise programme (6 months, three times weekly) was employed after careful instruction. OT programmes were provided for 1 h per fortnight, for 6 months.

Statistical analysis

Student's independent or paired *t*-tests assessed continuous variables. Mann-Whitney *U* and Fischer's Exact tests assessed ordinal variables. Results are reported as mean \pm standard error of the mean (SEM), with $P < 0.05$ considered significant. Effect size calculations (Cohen's *d*), performed using G*POWER Software Version 3.0.10 (Heinrich Heine University, Dusseldorf, Germany) [7], were interpreted as small ($d = 0.20$), medium ($d = 0.50$) or large ($d = 0.80$).

Results

Fifty-six patients with HD were approached, and 25 volunteered to participate. Three withdrew prior to randomization (frailty, falls, delusions) and two prior to completion (no wish to continue: I 1; C 1), with one participant transferred to the control group due to an adverse medication reaction. No statistical between-group differences existed for baseline demographics, depression, motor or cognitive assessments (Table 1). Participants demonstrated high adherence to clinical exercise and OT sessions (85%), and moderate adherence to the home-based exercise programme (56%). No adverse events were reported.

Rehabilitation produced a medium-large effect on UHDRS-TMS scores (Fig. 1a), impacting on chorea (medium-large effect) and tandem walking ($P = 0.015$) components. Significant between-group differences were observed for fat mass, fat-free mass, lower/upper body strength, written errors (SDMT) and for the walking-up-and-down-stairs component of the ABC-UK, with a large effect for the walking-around-the-house component (Table 1; Fig. 1b-d). Small-to-medium effects were noted for D-KEFS, HVLT-R, BDI-II, QOL and postural stability (Table 1; Fig. 1). GAS revealed partial or complete achievement of goals in seven out of nine intervention participants.

Discussion

This pilot study demonstrates the feasibility and safety of a 9-month multidisciplinary rehabilitation

Table 1 Participant characteristics (*n*; I = 9; C = 11)

Variable	Intervention		Control		<i>P</i>
Demographics					
Age (years)	53.8 ± 2.9		52.2 ± 2.6		>0.05
CAG (<i>n</i>)	43.1 ± 1.1		43.7 ± 0.7		>0.05
CAG index	399.0 ± 53.7		416.1 ± 23.3		>0.05
Body composition					
	Baseline	Final	Baseline	Final	<i>P</i>
Fat-free mass (kg)	52.1 ± 3.9	53.4 ± 4.2	55.4 ± 3.2	54.6 ± 2.9	0.047
Fat mass (kg)	21.6 ± 2.5	22.5 ± 2.6	21.9 ± 2.6	20.4 ± 2.6	0.014
Total mass (kg)	73.7 ± 4.6	75.8 ± 5.0	77.3 ± 3.8	75.0 ± 3.3	0.017
Body mass index (kg/m ²)	26.2 ± 1.3	26.9 ± 1.4	27.1 ± 1.3	26.7 ± 1.3	0.070
Bone mineral density (g/cm ³)	1.1 ± 0.0	1.1 ± 0.0	1.1 ± 0.0	1.1 ± 0.0	> 0.05
SDMT					
Written					
Correct	30.0 ± 4.9	27.4 ± 3.9	25.4 ± 3.3	23.3 ± 2.8	> 0.05
Incorrect	2.6 ± 0.8	1.2 ± 0.3	0.6 ± 0.3	1.4 ± 0.6	0.042
Oral					
Correct	35.8 ± 5.4	30.8 ± 5.3	25.9 ± 3.2	28.0 ± 3.4	> 0.05
Incorrect	3.0 ± 0.9	2.1 ± 0.8	5.6 ± 5.0	1.0 ± 0.4	> 0.05
HVLT-R					
Total recall	19.2 ± 1.8	16.3 ± 2.6	14.3 ± 1.7	14.7 ± 1.6	> 0.05
Delayed recall	5.9 ± 0.7	5.8 ± 1.3	5.4 ± 0.7	4.5 ± 0.7	> 0.05
Retention	80.3 ± 7.7	75.9 ± 10.8	85.3 ± 5.9	68.7 ± 10.1	> 0.05
RDI	8.3 ± 0.9	7.3 ± 1.3	7.3 ± 0.9	7.9 ± 1.0	> 0.05
D-KEFS					
TMT					
Visual scanning	34.3 ± 5.3	43.2 ± 6.7	31.4 ± 3.5	36.8 ± 4.2	> 0.05
Number sequencing	55.6 ± 6.2	63.8 ± 9.6	59.9 ± 5.8	57.5 ± 7.7	> 0.05
Letter sequencing	67.9 ± 14.0	71.0 ± 14.3	78.2 ± 17.0	65.2 ± 11.3	> 0.05
Number/letter switching	150.4 ± 21.7	144.3 ± 27.8	192.0 ± 27.1	122.2 ± 17.9	> 0.05
Motor speed	54.1 ± 9.4	61.4 ± 11.2	69.5 ± 11.8	60.8 ± 7.7	> 0.05
CWIT					
Colour naming	46.6 ± 6.7	50.63 ± 8.2	42.8 ± 4.4	47.8 ± 5.8	> 0.05
Word reading	33.8 ± 3.8	33.25 ± 4.1	30.2 ± 3.1	29.9 ± 3.7	> 0.05
Inhibition	90.9 ± 16.9	90.9 ± 17.0	87.3 ± 7.0	86.2 ± 8.1	> 0.05
BDI-II	10.8 ± 3.2	5.6 ± 1.6	12.9 ± 2.6	10.0 ± 2.5	> 0.05
ABC-UK					
Walking around the house	81.1 ± 8.7	87.1 ± 6.0	81.4 ± 5.9	75.6 ± 9.6	0.077
Walking up or down stairs	63.3 ± 12.9	72.7 ± 12.6	71.8 ± 8.2	63.3 ± 13.4	0.024

