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Sensory Evaluation of the Hands in Patients with Charcot-Marie-Tooth Disease Using Semmes-Weinstein Monofilaments

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ABSTRACT: In this study, the intra- and interobserver reliability of the Semmes-Weinstein monofilaments (SWMFs) was determined in the hands of 15 patients with Charcot-Marie-Tooth disease. In addition, the amount and distribution of sensory loss in the hand, and the relation between sensory loss, intrinsic muscle strength, and hand dexterity was explored in 45 patients. SWMF testing had good intra- and interobserver reliability with intraclass correlation coefficients of 0.91 and 0.86, respectively. The SWMF testing revealed normal sensory function in 43% of all six locations. The average loss of the intrinsic hand muscle strength was 57%. Poor strength was found in patients with both poor and with good sensory function. The correlation between the measurements of intrinsic muscle strength and the Sollerman test for dexterity was 0.70.

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INTRODUCTION

In patients with Charcot-Marie-Tooth disease (CMT, also referred to as Hereditary Motor and Sensory Neuropathy), functional deficits in hands and feet are caused by damage to the large diameter axons.[1,2] This results in loss of both muscle strength and sensory function (touch and vibration).[3]

The history of instruments to assess touch goes back to the late 1800s,[4] when Max von Frey[5] used horsehairs of varying thickness for sensory testing. Later, in the 1950s, Josephine Semmes et al. used nylon filaments for this purpose (the Semmes-Weinstein monofilaments; SWMFs).[6] Weinstein further improved the SWMF by rounding the filament tips and adding a coating to reduce slipping on application.[7] SWMFs have been widely used[8–14] and have good reliability in, for example, leprosy[14] and nerve injuries,[15] although this has been debated by others.[16] Research on sensory loss in the hands of patients with CMT has explored joint position sense,[1,17] vibration,[18–24] and two-point discrimination.[21,25] However, to our knowledge, quantitative assessment of touch using an instrument like the SWMF has not yet been investigated.

This study aimed to establish the intra- and interobserver reliability of sensory testing using the SWMF in the hands of patients with CMT to quantify the amount of sensory loss in a population of patients with CMT, and to explore the relation between sensory loss, intrinsic muscle strength, and hand dexterity.

MATERIAL AND METHODS

Patients with various types of CMT, diagnosed by neurologists on the basis of clinical electrophysiological and DNA analysis, were recruited from the outpatient clinic of the Department of Rehabilitation Medicine (Erasmus MC - University Medical Center, Rotterdam). Of the 50 eligible patients on record, 45 patients (90%) agreed to participate (Table 1); these were 25 males and 20 females with an average age of 45 (range 18−80) years. Most subjects had CMT type 1 and 2. The main reasons for declining participation (five subjects) were lack of time due to work and/or no interest in participation.

Patients were excluded when they had comorbidity that may have interfered with hand function. Of

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TABLE 1. Characteristics of the Study Population ($n = 45$)

Variable	*Group Descriptive Data*
Age (yr)	45 ± 15.1 (18–80)
Gender (male/female)	25/20
Type CMT	
1 (Male/female)	15 (7/8)
2 (Male/female)	17 (9/8)
3 (Male/female)	2 (1/1)
Unknown (male/female)	11 (8/3)

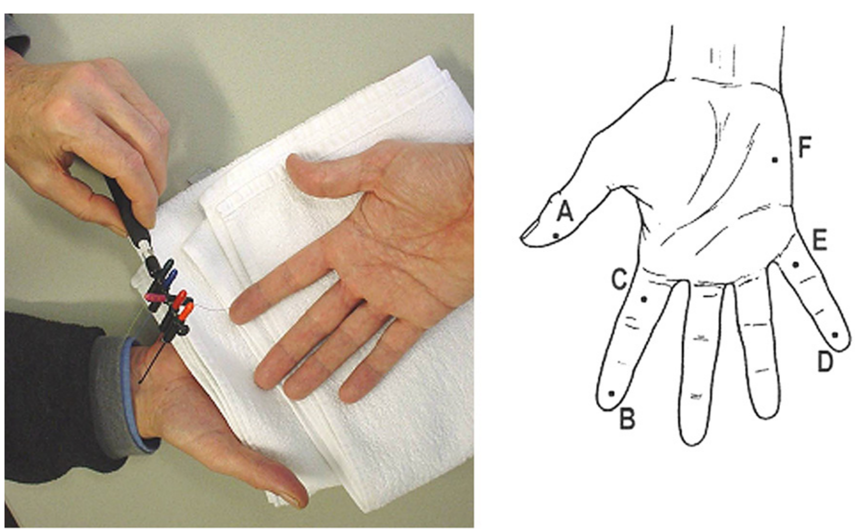
CMT = Charcot-Marie-Tooth disease.
Values indicate the mean ± standard deviation (range) or numbers.

