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Physiotherapy for Patients with Huntington´s Disease:

Effects of a Treatment Program with focus on balance and transitions and the Intercorrelation between Assessment Tools

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ABSTRACT

Objective: To evaluate the effect of a physiotherapeutic exercise programme for patients with Huntington's Disease (HD) concerning motor function and disability, balance and fall related self-efficacy, and to investigate the correlation between the seven assessment tools.

Participants: Twelve persons with genetically confirmed HD at an early or middle stage of the disease and with a mean age of 52 (16) years.

Methods: The intervention comprised physiotherapy (PT) focused on training of transitions, balance and fall-related self efficacy, twice a week for six weeks. Each treatment session lasted for one hour, was individual and took place at an out-patient clinic. Baseline assessments including five clinical tests and two questionnaires were made 6 and 0 weeks prior to the intervention and 0 and 6 weeks after the intervention.

Outcome measures: Motor function and disability were measured with the Unified Huntington's disease Rating Scale; the Total Motor Score and the Total Functional Assessment. Static and dynamic balance was measured with the One- leg stance-test, the Timed Up and GO Test, the Figure of Eight-test and the Berg Balance Scale. Fall-related self-efficacy was measured with the Falls Efficacy Scale.

Results: The physiotherapeutic exercise programme demonstrated a significant improvement in balance measured with the Berg Balance Scale ($p=.045$). The significant correlation coefficients between the different measurements of motor function, disability, balance and fall related self-efficacy ranged from 0.68 to 0.87.

Conclusions: The contents of the out-patient clinic physiotherapeutic exercise programme, with a focus on balance and transitions, seemed to have clinical relevance. PT in different kinds of settings should be studied further to get a better knowledge about the effects of PT and physical activity at home, at an out- patient setting or at the hospital for patients with HD.

Key Words: Huntington's disease; Physiotherapy; Motor function; Disability; Balance; Fall- related self efficacy.

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1. INTRODUCTION

1.1 Background

Huntington's disease (HD) is an inherited, progressive neurodegenerative brain disorder. At present, there is no cure for the degenerative process. Therefore, offering optimal treatment and care for patients with Huntington's disease is important. Rehabilitation and training, enriching environment, optimal care, support of relatives and staff are important fields that need to be developed.

The prevalence in Europe has been reported to be 4-9 per 100,000 inhabitants (1). In Sweden, about 1000 patients have the disease, and another 5000 persons are at risk (2). Most patients develop symptoms of HD in their middle, adult life with a mean age onset around 40 years. The symptoms start often between 30 and 60 years, but approximately 10 % of the patients have onset before 20 years (Juvenile HD) and 10 % have onset after the age of 55 (3). HD is characterized by an autosomal dominance. This means that a child to a sick parent is at 50% risk to get the disease. Only a child, who inherits the HD gene from one of the parents, is at risk of developing the disease. There are no gender differences regarding illness inheritance and illness development (4).

The disease leads to neuronal cell loss preferably in the basal ganglia. There is also a degenerative cell loss in cortex, thalamus and hypothalamus. These neuronal cell changes will eventually lead to a triad of symptoms consisting of motor, cognitive and psychiatric symptoms typical for HD. According to what neurons are affected the symptoms will vary. Motor symptoms can consist of gait changes, chorea, dystonia, decreased coordination, balance deficits and falls, voluntary movement abnormalities and bradykinesia (5). At the beginning of the the disease, the symptoms are mild with for instance slight gait changes and chorea. In the later stages chorea and dystonia can be increased and in the later stages, there might be severe symptoms of bradykinesia, rigidity (and sometimes spasticity), movement abnormalities, dysarthria and dysphagia (4, 5). Incontinence is common. While involuntary choreatic movements are the most

characteristic and prominent motor symptom of HD, bradykinesia, dystonia, sequencing problems, and motor impersistence are often more disturbing for the patients (6,7,8,9,10). Cognitive symptoms can vary from difficulties with complex thinking tasks to problems with planning, sequencing, organizing and prioritizing tasks. Intellectual decline, memory loss, perceptual problems, lack of insight or self awareness and difficulties with dual tasking may occur later in the disease. Psychiatric symptoms might start with depression, aggression, and irritability. During the course of the disease, sadness, apathy and impulsivity may occur. At a late stage of the disease, symptoms like antisocial and suicidal behaviour, paranoia, delusions, hallucinations and delirium can be part of the symptoms (5, 11). The combination of this triad of motor, cognitive and psychiatric symptoms makes HD complex for patients as well as for all people meeting a patient with HD.

HD is divided into four main stages: pre-manifest, early, middle and late. Based on the Total Functional Capacity Score (TFC), patients can be classified into early, middle and late stages of the disease. Early stage corresponds to stage 1, middle stage corresponds to stage 2 and 3, and late stage corresponds to stage 4 and 5 (12). Motor function during the different stages can be described in four phases. The premanifest phase (stage 1) means that a patient has a positive gene test for HD, but has not yet developed any clinical symptoms. The early stage (stage 2) includes motor symptoms with minor involuntary movements like chorea, decreased coordination and slight increase of tone. Gait and transfers might be affected already at an early stage of the disease, as well as in later stages (13). At the middle stage (stage 3) involuntary movements are enhanced, i.e. chorea, and dystonia. Voluntary motor control becomes more and more difficult to perform, balance problems are evident and there might be a risk of falling (12). Fall-related complications may result in hospitalization and/or a nursing home placement (14). At the late stage (stage 4), motor symptoms like chorea and dystonia increase, but also rigidity and Parkinsonism dominate more and more with time (11,12).

