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DETERIORATION OF MOTOR FUNCTION IN MYOTONIC DYSTROPHY AND HEREDITARY MOTOR AND SENSORY NEUROPATHY

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ABSTRACT. In order to obtain more information about the deterioration of motor function in patients with myotonic dystrophy and in patients with hereditary motor and sensory neuropathy, changes in strength and functionality were determined at one year intervals, over a follow-up period of 1 to 5 years. Twenty-five myotonic dystrophy patients and 16 hereditary motor and sensory neuropathy patients participated. Strength measurements were restricted to knee extension and flexion torques measured isokinetically on a dynamometer at two velocities (120 and 60°/s). Functionality was measured as scaled time scores for rising from sitting, rising from supine, walking and stair climbing. Myotonic dystrophy patients showed a reduction of knee extension torques at 60°/sec (mean decrease per year 5.7 Nm, or 9%) as well as a decrease in functionality. Hereditary motor and sensory neuropathy patients showed no statistically significant changes in torques or functionality. The correlation between isokinetically measured knee extension torques and functional scores was statistically significant in myotonic dystrophy but not in hereditary motor and sensory neuropathy. No correlation was found between changes in torques and changes in functional scores.

Key words: neuromuscular disorders, follow up, strength, functionality, HMSN, myotonic dystrophy.

INTRODUCTION

Myotonic dystrophy (MyD, Curschmann-Steinhert disease) and hereditary motor and sensory neuropathy (HMSN, Charcot-Marie-Tooth disease) both have a clinical picture characterized by slowly progressive reduction of muscular strength and loss of functionality. However, data quantifying this process are lacking. Functional testing to document natural history in neuromuscular disease studies has been strongly recommended (16, 17). Knowledge of the natural history is important for the purpose of prescribing aids and appliances during rehabilitation as well as for that of deciding how many participants are needed in efficacy studies (5). The present study is a side-line of our research on the trainability of subjects with slowly progressive neuromuscular disorders. So far, longitudinal studies of the rate of muscular strength loss and loss of functionality have not been performed in adults with MyD and HMSN, although these diseases are the most common neuromuscular disorders (7).

Depending on the age of onset, four types of MyD are distinguished: childhood, early adult, late adult, and senile onset. These types differ in clinical signs and prognosis (13). The most common types of HMSN are called type I and type II, with type I having more serious clinical signs than type II (11).

In order to learn more about the natural history of MyD and HMSN, isokinetically measured knee torque and leg function were repeatedly determined, at one year intervals.

MATERIAL AND METHODS

Twenty-five MyD patients participated in the study (16 men, 9 women). At the first measurement session, ages ranged from 16 to 70 years. Two subjects had the childhood type of MyD, the others an adult type. Sixteen patients with HMSN participated (9 men, 7 women; aged 23–67 years). Of these patients 13 had HMSN I, the others HMSN II. Twenty healthy subjects were measured with the same procedure. The patients were known at the rehabilitation department of the University Hospital Maastricht or belonged to the control group of a clinical trial studying the effects of strength training. Patients with concomittant diseases that influence leg function were excluded. All subjects participated

Table I. *Numbers of follow-up measurements (= numbers of years) and numbers of patients (n) followed during this period*

Total number of subjects: MyD $n = 25$, HMSN $n = 16$.

Number of follow-up measurements	MyD (*n*)	HMSN (*n*)
1	18	11
2	1	1
3	4	3
4	2	0
5	0	1

in an instruction session organized about 2 weeks before the first measurement.

After the initial measurements, follow-up studies were performed at one year intervals. For the MyD group this resulted in a total of 65 measurements, while 43 measurements were available for the HMSN group. The numbers of subjects and the numbers of follow-up measurements are presented in Table I.

Strength was measured by isokinetic dynamometry because *i*) test-retest reliability is high, especially for knee torques (1, 15, 20); and *ii*) sensitivity to change is high compared to manual muscle testing, especially in the MRC (Medical Research Council) ranges 3–5 (9, 19). All muscle strength measurements were performed on a Cybex II isokinetic dynamometer (Lumex, Bay Shore, Inc. NY). Damping was set at 2. Analysis was performed on the Cybex Data Reduction Computer (CDRC). The algorithm of the CDRC takes limb weight into account and selects the highest peak torque. Subjects were positioned in the seat of the Cybex II according to standard procedure (8). The left leg was tested first. Isokinetic maximum knee extension and flexion torques were measured at velocities of 120 and 60 degrees per second. In order to allow subjects to adapt to the experimental situation, they were instructed to extend and flex the knee as forcefully and rapidly as possible three times in a row. After one minute of rest, the same instructions were given, but now for the purpose of recording the isokinetic movements.