the 45 patients who participated, three patients were operated on the dominant hand and two patients were operated on both hands, during which tendon transfers were performed to improve hand function.[26] Because this surgery influenced both muscle strength and dexterity, the measurements of these five patients were not included in the analyses of the relations between hand function, strength, and sensory function of the hands.

Patients were asked for the number of years since they first noticed problems in their hands. In addition, we scored the most disturbing disability in relation to hand function as experienced by each subject. A 10-cm visual analogue scale (VAS) was used to evaluate the amount of fatigue and pain. Written informed consent was obtained from all subjects.

Sensory evaluation was performed with five filaments, representing six different force levels (Figure 1) that were applied to the skin.[27] In a quiet room, the patients were seated at the opposite site of the table from the tester. The procedure was explained to the patients, asking them not to look but to verbally respond when they felt that they were being touched. We preferred not to use a screen to cover the hands of the patients because, in our experience, some patients are not comfortable with their hands hidden behind a screen. Therefore, we ask patients to close their eyes and turn their head away. We check if the patient is cheating by sometimes applying a ''sham movement,'' that is, we pretend to touch the hand and see what response is given.

The hand of the patient was supported by the hand of the tester (with a towel in between; Figure 1). The lightest filament was used first. If the patient detected two out of three stimuli, this filament number was recorded. Otherwise, a thicker filament was used following the same procedure. Tests were performed with random time intervals and with a random order to minimize the possibility that the patient might guess the answer. Six locations divided over the palm and fingers (Figure 1) were tested on both hands. The six locations were grouped into a radial



Force (g)	Log number	Number	Interpretation
0.07	2.83	5	Normal
0.20	3.61	4	Residual Texture
2	4.31	3	Residual Protective sensory function
4	4.56	2	Loss of Protective sensory function
300	6.65	1	Residual Deep Touch
>300	--	0	No sensory function

FIGURE 1. Illustration of the Semmes-Weinstein Monofilaments testing. The hand is well supported to prevent any movement of the fingers. The right-hand panel shows the six locations of sensory testing. The lower panel shows the description of the five filaments in gram force (needed to buckle the filament), the log number of the force, the number (0–5) used for statistical analyses, and the clinical interpretation of each filament.

area (points A, B, and C) and an ulnar area (points D, E, and F). Similarly, the locations were grouped into a distal area (A, B, and D) and a proximal area (C, E, and F).

Although the values of the logarithmic transformation of the force are often presented (2.83, 3.61, etc.), we preferred the approach suggested by Rosen and Lundborg,[10] in which the lightest filament is scored as 5, the next as 4, etc. If the patient could not feel the heaviest filament (200 g), a zero was scored. This created a congruent scale for motor and sensory function of six grades on a 0–5 scale in which a 0 indicates complete absence of function and a 5 indicates normal function.

Reliability of the SWMF tests was determined in the hands of 15 of the CMT patients in a separate session using the same protocol. Patients were tested twice by two observers: the first author (TARS) is an experienced hand therapist and the third author (BTJvG) is a movement scientist with no previous experience in evaluating hand function.

Repeated measurements, that is, undergoing the same test four times, will certainly be demanding for many patients with CMT and moreover, there is a definite chance of the patient loosing concentration causing insufficient responses from the patient. To prevent this problem, we selected three points (A, B, and D) out of the six, firstly because we think these are the most relevant for hand function in regard to sensory function. Secondly, there is no reason to believe that reliability in these points is different from the other three points. Thirdly, to save time and prevent wrong answers due to loss of concentration.