1.2 Physiotherapy for patients with Huntington's disease

Physiotherapy (PT) is an important component in the multidisciplinary care of patients with HD (15,16,17,18). To ensure an evidence based physiotherapeutic treatment for patients with HD, it is of urgent need to investigate the effects of PT for patients with HD. There are several well designed studies assessing the effect of PT within basal ganglia disorders in Parkinson's disease (PD). Some of these studies showed positive impact of PT on motor function (19,20,21,22,23), and on physical functioning, health-related quality of life, strength, balance and gait (24,25). Regrettably, scientific evidence proving the effect of PT for patients with HD is not yet convincing. Very small amount of evidence about PT within HD has been described in two reviews, but they have methodological weaknesses (26, 27). One review (26) concluded that there is some low level of evidence for physiotherapy for deficits in balance, muscle strength and flexibility. The authors stated that there is insufficient evidence for strong recommendations regarding the usefulness for physiotherapy, occupational therapy or speech pathology for HD patients. In the other review (27), the authors highlighted the need for more systematic studies concerning PT for HD patients and the need for good objective assessment tools. Even if there are some older studies about PT in HD (29-31) and some more recent (32-34) there is still a need for more studies evaluating the effect of PT in HD regarding both assessment and treatment. Peacock performed a before and after observational study (29) with 10 patients who received PT once a week for 12 weeks. The intervention included therapist led exercises for functional ability, flexibility, coordination, balance, breathing control and strength. All participants improved flexibility, coordination and breathing control, but the outcome measures being used are not presented in detail, and validated outcome measures were not included (29). Binswanger (30) made a pilot study with five patients in a home based setting where a physiotherapist delivered individually tailored programmes. Intervention included neurophysiologic techniques, range of motion exercises, strengthening exercises, gait rehabilitation and breathing control, but the intervention was not presented in detail. Outcome measures were not clearly defined. Results showed increased alertness, ability/willingness to engage in activities, and improved balance leading to safer ambulation among the enrolled patients (30). A single case study with a home-based observational

design (32) described a 14 weeks video based home training programme with warm up exercises, leg- and arm exercises, floor exercises, and cools down. Used outcome measures were the Falls Efficacy Scale (FES), the Berg Balance Scale (BBS) and the Unified Huntington's Disease Rating Scale – Total Motor Score (UHDRS-TMS). The results showed a reduced level of disability, reduced number of falls and a higher walking speed. Improvement was seen at FES, BBS and UHDRS-TMS (32).

A qualitative study where physiotherapists working with HD, either were interviewed (n=8) or filled out questionnaires (n=49), identified three main themes that need to be developed within the PT field in HD. The three main themes were: 1. Insufficient use of routine outcome measures for PT in HD; 2. Under-utilization of PT in HD (particularly in the early stages); 3. Management of falls and mobility-deficit progression (35).

The European Huntington's Disease Network (EHDN) is a European network for professionals as well as for patients with HD and their relatives. Within the EHDN, working groups are established. One of them is the Motor Phenotype Working Group, and another is the Physiotherapy Working Group.

The EHDN has a Scandinavian Group, and there is also a national Swedish HD Group. In Sweden there are multiprofessional teams for HD patients in Stockholm, Uppsala, Umeå, Göteborg and Lund. The team in Uppsala was established in 1991, and consists of a neurologist, a nurse, a neuropsychologist, a physiotherapist, an occupational therapist, a dietician and when needed a social worker and a speech therapist. The Huntington clinic of the University Hospital in Uppsala has regular contacts with approximately 50 patients in the region of Uppsala and Stockholm (2).

1.3 Definitions of terms

Below, there are some definitions of terms that are central aspects of physiotherapy for HD patients. The terms are postural control, postural orientation, postural stability, and balance (static and dynamic).

Postural control is the ability of a human being to be able to control balance, in contrast to an inanimate object. The ability of postural control is necessary to

maintain posture in activity (36). Postural control involves the control of the body position in space for the purpose of stability and orientation. Stability and orientation are two very important aspects of postural control. Postural control requires a complex interaction of musculoskeletal and neural systems and coordination. Even cognitive aspects have an influence on postural control (37).

Postural orientation is the ability to maintain an appropriate relationship between the body segments and between the body and the environment when performing a task (37).

Postural stability is a type of balance, i.e. the ability to maintain the body in equilibrium. At rest it is called static equilibrium, and at steady state motion it is called dynamic equilibrium (36).

The term balance (or equilibrium) is defined as the state of an object when the resultant load actions (forces or moments) acting upon it are zero (36).

Static balance is the ability to maintain balance in a static situation. It is related to the position of the centre of mass (even called the centre of gravity), and to the area of the base of support of the object. The object is in balance, when the line of gravity falls within the body of support of that object. If the line of gravity is displaced, the object becomes unbalanced and might fall (36).

Dynamic balance is closely related to the ability of having postural control and voluntary movement. It is the ability to keep balance while moving between objects. It is a matter of achieving the line of gravity within the base of support while moving, for example ambulation like transferring from lying to sitting, from sitting to standing and from standing to walking (37).

1.4 Outcome measures (i.e. Assessment tools)

There is no consensus between physiotherapists of today, on what outcome measures that should be used in the clinic or in research. Hence, there is an obvious need for finding suitable assessment tools for patients with HD in order to be able to evaluate PT treatments. There are several assessment tools for assessment of balance and transitions that physiotherapists can use, and to correlate some of the most appropriate of them would be important in order to be

able to select only a few tests that really give the optimal information within the HD field.

Only a few outcome measures commonly being used in physiotherapy have been tested on patients with HD (33, 34, 38, and 39). Rao et al. (33) examined validity and responsiveness of three clinical tests of mobility and balance in HD. The tests were The Berg Balance Scale (BBS), Timed Up and Go test (TUG) and Functional reach test (FRT). The results showed that the FRT, TUG and BBS scores were correlated with quantitative gait measures. All tests were correlated with functional limitations, and all tests were responsive to disease severity. In another study, mobility and falls in HD were studied (34). BBS and TUG were used to measure balance. Also, 10 meters walking speed and data about falls and stumbles in the previous 12 months were used. Results showed that recurrent fallers had worse balance scores on BBS and TUG than the non fallers. Patients with HD had an increased risk of falls if TUG was more than 14 seconds and BBS score lower than 40 points (34). One observational study (38) investigated isometric muscle strength of six different muscle groups in the lower limbs with a hand held dynamometer. Results showed that reliability of strength testing was very good (ICC 0.86 to 0.98), and that HD patients had about half the strength of healthy matched controls. UHDRS motor scores and strength scores correlated significantly (38). A Dutch study investigated falls and gait disturbances in HD (39). Balance and gait measures (UHDRS-TMS and BBS) were compared between patients and a healthy control group. A high proportion of falls (72.5%) caused minor injuries. Fallers showed higher scores for chorea, bradykinesia and aggression as well as lower cognitive rates compared to non fallers (39). The Unified Huntington's Disease Rating Scale (UHDRS) is a clinical rating scale which is commonly used at the clinic as well as in research in the medical field (40). Lately, the scale also is being used in PT research (32, 38, 39). However, the UHDRS scales are not PT specific.