Functionality was assessed by means of that part of the Appel test which relates to lower extremity function (2).

This test includes four time scored activities. Depending on the time it took the person to perform the four activities, a performance score was given. The remaining two test items are of a qualitative nature and were scored by the observer. The scores for the six items were added to get an overall score. The range of this functional score is from six points (good functionality) to 35 (poor functionality).

Table II. *Part of the Appel test relating to lower extremity function*

Activity	Points
Rising from a chair at lower limb height (s)	
0–1	1
1.5–3	2
3.5–5	3
> 5	4
Unable	5
Rising from supine (s)	
≤ 2	1
2.5–4	2
4.5–6	3
6.5–10	4
> 10	5
Unable	6
Walking 6 meters (s)	
≤ 8	1
8.5–12	2
12.5–16	3
> 16	4
Unable	5
Climbing and descending 4 standard steps (s)	
≤ 5	1
5.5–8	2
8.5–12	3
12.5–18	4
> 18	5
Unable	6
Need for assistive devices	
None	1
AFO/cane/boots	2
Walker, crutches, and/or occasional wheelchair	3
Confined mostly or always to wheelchair	4
Confined to bed	5
Hips and legs	
Walks and climbs stairs without assistance	1
Walks and climbs stairs with aid of railing	2
Cannot climb stairs but walks unassisted and rises from chair	3
Cannot climb stairs but walks unassisted with either AFO or cane	4
Cannot climb stairs but walks with minimal assistance or walks unassisted with crutches or walker	5
Cannot climb stairs but walks with crutches or walker with assistance or walks with total support	6
Confined to wheelchair	7
Confined to bed	8
Total	6–35

Statistical analysis

Only the highest peak torque values of the three movements per velocity and per leg were registered. For each participant, the mean of the peak forces for each velocity of both legs were used for further calculation. For persons with more than one follow-up measurement, simple linear regression analysis was used to calculate the mean change per year; for the other participants, further analysis was based on the change over one year. A paired *t*-test was performed to compare initial values with values after one year follow-up. The initial value for the torque variables was subtracted from the value after one year. The value of the functional scores after one year was subtracted from the initial value, because of the inverse relation between sign and clinical meaning. This calculation of changes results in a negative sign for deterioration for all variables. In addition changes in torques, calculated as a percentage of the initial torque, were analysed. The relation between mean knee torque and

Table III. *Initial values for mean peak torques (Newtonmeters) and functional scores*

Standard deviations are given in brackets.

	MyD ($n = 25$)	HMSN ($n = 16$)	Healthy ($n = 20$)
Extension 120°/sec	53 (36)	77 (33)	122 (35)
Range	9 to 142	0 to 127	70 to 204
Extension 60°/sec	72 (47)	100 (39)	153 (45)
Range	11 to 199	6 to 157	106 to 247
Flexion 120°/sec	21 (15)	28 (17)	60 (23)
Range	2 to 62	1 to 71	27 to 112
Flexion 60°/sec	34 (21)	43 (22)	79 (29)
Range	7 to 101	4 to 94	42 to 151
Functional score	11 (4)	10 (3)	6
Range	6 to 25	6 to 17	6 to 7

functional score was investigated within each diagnostic group. Because of the non-linear relation between knee torques and functionality scores, this relation was analysed using the non-parametric Spearman rank correlation and its corresponding significance test (r). Spearman r was used to quantify the influence of the change in mean knee extension torque on the change in functional score.

RESULTS

Initial values for torques were lower in MyD than in HMSN patients (Table III). Compared to healthy subjects, both patient groups had lower torques. The functional scores of the two patient groups, however, were nearly equal. The changes in knee torques and functional scores over 1 year have been expressed as absolute values in Table IV. No relation was found between initial values and changes over time.

Table IV. *Changes in peak torques (Newtonmeters) and functional scores over one year.*

Mean values and standard deviations given in brackets. Negative signs indicate a decrease. *p*-values are based on a paired *t*-test; significant values are printed in **bold** type and marked with *.