ABC-UK, Activities-specific Balance Confidence Scale; BDI-II, Beck Depression Inventory-II; CAG, cytosine-adenine-guanine; CWIT, Colour Word Interference Test; D-KEFS, Delis-Kaplan Executive Function System; HVLT-R, Hopkin's Verbal Learning Test-Revised; RDI, Recognition Discrimination Index; SDMT, Symbol Digit Modalities Test; TMT, Trail Making Trials.

programme in 20 patients with HD. Relative to control subjects, intervention recipients exhibited reduced motor and postural stability deterioration, and significant increases in fat-free mass and strength. Strength improvements have not been reported to-date, perhaps because previous programmes spanned only 8 weeks [8]. The minimal impact on cognitive outcomes observed here may be obscured by lack of sensitivity of testing procedures, normally requiring large sample sizes [9]. Changes in QOL perceptions reflected functional outcomes.

Although positive, the pilot study has significant limitations, including lack of long-term follow-up (precluding examination of a carry-over effect on ces-

sation), limited sample size and low frequency of supervised rehabilitation, optimally requiring two–three sessions per week. Assessment tools may also lack sensitivity to detect subtle changes.

In conclusion, we demonstrate that patients with early-to-middle-stage HD can successfully participate in prolonged multidisciplinary rehabilitation as an adjunct to medication, and further explorative, larger studies are warranted. Encouragingly, despite the small sample size and low exercise frequency, small improvements were detected. Future studies would benefit from more frequent rehabilitation, including a high-intensity aerobic component [10] to maximize cognitive improvements.