1.5 The hypothesis of the study

The hypothesis of this study was that the set of physiotherapeutic exercises used in the study would improve motor function and balance in patients with HD and might have an impact on the patients' level of disability and fall related self-efficacy.

1.6 Aim of the study

There were two aims of the study; 1. To evaluate the effect of a physiotherapeutic exercise programme for patients with HD concerning motor function and level of disability, balance, and fall related self-efficacy, 2. To investigate the correlation between the seven assessment tools used in the study.

1.7 Questions

1. To what extent did motor function, level of disability, balance and fall related self-efficacy measured with UHDRS-TMS, UHDRS-Functional Assessment, One Leg Stance, Timed Up and Go, Figure of Eight- test, Berg Balance Test and Falls Efficacy Scale change during baseline with measurements 6 and 0 weeks prior to the intervention (test 1 and 2)?
2. To what extent did over all motor function measured with UHDRS-TMS and level of disability measured with UHDRS-Functional Assessment change in patients with HD from baseline to post intervention and at follow-up?
3. To what extent did static balance measured with One Leg Stance change in patients with HD from baseline to post intervention and to follow-up?
4. To what extent did dynamic balance and walking measured with timed up-and-go-test, Figure of Eight- test and Berg's balance test change in patients with HD from baseline to post intervention and to follow-up?
5. To what extent did fall related self-efficacy measured with Falls Efficacy Scale change in patients with HD from baseline to post intervention and to follow-up?
6. To what extent did the used instruments correlate with each other in patients with HD?

2. METHODS

2.1 Design

The study had a quasi experimental within-group design as an intervention effect without a control group was evaluated. The study had also a correlational design.

2.2 Patients

Inclusion criteria

Genetically verified HD, patients should be at an early or middle stage of the disease (stage 2 and 3), be adult (over 18 years old), and be able to participate in treatment at the center twice a week for six weeks, and be able to take part in four assessments at the study center. Patients should be able to give written informed consent to participate in the study and should have no change of neurologic and psychiatric medication 4 weeks prior to beginning of the trial.

Exclusion criteria

Patients who already were receiving regular PT within the last three months, were at a premanifest (stage 1) or at late stage of the disease (stage 4), suffered from Juvenile HD or were suicidal or exhibited signs of active psychosis.

Patients with HD were recruited from the outpatient clinic of the Department of neurology at the University Hospital in Uppsala, Sweden.

2.3 Patient characteristics

Among a total of twenty symptomatic patients with HD fulfilling the inclusion criteria, eventually eighteen patients wished to enter the study. Out of the eighteen patients who were enrolled, there were only twelve patients who completed the study. The patients who completed the programme had a mean age of 53 years (SD=16, range 32.0-83.0). Seven of the patients were women and five men. Eight patients were in the early stage of the disease (stage 1), and four patients were in the middle stage (stage 2 and 3). Eight were married/living together, and four were living alone (one was single, two were widows and one was divorced). All of the patients had family with whom they had contact. Four of the patients had a job; one worked full time, three patients part time and had sick

leave part time. Four patients reported other diseases such as high blood pressure, lumbago and eczema. At least five of the patients reported previous falls, or risk of falls, before the study according to medical charts. See Table 1.

Table 1: Patient characteristics.

Variable (number of)	Participating patients (n=12)
Mean age (SD), range	53 (16), 32-83
Women/men	7/5
Early stage/ middle stage	8/4
Married or living together	8
Living alone	4
Family in contact	8
Treatment in Uppsala/Stockholm	7/2
Treatment in Eskilstuna	2
Treatment in Gnesta	1
Having a job/not having a job	4/8
Working full time/part time	1/3
Full time sick leave	4
Retired	4
No other diseases	8
Other diseases	4
Reporting previous falls	5

2.4 Outcome measures

The seven assessment tools that were used included motor function, level of disability, static and dynamic balance, and fall related self- efficacy. These outcome measures will be presented below.

2.4.1 Motor function and level of disability

The Unified Huntington's Disease Rating Scale (UHDRS) is a clinical rating scale which is commonly used at the clinic as well as in research (40). The scale is aiming to quantify the severity of the patients with HD. The scale consists of four domains: motor function, functional capacity, cognitive function and behavioral abnormalities (psychiatric function). Motor function of the UHDRS assesses motor features of HD with standardized ratings. The functional assessments include Total Functional Capacity Score, Total Functional Assessment and The Independence Scale. There is a high degree of internal consistency between the four domains (40). In this study, only the scale for motor function (UHDRS-Total Motor Score) and functional capacity (UHDRS-Total Functional Assessment) were used.

Unified Huntington's Disease Rating Scale - Total Motor Score (UHDRS-TMS) (40)

The UHDRS motor function scale consists of 15 items with a scale ranging from 0-4. 0 is normal and 4 mean severe symptoms. The total motor score is 60, where 0 points is normal and 60 points mean a severe, advanced stage of the disease. The 15 items to be tested are ocular pursuit, saccade initiation, saccade velocity, tongue protrusion, finger taps, pronate/supinate-hands, Luria, rigidity-arms, bradykinesia-body, maximal dystonia, maximal chorea, gait, tandem walking, and retropulsion pull test. After the rating, the level of diagnostic confidence should be assessed, where a 0 means no abnormalities and a 4 means motor abnormalities that are unequivocal signs of HD. No validity studies have been made, but one study showed a high degree of internal consistency within each of the four domains of the UHDRS (40). There were also significant correlations between the domains of the UHDRS, except for the behavioral score, and the interrater reliability for the motor scores was good (40).