	MyD ($n = 25$)	HMSN ($n = 15$)
Change extension 120°/sec	−3.7 (11)	−5.0 (13)
Range	−26 to +35	−38 to +15.5
p	0.11	0.17
Change extension 60°/sec	−5.7 (7.4)	−1.1 (10.6)
Range	−24 to +6.3	−25 to +18
p	**0.001***	0.69
Change flexion 120°/sec	−0.4 (6.7)	−0.92 (5)
Range	−12.5 to +21.5	−7.9 to +8
p	0.76	0.5
Change flexion 60°/sec	−0.28 (7.8)	−0.08 (5.8)
Range	−13 to +21.5	−9.6 to +12.5
p	0.86	0.96
Change function, score range	−1.0 (2.0)	0.4 (0.9)
p	−9 to +3	1 to +2
	0.03*	0.09

One HMSN patient (the eldest, a 67-year-old woman) was excluded from the calculations because she had extremely low initial torques (mean extension torque 3 Nm). Torques in this range do not allow reproducible measurements.

Statistically significant deteriorations of the extension torques at 60°/sec and of the functional scores were found in the MyD group. A knee extension torque reduction was observed in 20 of the 25 patients (80%).

Changes in torque, calculated as percentages of the initial torques, showed considerable variation, mainly because of the low initial values in some patients. The mean decrease in the extension torques at 120°/sec was 11% (SD 28%, range −100% to 55%) of the initial value. At 60°/sec, this decrease was 9% (SD 11%, range −33% to 15%). The mean decrease in flexion torque at 120°/sec was 5% (SD 43%, range −100% to 127%). The mean decrease in flexion torque at 60°/sec was 8% (SD 25%, range −60% to 32%). A deterioration of functional score was observed in 14 patients (52%). Seven patients showed no changes and four showed improvement.

In HMSN there was a tendency towards decreasing extension torques, which was, however, not statistically significant. Of the 15 HMSN patients 10 (66%) showed a reduction. The mean decrease in the extension torques at 120°/sec was 4% (SD 13%), that at 60°/sec 0.6% (SD 9%). The mean decrease in flexion torques at 120°/sec was 2% (SD 20%); that at 60°/sec 0.4% (SD 13%). Remarkably, there was a slight improvement in functional performance in eight HMSN patients, while a deterioration occurred in only two subjects. The improvement was not statistically significant. The same tendencies were found in the subgroup of patients with a follow-up of more than one year.

The relationships between mean knee extension torques and functional scores (Fig. 1*a* and *b*) were described for the initial values. Statistically significant correlations were found in MyD (for 120°/sec $r = -0.62$, $p = 0.002$, for 60°/sec $r = -0.65$, $p = 0.001$), whereas this correlation was non-significant in HMSN (for 120°/sec $r = -0.11$, $p = 0.67$, for 60°/sec $r = -0.10$, $p = 0.71$).

Fig. 2*a* and *b* presents the changes in functional scores over one year versus the changes in extension torques for the MyD group and the HMSN group. Of