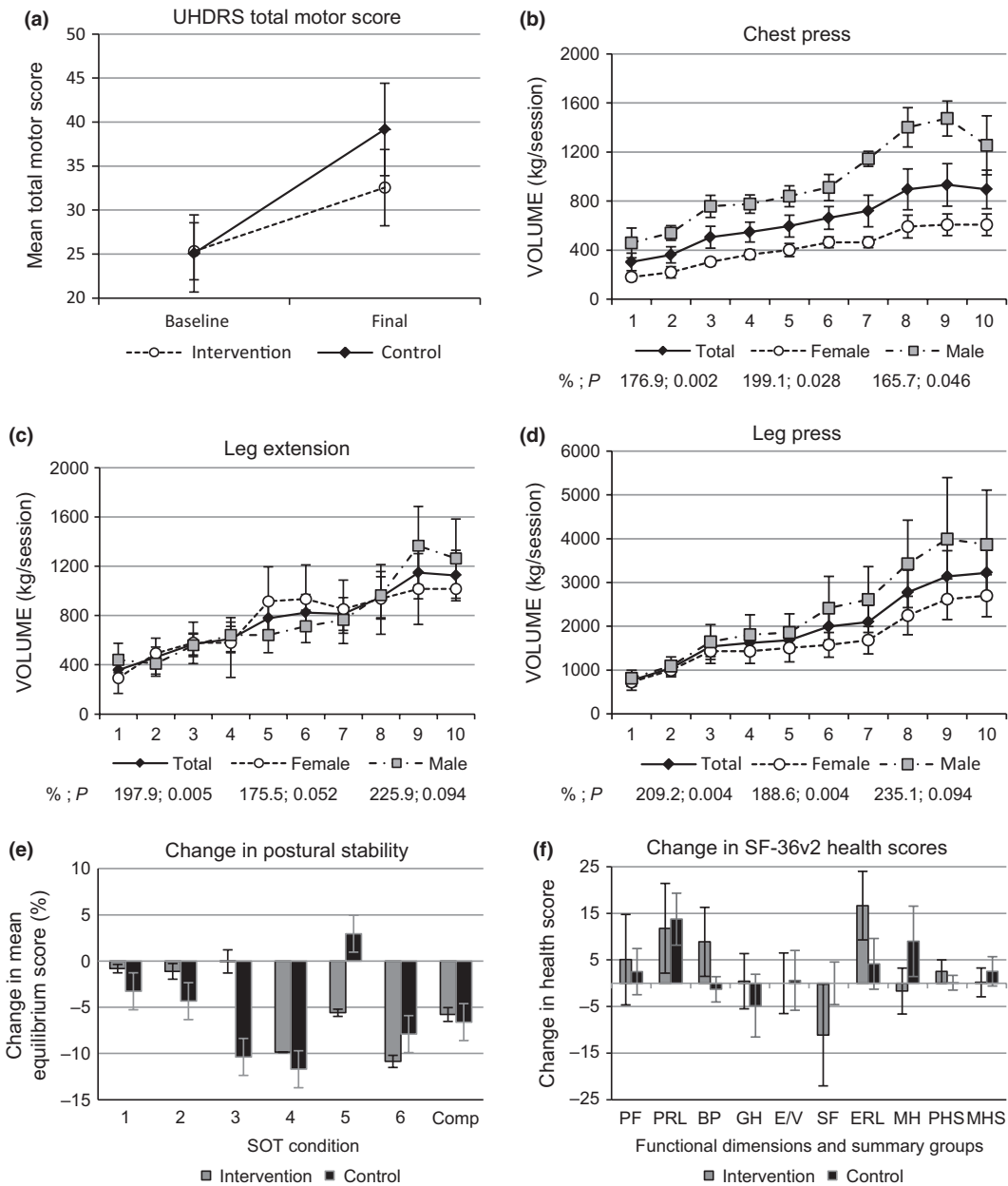


Figure 1 (a) Unified-Huntington’s-Disease-Rating-Scale-Total-Motor-Score (UHDRS-TMS) at baseline and final assessment (n ; I = 9; C = 11). (b–d) Strength outcomes for upper and lower body (n ; I = 9; C = 11); values are shown for the intervention group as a whole, and for female and male sub-groups to indicate gender response. Percentage of overall change (%) and statistical significance (P) from commencement of maximal training (point 3) to final assessment are also indicated. (e) Changes in postural stability at final assessment relative to baseline (n ; I = 9; C = 11). (f) Changes in SF-36v2 health scores at final assessment relative to baseline (n ; I = 9; C = 11). (Functional Dimensions: PF, Physical Functioning; PRL, physical role limitations; BP, body pain; GH, general health; E/V, energy/vitality; SF, social functioning; ERL, emotional role limitations; MH, mental health. Summary Groups: PHS, physical health summary; MHS, mental health summary)

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