Unified Huntington's Disease Rating Scale - Total Functional Assessment (UHDRS-TFA) (40)

The UHDRS-TFA measures patients' level of disability and functional capacity. The scale contains 25 questions that can be answered with yes or no. A no answer gets 0 points and a yes answer gets one point and maximum points are 25. When the score is added, the patient's level of disability is calculated in percent. 100 % means that no special care is needed. 10% means tube fed, and total bed care. The questions include whether the patient can work (3 questions), can manage his finances, can shop groceries and handle money transactions, can supervise children, can drive a car, can manage housework, can prepare meals, and can use the telephone without any help. Three questions include personal care and two questions the ability to use public transportations and to walk in the neighborhood without help. The last seven questions ask whether the patient can walk without falling or without help, about transitions at home, using the toilet without help, and whether the patient's care still can be provided at home. It can be marked on the scale whether it was the patient who answered the questions, or whether it was the patient with help of family/companion. Concerning validity, research indicates that the scale might be of help when tracking changes in the clinical features in HD over time (40). The reliability of the test has not yet been reported (40).

2.4.2 Outcome measure for static balance

The one- leg stance- test (OLS) (41)

The patient is asked to stand on his right leg with eyes open and closed (if possible). Then the left leg is tested in the same way. The test is timed in seconds. If the patient stands >30 seconds, the test is stopped. In this study, the patients were standing in a corner with the investigator in front of the patient for safety reasons. Patients were only tested on the floor (no cushions for example). Patients were instructed to let their arms hang vertically along the sides of their body during the test, if possible. Validity of this test was not described, but reliability tests show good inter-rater and test-retest reliability in healthy patients (42), and in disabled and non-disabled elderly (43). In this study, only standing with eyes open was used.

2.4.3 Outcome measures for dynamic balance

Timed Up and Go Test (TUG) (44)

Patients were instructed to stand up from a chair, walk 3 meters, and then turn around, walk back to the chair and sit on the chair again. The whole test is timed. Assisted devices were allowed if needed and regular footwear should be used. No physical assistance was given. The test was repeated twice, and the average score for both tests was documented. Validity is not tested, and test-retest reliability tests show an ICC of 0.85 (in patients with PD) and a minimal detectable change in 11 sec (in patients with PD) (45).

The Figure of Eight- test (46)

The patient walks in a figure of two circles put together to form an eight (inner diameter 1.5 m and outer diameter 1.8 m). The space between the lines should be 15 cm. The patient was instructed to walk between the lines of the figure twice at a comfortable speed or at a speed given by a metronome. The number of incorrect steps outside the line was counted and time in seconds was measured. Incompleted tests were noted. In this study, patients walked without shoes at their self-chosen speed and step length. Steps outside the line, but not on the line, were counted as incorrect. Validity is not tested, but it has been shown good inter-rater and test-retest reliability for elderly women. Intraclass correlation coefficient (ICC) was 0.93 (46).

Berg Balance Scale (BBS) (47)

This is a 14-item scale, and it was designed to measure balance and risk of falling in older adults in a clinical setting. The subtests of the scale consist of various activities related to postural control. The subtests include static postures (e.g. sitting, standing), transitions (e.g. sitting to standing) and challenging positions (e.g. standing with eyes closed). The equipment needed is a ruler, two standard chairs, footstool or steps, stopwatch and a 15 ft walkway. Quality of performance is scored on a five-point ordinal scale ranging from 0-4, where "0" indicates the lowest level of function and "4" indicates the highest level of function. Score ranges between 0-56. If the patient has 41-56 points, there is a low fall risk; 21-40 points mean a medium fall risk, 0 and 20, a very high risk of falling. The test takes

about 15-20 minutes to administer. Validity has not been tested in HD, and reliability test shows an ICC less than 0.90 (PD) (45), and a minimal detectable change of 5 pts (PD) (45).

2.4.4 Outcome measures for fall related self-efficacy

The Falls Efficacy Scale (FES) (48)

FES has been used to detect changes in the patient's own perceptions of his/her balance. FES can measure fear of falling in individuals and reflects subjective balance. It can be seen as a complement to objective balance assessment. FES consists of ten activities that should be scored how confident the patient is to do certain activities without falling. The scale ranges from 1=very confident to 10=not confident at all. A total score > 70 indicates that the patient has a low fall-related self-efficacy. The activities measured include taking a bath or shower, reach into cabinets or closets, walk around the house, prepare meals, get in and out of bed or a chair, answer the door or telephone, getting dressed and undressed, personal grooming and getting on and off the toilet. Validity has shown to be good on healthy elderly patients, and reliability tests show good test-retest reliability (Pearson's correlation 0, 71) in healthy elderly patients (48).

2.5 Intervention

The physiotherapeutic intervention in this study aimed to improve motor function, level of disability, balance and fall-related self-efficacy. The focus of the treatment was laid on training of static (such as standing on one leg) - and dynamic balance (such as transitions and walking), postural training and orientation (such as alignment of posture and coordination) and relaxation (see appendix 1). The treatment programme was set up and formed by the author who is an experienced PT in HD. For an overview of the treatment being used in the study, see appendix 1. Patients received PT twice a week for six weeks. Each treatment session lasted for one hour, and each treatment was individual and took place at an out-patient clinic. Each patient had the same physiotherapist throughout the whole study. One whole session with a patient has been videotaped to make it possible to see the programme performed "live" in detail with a patient.

2.6 Procedure

Both the assessments and the intervention took place during the summer and fall of 2008 and the whole year of 2009. All assessments were conducted at the University Hospital of Uppsala, Sweden.

Baseline assessments were made 6 weeks and 0 weeks prior to the intervention. Then, there was a 6 week long treatment period (intervention). Thereafter, the same tests, as used before the intervention, were used 0 and 6 weeks after the intervention, see Figure 1.

Figure 1. Time schedule for assessments

Test 1..... Test 2 - treatment for 6 weeks- Test 3 Test 4
6 weeks.....0 weeks _____ 0 weeks 6 weeks

All the assessments were made by the same investigator, who was not involved in the treatment part of the intervention. The tests were performed in the following order for practical reasons: UHDRS-TMS, UHDRS-TFA, TUG, Figure of Eight, BBS, The one- leg stance- test, FES. Some of the patients had travelled far (150-200 km) to come to the testing, so the testing had to be done even if the patient was tired when the testing started. On an average, each testing procedure took approximately two hours. Parts of the assessments have been video recorded.