Muscle strength was determined by manual muscle strength testing using the 0–5 grading system as recommended by the Medical Research Council (MRC)[28–30] and a hand-held dynamometer (Rotterdam Instrinsic Hand Myometer [RIHM]) to measure intrinsic hand muscle strength in Newtons.[31,32] Maximal strength of three intrinsic muscle groups was measured: palmar abduction of the thumb (mainly abductor pollicis brevis muscle), abduction of the index finger (first dorsal interosseous muscle), and abduction of the little finger (hypothenar muscles). These measurements have excellent intra- and interobserver reliability, with intraclass correlation coefficients (ICCs) ranging from 0.86 to 0.98 for the different muscle groups.[33] For all strength measurements with the RIHM dynamometer, the mean of three maximum voluntary contractions was recorded.

For hand dexterity, the standardized Sollerman hand function test was used, which includes several tasks based on the most common handgrips.[34] This test was originally developed for the evaluation of hand function in patients with tetraplegia,[34] but is also used in patients with nerve injuries to the hands.[10,12,13,35] For the present study, three of the most relevant tasks for assessing fine manipulation of the hand (picking up coins from a purse, putting nuts on bolts, and doing up buttons) were selected. All tests were done with the dominant hand. For each task, the range is 0–4. A "0" indicates that the task cannot be performed and a "4" indicates that the task is completed without any difficulty within 20 seconds and with the prescribed handgrip of normal quality. The total score is the sum of the three items (range 0–12).

Data Analysis

The ICCs (2,1) were calculated (SPSS 12.0.1; SPSS, Inc., Chicago, IL). for each individual location for both the intraobserver and interobserver reliability of the sensory testing. Paired t-tests were used to study differences in SWMF tests between both hands and between proximal and distal, and radial and ulnar locations of the hand. To study the relation between sensory loss, intrinsic muscle strength, and hand dexterity, Pearson and Spearman's correlation coefficients were calculated. In addition, a stepwise multiple regression analysis (SPSS 12.0.1) was performed to determine whether sensory function and muscle strength independently predicted dexterity as measured with the Sollerman test. For muscle strength, the mean of the dynamometry measurements with the RIHM of the three intrinsic muscle groups was used as input for the multiple regression analysis. For sensory function, the mean of three locations (A, B, and D) was used.

RESULTS

Problems in manipulating small objects were reported by 63% of the patients. Fatigue and loss of strength were mentioned as major hand problems in 29% and 24% of the patients, respectively. The VAS score (range 0–100) for fatigue was 31 mm ± 18.6 (mean, SD) and for pain 51 mm ± 29.1. The average time since the patients first noticed their hand problems was 12.4 (range 1–45, SD 12.6) years.

TABLE 2. **Reliability of SWMF Testing in Both Hands of 15 Patients with CMT at Three Locations (Thumb, Index, and Little Finger)**

Location	*Hand*	*Intraobserver ICC*	*Interobserver ICC*
Thumb (A)	Right	0.98	0.89
	Left	0.97	0.95
Index finger (B)	Right	0.91	0.97
	Left	0.85	0.89
Little finger (D)	Right	0.78	0.73
	Left	0.95	0.74
Mean		0.91	0.86

SWMF = Semmes-Weinstein Monofilaments; CMT = Charcot-Marie-Tooth disease; ICC = intraclass correlation coefficient.
ICC values for intraobserver and interobserver reliability are presented.