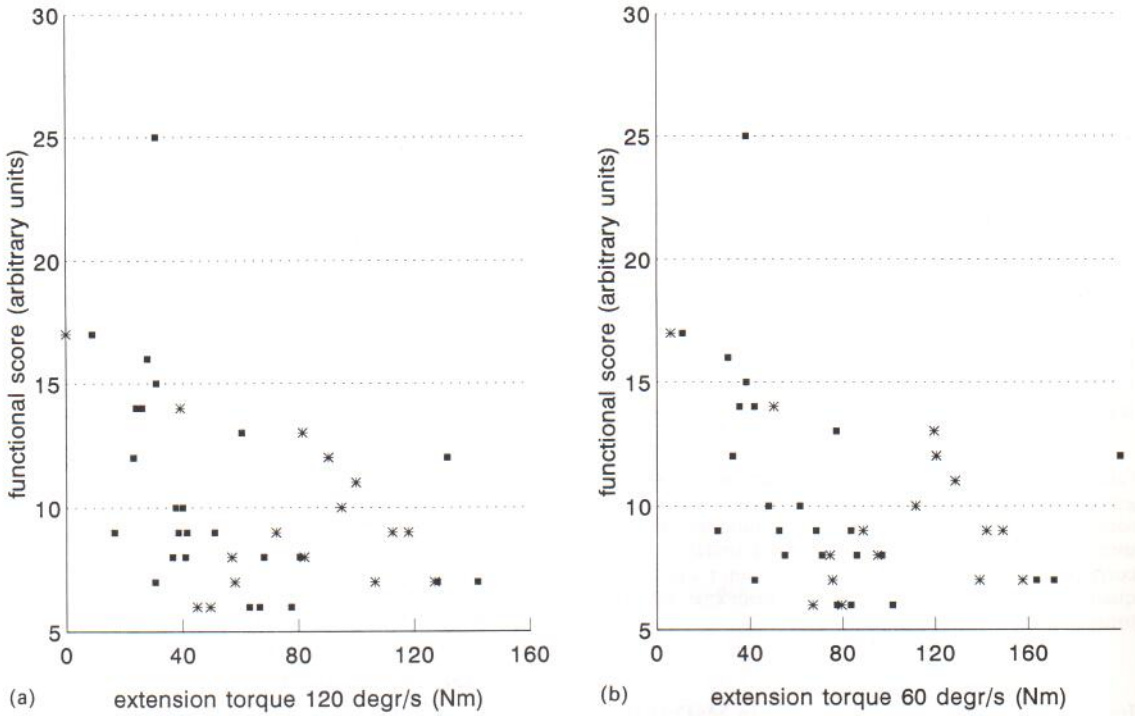

Figure 1. a and *b* Relationship between peak extension torques and functional scores at the initial measurement session. Nm = Newtonmeter. Each symbol represents one subject. ■ = MyD ($n = 25$), ✳ = HMSN ($n = 16$).

the 20 MyD patients with a decreased torque, 11 also showed a decreased functional score. None of the MyD patients showed increases in both torque and function. Of the ten HMSN patients with a decreased torque, only two had a decreased functional score. Two HMSN patients showed an increase in both torque and functionality.

The correlation between changes in functional score and changes in mean torque were weak and statistically non-significant (MyD for 120° and 60°/sec $r = 0.09$, $p = 0.66$, HMSN for 120°/sec $r = 0.25$, $p = 0.35$, for 60°/sec $r = 0.29$, $p = 0.27$).

DISCUSSION

The aim of this study was to gather more information about changes over time in strength and functional abilities in subjects with MyD and HMSN, and about the possible relation between these changes in strength and functionality.

The MyD group showed a considerable reduction in extension torques (significant at 60°/sec) and functionality over a one-year period, while the change in flexion torques was not significant. The lack of statistical significance for extension torques at 120°/sec would seem to be due to the large degree of variation. The HMSN patients tended to show a relatively small decrease in extension torques. The lack of statistical significance for this change may be due to slow deterioration, combined with a relatively small number of participants and a short period of follow-up. Again, no change in flexion torques was found. Strength is known to decrease with age in healthy subjects (4), but the decrease in one single year is negligible. This means that strength decrease because of normal ageing cannot explain our observations in MyD patients.

There have not been any studies of progress in MyD by measuring knee torques, but values at 120°/sec have been published before (10). Most of our patients were mildly affected, and their torque data are in agreement with those of the earlier study. The findings in our longitudinal study are in agreement with the results of a cross-sectional study (14) which found increased muscular dysfunction in patients with the classical form of MyD, with disease onset in adolescence or early adulthood. Recently, a decrease in walking speed, but no decrease in knee torques (at