The major part of the physiotherapy treatment took place at the University Hospital in Uppsala at the Department of Physiotherapy (7 patients). Those patients, who were treated in Uppsala, received their PT treatment by the same physiotherapist throughout the whole study. Due to the home city of the patient,

some treatments were made in other Swedish cities (5 patients). It would have been too tiring to travel twice a week for physiotherapy treatment for those patients. Therefore, treatment at their home hospitals was arranged. Two patients received their treatments at the hospital in Eskilstuna, one patient got treatment at an outpatient clinic in Gnesta, and two patients were treated at two hospitals in Stockholm.

The five physiotherapists, who took part in this study from outside of Uppsala, were taught by the physiotherapist in Uppsala how the treatment was going to be performed. They were offered a visit at their home clinic or a visit in Uppsala, in order to go through the material and discuss details in the treatment sessions. However, the physiotherapists involved in these three cities thought that telephone consultations and discussions based on the treatment programme over the phone or e-mail was sufficient throughout the study to be able to do the treatment reliable and in the same way.

Compliance to treatment sessions was good among the patients. 6 patients came to all 12 sessions, 4 patients came to 10 sessions, and 2 patients came to 9 out of the 12 sessions. The average compliance was 91%.

2.7 Ethics approval

Ethics approval for the study was obtained through the Regional Ethical Committee of Uppsala (2008-05-14; Dnr 2008/092). If patients agreed to participate, they were invited to a screening visit. Written informed consent was obtained prior to enrollment in the study.

2.8 Statistical Analysis

To analyze sample characteristics for patients, descriptive statistics was used. The effect of intervention was analyzed with Friedman ANOVA for ordinal data and ANOVA repeated measures for continuous measures. To ensure a stable baseline between test 1 and test 2, a nonparametric test for related samples was made with Wilcoxon Signed Ranks Test. In addition, correlation analysis was performed by Spearman correlation coefficients. A correlation exceeding 0.70 was

considered high according to Polit and Beck (49). Statistical significance was set to $p \leq 0.05$. The statistical analysis was performed using SPSS.

3. RESULTS

3.1. Baseline stability

At baseline, there was no significant difference between results at test 1, (6 weeks prior to intervention) and test 2 (0 weeks prior to intervention), except for the test One Leg Stance on the left foot (OLSL) and the FES. OLSL significantly improved from test 1 to test 2. OLSL had a mean value of 12.24 and median of 7.00 at test 1 and a mean value of 11.29 and median of 7.55 at test 2 ($p = 0.005$). Patients had a lower fall-related self-efficacy at test 1 than at test 2, with a mean value of 83.67 and a median value of 94.00 at test 1 and a mean value of 67.92 and a median value of 79 at test 2 ($p = 0.005$). Since there was mostly no significant difference between results at test 1 and test 2 at baseline, only results from test nr 2 will be presented in the following.

3.2. Effects of the Treatment Programme

All 12 patients conducted test nr 2 and 4, but in test nr 3 there were only 11 patients completing the test. The results from baseline to post intervention and at follow-up (test 2, 3 and 4) are presented in table 2 for each assessment tool. *Motor function* measured with UHDRS-TMS had a positive development from baseline to post intervention and at follow-up, but the change was not significant (p -value 0,076). *Disability* measured with UHDRS-TFA showed a slight non-significant improvement. *Static balance* measured with OLS and *dynamic balance* measured with the TUG improved from baseline to post intervention and to follow-up but the change was not significant. *Dynamic balance* measured with the Figure of Eight- test, in seconds as well as number of steps, did not indicate any improvement from baseline to follow-up. BBT, on the other hand, showed a significantly positive change from baseline to post intervention and to follow-up with a p -value of 0,045. Especially at test number 3, scores were higher and the performance better, but this was also the case after test 4. Fall related self-efficacy, measured with FES, showed a non-significant change from baseline to post intervention and to follow-up (see table 2).

Table 2: Median values for motor function, disability, balance, and fall related self-efficacy before the training starts (test 2), after 6 weeks of training (test 3) and after 6 weeks follow-up (test 4).

Variabel	Test 2 (n=12)		Test 3 (n=11)		Test 4 (n=12)		p-value
	Median	(Q1-Q3)	Median	(Q1-Q3)	Median	(Q1-Q3)	
UHDRS-TMS	46,00	(20,00-70,00)	41,00	(15,00-64,00)	44,00	(21,00-68,00)	0,076
UHDRS-TFA	19,00	(13,00-22,00)	21,00	(11,00-23,00)	20,00	(10,00-23,00)	0,892
BBS	53,00	(37,00-54,00)	55,00	(49,00-56,00)	54,00	(44,00-56,00)	0,045*
OLSR	4,40	(1,12–9,87)	10,50	(2,22–30,00)	11,65	(1,87–26,02)	0,055
OLSL	4,00	(2,00–26,00)	6,30	(1,80–30,00)	12,80	(0,00-30,00)	0,889
EIS	17,50	(11,10-17,50)	18,10	(12,90-26,60)	15,80	(8,60–28,60)	0,739
EIST	9,00	(5,00–19,00)	12,00	(6,00–17,00)	8,00	(1,00–10,00)	0,513
TUG	8,20	(5,60–16,70)	7,20	(7,20–13,10)	7,00	(6,40–11,80)	0,178
FES	80,00	(62,00-95,00)	90,00	(78,00-100,00)	86,00	(70,00-100,00)	0,089

Abbreviations: UHDRS-TMS, Unified Huntington's Disease Rating Scale-Total Motor Score; UHDRS-TFA, Unified Huntington's Disease Rating Scale-Total Functional Assessment; BBS, Berg balance scale; OLSR, one leg stance right; OLSL, one leg stance left; EIS, figure of eight in seconds; EIST, figure of eight- number of steps; TUG, Timed Up and Go; FES, Falls Efficacy scale.

*Denotes a significant P value of 0, 05.