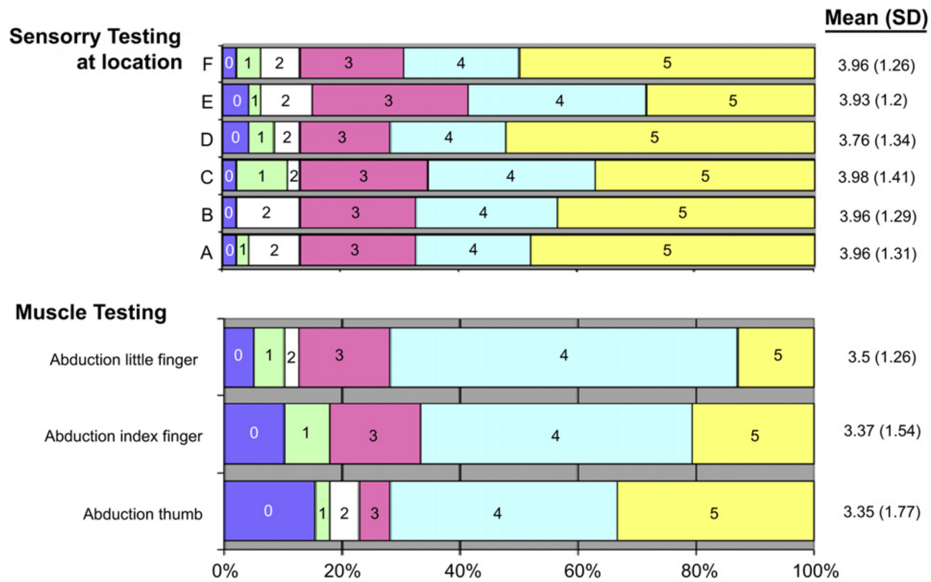


FIGURE 2. *Distribution of the results of the sensory testing with Semmes-Weinstein Monofilaments (numbers 0—5) at six locations (A—F on the y-axis) in the dominant hands of 45 patients with Charcot-Marie-Tooth disease and distribution of the results of the manual muscle strength testing (MRC grades 0—5) of three movements in 40 patients. In both scales, "0" indicates complete loss and "5" indicates normal function. The mean and SD of all individual locations and measurements are presented in the right-hand column.*

The mean intraobserver reliability of the SWMF measurements for both hands was 0.91 (range 0.78—0.98) for the different locations (Table 2). The mean of the interobserver ICCs was 0.86 (range 0.73—0.97). The lowest ICC data were found in the little finger.

For visual comparison, the MMST and SWMF values have been combined into one figure (Figure 2); this is possible because both have a scale of 0—5. The SWMF testing revealed that filament five (representing normal sensory function) was scored most often (43%). Normal sensory function in all six locations was found in 26% of the patients. Only one patient had near complete sensory loss and could not feel the thickest filament in five of the six locations. No significant differences were found between the six locations of the left and right hand. Similarly, no significant differences were found between the distal and proximal points, and between the radial points and the ulnar points.

Manual muscle testing of the three measurements revealed that only 7% of the patients had normal MRC values (i.e., MRC 5; Figure 2) for all three tests in both hands, whereas 4% had complete loss of muscle strength (i.e., MRC 0) in all three intrinsic muscle tests of the hand. Of all manual muscle strength measurements, 35% was less than or equal to MRC 3, whereas MRC 4 was scored most frequently (40%). Of these values, the corresponding quantitative values as measured with the RIHM dynamometer are given in Table 3. If the MRC was less than grade 3, no RIHM measurements could be performed and a "0" was recorded.[36] Compared with normal values, patients with CMT had an average strength loss of the intrinsic hand muscles of 57%.

Although a significant correlation (Pearson) between sensory function and strength of the intrinsic muscles was found ($r = 0.57$, $p < 0.001$), the scatter plot (Figure 3) of the individual patients shows a pattern in which a relatively high good sensibility can

TABLE 3. **Group Values for the Strength Measurements of CMT Patients ($n = 40$) Compared with Norm Values**

		Male		*Female*	
Movement		***CMT ($n = 20$)***	***Normal ($n = 54$)***	***CMT ($n = 20$)***	***Normal ($n = 43$)***
Abduction little finger	N	14.6 ± 10.6	32.8 ± 6.9	9.6 ± 7.6	21.4 ± 5
Abduction index finger	N	19.6 ± 19.4	47.5 ± 8.5	17.2 ± 12.8	34.2 ± 6.6
Abduction thumb	N	32.8 ± 28.3	85.2 ± 17.4	24.4 ± 17.5	59.2 ± 10.2

CMT = Charcot-Marie-Tooth disease.
Values indicate male and female group mean and standard deviation (dynamometry with RIHM in Newton, N). The norm values were obtained from 97 persons: 54 males/43 females with a mean age of 36 years. This group consisted of hospital staff, patients with uninjured hands, and persons accompanying the patients.