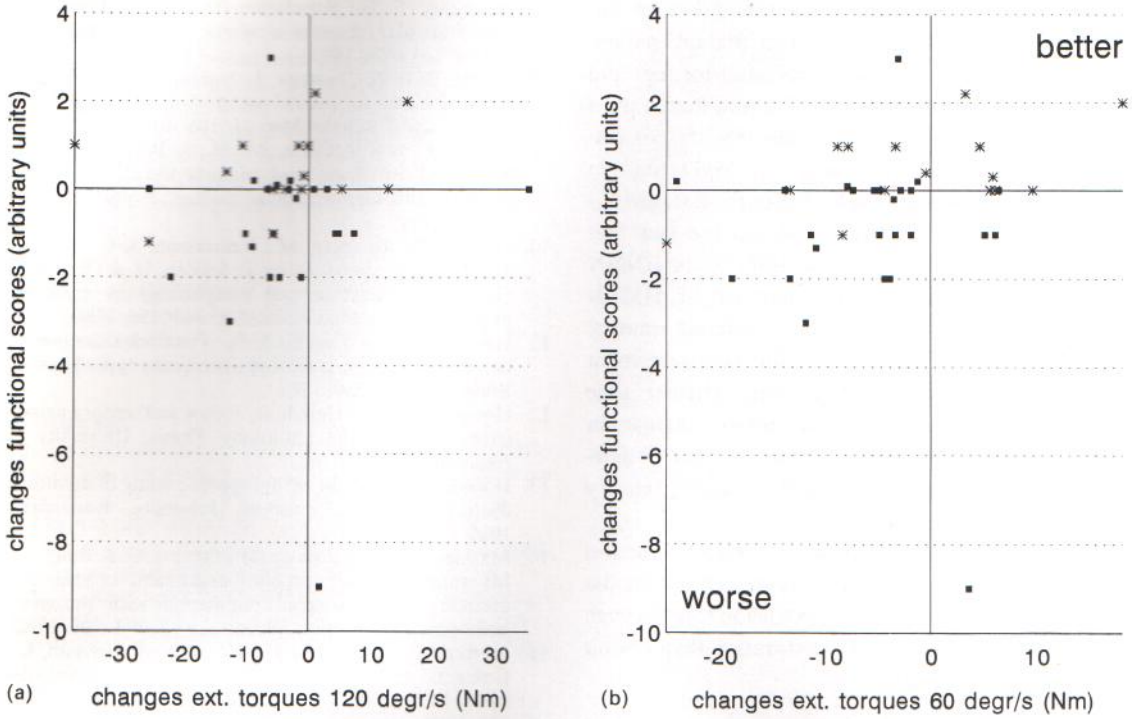

Fig. 2 a and *b* Mean change in peak extension torques and functional scores over one year periods. All data are presented in such a way that a deterioration is negative (see methods). Nm = Newtonmeter. Each symbol represents one subject. ■ = MyD ($n = 25$), ✱ = HMSN ($n = 15$).

120° and 30°/sec) was observed in an intervention study of MyD over a two-year period (18).

In the literature, studies of strength reduction in HMSN have shown contradictory results. In a longitudinal study of 31 subjects, the evaluated clinical severity index was found to increase most in subjects aged between 15 and 39 years (6). Most of the subjects in our group were older (median age 40 years), which may explain the slow deterioration. Two cross-sectional studies in HMSN type I patients reported no indication of a decrease (12) or only a slight deterioration (3) with increasing age. All three studies (3, 6, 12) used manual muscle testing in combination with other data to obtain a score for clinical severity. Important limitations of manual muscle testing are *i*) its inherent subjectivity, which may lead to serious bias, and *ii*) its grading in six points, causing a reduced differentiation of strength. Another cross-sectional study (11) suggested a relation between mean weakness score and duration of symptoms in HMSN I but not in HMSN II patients, but the weakness score in this study was not clearly defined. All studies, including the present one, confirm the clinical experience of a slower deterioration in HMSN than in MyD patients. Its high sensitivity and good reproducibility make isokinetic muscle testing superior to manual muscle testing in the monitoring of strength over a long period (15). Only one other study has been reported which involved longitudinal follow-up of isokinetic knee torques in a large group ($n = 44$) of neuromuscular patients, viz. polio survivors (1). No decrease over one year could be proved. Most tests to assess function in neuromuscular patients have been developed for children. We chose the Appel scale, which was originally developed to evaluate adult patients with amyotrophic lateral sclerosis (2). Only items concerning leg function were studied. Time scores for each activity were categorized to global performance scores. Although this procedure reduces the score's sensitivity to changes, a functional decrease was found in MyD patients over one-year follow-up intervals.

In an earlier study of a group of adult patients with various neuromuscular diseases, we found a relation between isokinetically measured knee torque and functional performance (20). As a result, we were

also interested in relations between (changes in) strength and functionality in the present patient groups. The relation between extension torques and functional scores was found to be non-linear, so a non-parametric test was used to describe the correlation. The relation was stronger in MyD than in HMSN. We suppose this to be due to the less obvious strength reduction in HMSN, and to the fact that other impairments influence functionality in HMSN as well. The relatively small number of HMSN patients showing a combination of reduced strength reduction and decreased functionality is in agreement with this weak relation. Moreover, whether time scores change will not only depend on changes in knee torques, but also on changes in other impairments, such as the strength of other muscles, sensory loss and lack of co-ordination.

In conclusion: Deterioration of motor function could be shown in the MyD group but not in the HMSN group. Isokinetic knee extension torques were more sensitive indicators of deterioration than flexion torques and functional scores.

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