3.3. Correlation between assessment instruments

The highest correlations were found between UHDRS-TMS and BBS ($r=0.87$), as well as between UHDRS-TMS and the One Leg Stance on Left foot (OLSL) ($r=0.87$). Also, the correlation coefficient between UHDRS-TFA and BBS was 0, 87. TUG correlated well with both BBS, $\rho = 0.87$, and UHDRS-TMS; $\rho=0.81$. On the contrary, there were low correlations between the test Figure of Eight- test and all other measures. See table 3.

Table 3: Correlation matrix for measurements of motor function, disability, balance, and fall-related self-efficacy.

	UHDRS-TMS	UHDRS-TFA	BBS	OLSR	OLSL	EIS	EIST	TUG	FES
UHDRS-TMS	1,00								
UHDRS-TFA	0,54	1,00							
BBS	0,72**	0,87**	1,00						
OLSR	0,75**	0,43	0,63*	1,00					
OLSL	0,87**	0,68*	0,80**	0,80**	1,00				
EIS	0,03	0,16	0,02	0,19	0,01	1,00			
EIST	0,12	0,04	0,20	0,13	0,02	0,72**	1,00		
TUG	0,81**	0,78**	0,86**	0,55	0,82**	0,03	0,20	1,00	
FES	0,55	0,51	0,69*	0,27	0,42	0,22	0,30	0,75**	1,00

Abbreviations: UHDRS-TMS, Unified Huntington's Disease Rating Scale-Total Motor Score; UHDRS-TFA, Unified Huntington's Disease Rating Scale-Total Functional Assessment; BBS, Berg's balance scale; OLSR, One Leg Stance right; OLSL, One Leg Stance left; EIS, Figure of Eight- test in seconds; EIST, Figure of Eight- test- number of steps; TUG, Timed Up and Go; FES, Falls Efficacy Scale.

* A significant correlation at $p\text{-level} \leq 0, 05$

** A significant correlation at $p\text{-level} \leq 0, 01$

4. DISCUSSION

4.1 Summary

The results of this study indicate that the treatment programme had a positive effect based on the results of the assessment tools from baseline to post intervention and to follow-up, and that the used assessment tools were well associated with each other.

Regarding the effect of the treatment programme, the BBS was the only test showing a significantly positive treatment effect from baseline to post intervention.

Regarding the association between the outcome measures, the highest correlations were found between UHDRS-TMS and BBS, as well as between the UHDRS-TMS and The One Leg Stance on Left foot. Also, the correlation between UHDRS-TFA and BBS was high. In addition, the TUG correlated well with both BBS and UHDRS-TMS.

4.2 Results

The aim of the study was fulfilled, and the research questions have been answered but it is not possible to draw any general conclusions because of the lack of a control group and the small sample size with several non-significant p-values.

The hypothesis of this study that the set of physiotherapeutic exercises would improve motor function and balance in patients with HD was supported by the result on BBS ($p=.045$). The impact on the patients' level of disability and fall related self-efficacy was not verified in this study. However, some of the tests indicated improvements even if they were not significant. Motor function (UHDRS-TMS) had a p-value of 0,076, static balance (One Leg Stance on the right foot) had a p-value of 0,055 and fall related self-efficacy (FES) had a p-value of 0,089 (see table 2).

Concerning baseline stability, there was no significant difference between results at test 1, (6 weeks prior to intervention) and test 2 (0 weeks prior to intervention), except for the test One Leg Stance on the left foot and the FES. It is hard to explain why only the One Leg Stance on left foot changed as all other the balance

measures did not change significantly. Change in FES might be explained by cognitive symptoms that could have had an impact on the patients' judgement and opinion from one assessment to another. However, the fact that all tests were performed by the same testing person, not involved in the intervention, for all the twelve patients makes the testing procedure reliable.

The effects of the treatment programme in our study demonstrated a significant increase in dynamic balance measured with BBS. A pilot study with a before-after design studied effects of an intensive rehabilitation programme on patients with HD. Treatment took place at an inpatient rehabilitation centre with a multidisciplinary approach, and patients were at an early to middle stage of the disease like in this study. The objective of the study was to investigate the effects of a rehabilitation programme, where PT was a part of the programme besides speech therapy, occupational therapy and cognitive rehabilitation. Consequently, the evaluation included not only PT but a team approach. The PT intervention had similarities to this study, including for instance exercises for gait, balance, transfers and posture, but the treatment period was three weeks and could be repeated three times a year. Outcome measures were not PT specific except for tests for motor function at baseline and post admission (the Tinetti balance scale and Physical performance Test). Treatment programmes were individualized, and not standardized as in our study. Treatment was both individual and in group. The results showed that each three-week period of treatment resulted in improvement in motor performance and daily life activities ($p = 0.0001$) and the function was maintained over time. The conclusion was that intensive rehabilitation may positively influence the maintenance of functional and motor performance in HD (28).

In our study five (42%) patients reported one or more previous falls. Prevention of falls is a very important area to develop in HD, and the physiotherapist's role is important in fall prevention in HD. Especially in stage 3 and 4 falls are common (12) and may lead to serious consequences such as fractures, concussion and subdural hematoma (50). A Dutch study investigated falls and gait disturbances in patients with HD (39). Falls were recorded in 45 early to middle stage HD patients both retrospectively and prospectively. At baseline, 60% of the patients reported two or more falls in the previous year and were classified as fallers. Balance and

gait measures were compared between patients and a healthy control group. Like in our study, the UHDRS and BBS were used. A high proportion of falls (73%) caused minor injuries. Fallers showed higher scores for chorea, bradykinesia and aggression as well as lower cognitive rates compared to non fallers. Patients had a decreased gait velocity and stride length, and they had increased stride length variability and a greater trunk sway in medial -lateral direction. These symptoms were significantly higher in fallers compared to non fallers in the patient group (39). Another study investigated the relationship between fear of falling and fall frequency among patients with PD, not HD (51). One interesting finding was that the patients who had the tendency to fall most often did not report the most fear. The combination of lack of fear of falling but frequent falls in a small subgroup suggested that this group may need help and support and suitable caution to prevent falls (51). Studies similar to the above described on PD, but on patients with HD, would be important to do in a future to penetrate these problems more in HD and to develop good clinical standards for fall prevention in HD. In our study, patients scored relatively high on FES. Several of the patients scored over 70 points on the FES, which indicates that the patients really had a low fall related self-efficacy. In another study, mobility and falls in HD were studied (34). Like in our study, BBS and TUG were used to measure balance. Results showed that recurrent fallers had worse balance scores (BBS and TUG) than the non fallers, and both TUG and BBS were important predictors of falls in the study. Also, people with HD had an increased risk of falls if TUG was more than 14 seconds and BBS score lower than 40 points. In conclusion, the BBS and TUG appeared to be useful in fall risk assessment (34). These findings support the suggestions from our study to use BBS and TUG for balance evaluation in HD, and might also be useful clinically to identify an increased risk for falls in patients with HD.