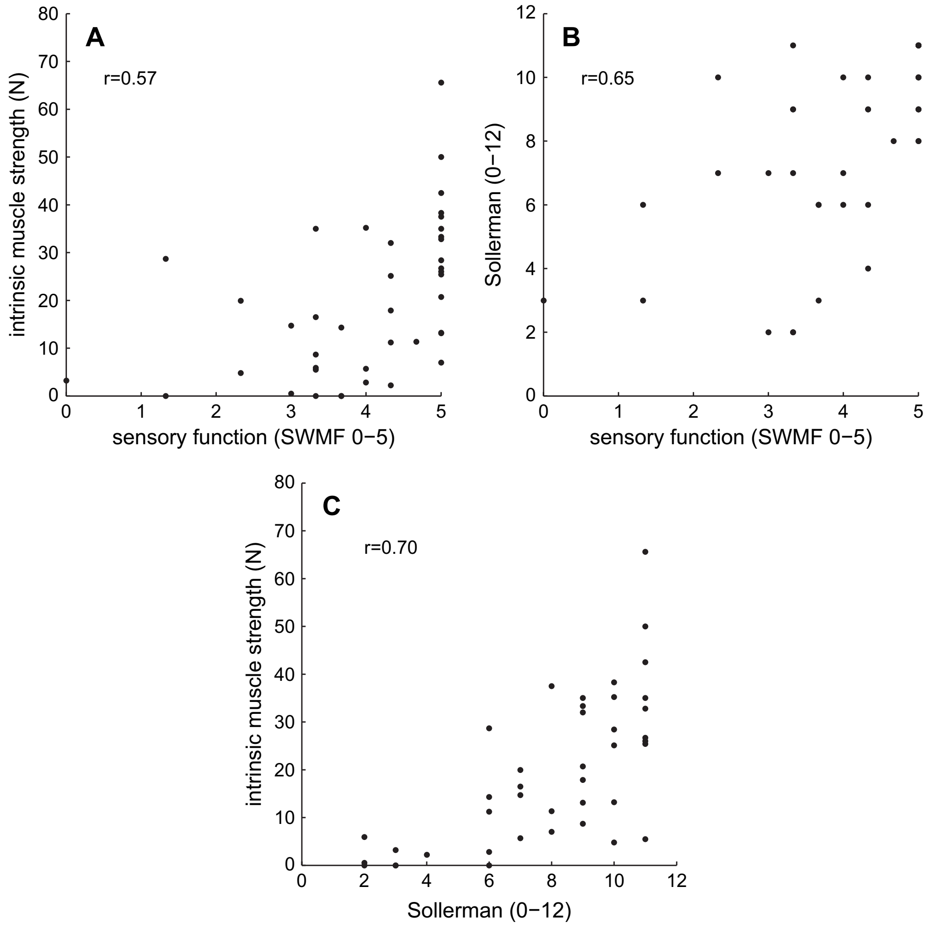


FIGURE 3. Scatter plot of the relation between sensory function (values on the x-axis are the mean of three points, i.e., A, B, and D; "0" indicates no sensory function and "5" indicates normal sensory function) and intrinsic muscle strength (N) measured with the RIHM dynamometer (values on the y-axis are the mean of three tests; abduction thumb, index, and little finger).

correspond with both a high and low intrinsic muscle strength. In other words, where patients with a poor sensibility always have a low intrinsic muscle strength, a good sensibility does not necessarily correspond with a good strength of the intrinsic muscles.

The correlation (Spearman) between the RIHM measurements of intrinsic muscle strength and the Sollerman test for dexterity was 0.70, which was slightly higher than the correlation between sensory function and dexterity (0.65). Scatter plots are presented for both correlations (Figure 3). Stepwise regression analyses indicated that both sensory function (SWMF measurements) and muscle strength (RIHM measurements) were significant ($p < 0.05$) predictors for hand dexterity. The standardized regression coefficient for the intrinsic muscle strength (0.51) was higher than the coefficient for sensory function (0.37).