Since HD is a progressive degenerative disease, time is a valuable factor in treatment. Studies when PT should start are important, in order to investigate if motor function and physical activity can be maintained longer with a PT intervention. Whether PT should start already at stage 1 or 2 should be examined. The role of the physiotherapist as an inspiration for movement and to make the patient more initiative when it comes to physical training is important to study in all stages of the disease. The patient already at an early phase of the disease might

have cognitive and psychiatric symptoms, for instance executive problems and depression. The patient might need help from the PT to find a suitable way for daily exercising, but also get individual advice about specific needs for training based on a thorough PT examination. The treatment programme in our study was easy to administer, and all the involved physiotherapists reported no problems understanding how the exercises were supposed to be performed. The fact that the programme was standardized helped the PT to know what exercises to do. Seven of the twelve patients had the same PT, which is good in terms of reliability of the treatment. The patients liked the programme, and could well endure the whole one hour session. Patients' adherence to the programme was good. To maintain the ability to walk was the most common individual goal of the patients for the treatment period. Training diary was asked for during the treatment period, as well as individual goal setting, but the diaries were not completed during the treatment period and the goal setting was not consequent and therefore this material was of little use in the evaluation of the treatment programme. Maybe self-reported scales and questionnaires are not suitable instruments for patients with HD, taking into account possible cognitive and psychiatric symptoms.

Regarding the association between the outcome measures in our study, the highest correlations were found between UHDRS-TMS and BBS, as well as between UHDRS-TMS and The One Leg Stance on Left foot (OLSL). Also, the correlation between UHDRS-TFA and BBS was also high. Both UHDRS-TMS and UHDRS-TFA are commonly used instruments in clinical work as well as in research. Based on the results of this study, BBS should be a suitable complement to the motor function evaluation in order to evaluate balance more thoroughly. One Leg Stance (OLS) is a part of BBS (last item), so OLS could be excluded in favor of BBS. The TUG correlated well with both BBS and UHDRS-TMS, and therefore TUG also could be excluded. However, TUG might be a good instrument in the assessment and prediction of falls (34). There was a very low correlation coefficient between the One Leg Stance on the Left Foot/Right Foot and the Figure of Eight- test in seconds ($\rho = 0,01/0, \rho=190$), and that might indicate that the Figure of Eight- test is a test that can capture aspects that the other instruments do not. In what way, is still yet to be found.

The reason why the correlation between instruments at test 2 were examined, was that at test 2 patients were slightly more accustomed to the testing procedure, but they had no training effect since the intervention had not yet started. It would have been an option to use test 3 or 4, but then the level of performance might have been influenced by the treatment.

Rao et al. (33) examined validity and responsiveness of three clinical tests of mobility and balance in HD. The tests were BBS, TUG and Functional reach test (FRT). The results showed that the FRT, TUG and BBS scores were correlated with quantitative gait measures. All tests were correlated with indications of functional limitations, and all tests were responsive to disease severity. The authors conclude that all three tests should be routinely included as a complement to the UHDRS motor section (33), which is similar to some of the conclusions from our study.

It appears that the testing part was too exhausting for some of the patients in our study. The patients were very tired after the two hours testing, which was both demanding physically and mentally. Since the testing part was so comprehensive, it might also have resulted in a training effect that could have influenced the results of our study. Finding valid, reliable and effective assessment tools is therefore important in HD clinical work as well as in research, in order not to bother patients too much with testing.

The big difference in age among the patients might have had an impact on the results. The younger patients might have engaged in the treatment programme more easily, and had a higher endurance to go through the testing without getting too tired. The oldest patient was 83 years old. Some of the tests were too hard for that patient to pursue, e.g. the One Leg Stance. Questionnaires were also very hard to answer for that patient. However, data on all patients in our study indicate that the most important factor for the results on the tests and maybe also the ability to engage in treatment is the stage of the disease, not the age.

4.3 Methods

There were two major limitations to this study. The first limitation is the lack of a control group. Uncontrolled interventional studies always have a limitation in the risk for a placebo effect of the patients with an expectancy effect. The other limitation was the small number of patients. This study only included twelve patients which is a too small sample size to obtain statistical power and that increase the risk for rejection of the study hypothesis.

Another limitation to this study is that only a few of the used assessment tools have been tested on patients with HD in terms of validity and reliability.

The external drop out range was regrettably high. From the beginning, there were supposed to be at least 20 patients in our study in order to get power according to the within-group design. Unfortunately, only 12 patients completed the study. There can be many reasons for that. There was a problem to recruit patients that would fit to the inclusion- and exclusion criteria. For instance, one patient wanted to enroll but he was found to be in a too advanced stage of the disease in order to be able to participate. Another patient did not want to stop her ongoing physiotherapy treatment for 3 months, as requested, and therefore she did not want to enroll. Some patients came to the first one or 2nd test, but then dropped out. The reason for this is not completely known, but several of the patients dropping out mentioned that the testing was very time consuming and tiring. Since the testing itself was very comprehensive and like an exercise itself, further engagement might have appeared deterrent. The treatment intervention was an intensive task with two weekly training occasions for six weeks for the patients. Maybe some of the patients also dropped out because the treatment appeared too demanding. For some of the patients, structured training at home might have been a good complementary treatment alternative. For example, daily home training and physical activity combined with treatment at the clinic once a week over a period of 12 weeks might have been less demanding for the patients. However, home training is not always easy to perform for those patients who lack the ability to take initiatives of their own and for those with little support at home from relatives and friends. Also, patients with severe chorea and balance

problems need training under supervision. PT at home might be another treatment option.

The internal drop out range was low. There was only one drop out from the testing, as only 11 of the 12 patients came to test number 3. All 12 patients were present at all the other three testing occasions, so this small internal drop out should not have a significant impact on the results.

Patients were treated with physiotherapy twice a week for six weeks at the clinic. Indeed, a longer treatment period would have been to prefer since a treatment period of six weeks might be considered to be too short of a training period in order to draw any conclusions from the effect of the intervention (52). In a home based observational single case study, there is a description of how one patient with HD gets a 14 weeks exercise programme. The programme was a video based home programme with exercises similar to our study with warm up, leg- and arm exercises, floor exercises and cools down. Like in our study, some of the outcome measures that were used were FES, BBS, and the UHDRS-TMS. The results showed a reduced level of disability, reduced number of falls and a higher walking speed. Improvement was seen at FES, BBS and UHDRS-TMS (32).

Our study had its focus on an outpatient setting at the hospital. PT in different kinds of settings should be studied further on. Whether it is better to give PT at home, at an out- patient setting or at the hospital is still not known, and it might differ from patient to patient and from time to time. The cost-effectiveness of the different treatment settings is an important factor to take into account as well. Suitable home based physiotherapy for patients at earlier stages of the disease should be generated and evaluated. At the middle stage, it might be inspiring for the patient to come away from home to an outpatient setting to get PT on a regular basis, since lack of initiative and passivity can be a problem at home. In ward treatments also need to be evaluated and developed. Especially for patients at advanced stages of the disease in ward treatments could be relevant, but maybe also for earlier stages (28). Therefore, the role of the physiotherapist already at an early stage of the disease is important to study in the future.

The time factor is also important to consider, when designing HD studies. Change over time will not necessarily always result in improvement because of the

degenerative process of the disease, even if the intervention itself is effective. Therefore, long time follow ups are probably hard to use evaluating effects of PT in HD. The level of motor performance of the patients can also differ from day to day, which means that evaluation has to be done frequently over a short period of time to be of use in treatment evaluation. If evaluation is made with testing with a low frequency, it might be hard to evaluate the effect due to natural variation and the degenerative process. Motor performance can be markedly influenced by mental distraction, tiredness or other temporary diseases in patients with HD (11, 12). In our study for example, values varied from one testing to the other, for example from test 1 to test 2 with only six weeks in between and even though the intervention had not yet started. This indicates that testing should be done with a high frequency during a relatively short period of time in future studies in order to get representative values. Single case studies could be an option of design as frequent testing characterizes this design. Also, studies using a control group could possibly track whether the control group worsened but not the treatment group. This would correct for the possible natural degenerative course of the disease over time.

In order to get studies with statistical power, the number of patients has to be so high that multicenter studies would be the best design in future clinical studies about PT assessment and treatment of HD patients. According to the indicated results of this study, especially BBS should be used in future PT studies in HD. BBS should be tested for validity and reliability in HD patients in a multicenter study. Finding a good new assessment tool for PT in HD would of course also be very useful. Qualitative studies about PT in HD could also bring new important knowledge.

As a result of the collaboration within the Physiotherapy Working Group, guidelines for physiotherapy for patients with Huntington's disease have been developed during 2009 (2). Those can be of good use when designing new studies, e.g. multicenter studies within the Physiotherapy Working Group.

4.4 Clinical implications

The treatment programme being used in this study might be an inspiration for other physiotherapists working clinically with HD patients. The programme can be seen as a base to start from in the treatment of the HD patient, and individual adjustments need to be made depending on the patients needs and own goals.

Preferably, BBS should be used in PT assessment of balance in HD patients at the clinic as well as in research. It should be added to the assessment of motor function and disability. Even TUG might be useful as a complement to the assessment of balance and prediction of falls.

4.5 Conclusions

The physiotherapeutic treatment programme in this study indicated a positive effect on the patients´ motor function, level of disability, balance and fall-related self efficacy. The contents of the programme with a focus on balance and transitions seemed to have clinical relevance.

PT in different kinds of settings should be studied further on to get a better knowledge about whether to give PT at home, at an out- patient setting or at the hospital. The effects of physiotherapy at an early stage of the disease is also important to study in order to investigate if motor function, such as balance and transitions, can be maintained longer with PT and physical activity. Therefore, in future PT research, multicenter studies with control groups, as well as single case studies and qualitative studies should be made to bring more knowledge about the effects of physical activity in patients with HD.

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APPENDIX 1.

Physiotherapy Treatment Programme

60 minutes treatment sessions twice a week

Warming up (max 10 minutes):

- Training bike (or so called Kalmar tramp) approximately 5 min
- step-up 2-3 min

Transitions (max 15 min):

- from lying to sitting
- from sitting to lying again
- from sit to stand
- from standing to sitting
- from sitting to walking and then back again (as in the timed-up and-go)
- walking in different directions, walking between cones
- walking the stairs and uphill-downhill
-

Exercises for postural control (max 5 min):

- In sitting (pelvic tilt, feet on the ground, straighten up back)
- In standing (pelvic tilt, postural sway forwards-middle-backwards, finding center of gravity, straighten up, look forward and use a reference point)

Static balance (max 5 min):

- Romberg's test (eyes open, eyes closed)
- Sharpened Romberg (with right and left foot in front respectively)
- Standing on one leg (eyes open, eyes closed)

Dynamic balance (max 10 min):

- Figure of Eight- test 4 times
- tandem walking on a line on the floor
- walking between cones
- weight transfers sideways, back and forth

Balance and motor coordination (max 10 min):

- touch left hand and right foot/knee; touch right hand and left foot/knee in sitting, standing and walking (choose the alternative that suits the patient)
- throw balls to each other (small, big, high/low according to the ability of the patient)
- throw sand bags between right hand and left hand and look at the bag all the time (in standing or in sitting)
- eye movement exercises by looking at the lines of a cross to the right, to the left, upwards, downwards

Relaxation (max 5 min):

- patient in supine in a comfortable position
- breathing exercises with abdominal breathing
- practising to become heavy in the whole body towards the surface
- end the session with stretching arms and legs, yawning