DISCUSSION

The SWMFs have become one of the most commonly used quantitative measures in hand therapy practice.[12] According to Jerosch-Herold,[13] the touch threshold test using monofilaments such as the Weinstein Enhanced Sensory Test or SWMF, and the shape−texture identification test for tactile gnosis, are the only tests that meet criteria for a standardized test and for which the psychometric properties have been evaluated and quantified.

Despite the fact that quantitative sensory testing with SWMF has been shown valuable in patients with nerve injuries, nerve entrapments, and leprosy,[8−11,14] touch in CMT is often scored dichotomously as "present" or "absent." SWMFs are not commonly used in neurological examination, possibly because of the controversy concerning their reliability.[16] In the present study, the intra- and interobserver reliability of the SWMF in the hands of 15 patients with CMT was found to have good to excellent reliability, with a mean intraobserver ICC of the different locations of 0.91 and a mean interobserver ICC of 0.86. These reliability data are relatively higher than an earlier study on diabetic feet that reported ICC values for intra- and interobserver reliability of 0.80 and 0.77, respectively.[37]

We have no explanation for the finding in our study that the ICC values for the little finger were lower than those for the thumb and index finger.

Applying the SWMF, we found a relatively wide range of loss of sensory function in the hands of patients with CMT. Normal sensory function in all six locations of their hands was found in 26% of the patients. However, when taking only one location as reference, for example, the index finger location of the dominant hand, 58% of the patients had normal sensory function. These data seem to concur with a study on a large group of CMT patients that reported no demonstrable sensory impairment in 30% of CMT type I patients and in 60% of type II patients.[24] However, these data are difficult to compare because the latter study gave no details about the sensory testing of light touch.

Quantitative sensory testing using SWMF allows to investigate patterns of sensory loss, such as the difference between distal and proximal locations of the hands or between different nerve-innervated regions. Although CMT is recognized as a progressive disease developing from distal to proximal, in the present study we found no significant differences between the distal and proximal locations of the hand. Similarly, no differences were found between ulnar and radial points.

The present study also suggests that the clinical signs of sensory and motor loss do not develop equally. On the basis of the manual muscle testing, only 7% of the patients had normal muscle strength in all three muscle tests, whereas 26% of the patients had normal sensation in all locations based on SWMF testing (Figure 2). The scatter plot of the relation between SWMF and muscle strength measured with the RIHM revealed a nonlinear pattern (Figure 3). Moreover, poor sensory function was always found in combination with poor strength, whereas poor strength was found in patients with both poor and with good sensory function.

In our experience, most CMT patients attribute their loss of hand dexterity to muscle weakness, whereas few patients are aware of a loss of sensory function. A higher percentage of patients have normal sensory function (i.e., feel filament number 5) as compared to normal muscle strength (i.e., MRC grade 5). In the present study, both sensory and muscle function were significantly correlated with hand dexterity and the stepwise regression analysis indicated that both sensory and muscle function were independent predictors of hand dexterity, although muscle strength was a better predictor of hand dexterity than sensory function.

Future studies should explore the relationship between the sensory function of the feet and of the hands, and compare SWMF tests with vibration tests, to provide more insight into the sensory function of patients with CMT. A longitudinal study designed to investigate the use of SWMF to determine changes in sensory function of the hand would provide further information on the value of this quantitative sensory testing instrument.

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   a. intra and intertester reliability were identical
   b. intratester reliability was better than the intertester reliability
   c. intertester reliability was better than the intratester reliability
   d. both intra and intertester reliability were unreliable

#2. The average loss of hand intrinsic muscle strength among CMT subjects was approximately
   a. 85%
   b. 75%
   c. 65%
   d. 55%

#3. The correlation between dexterity and hand intrinsic muscle strength in this study was approximately
   a. 0.90
   b. 0.80
   c. 0.70
   d. 1.0

#4. Sensation was tested using a
   a. traditional complete set of SWMFs
   b. 5 piece set of SWMFs
   c. S2PD device
   d. M2PD device

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