The hand in Charcot-Marie-Tooth disease 1A
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Chapter Three

Manual dexterity and related functional limitations in Hereditary Motor and Sensory Neuropathy. An explorative study

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ABSTRACT

**Purpose:** To explore impairments in manual dexterity and perceived limitations in upper extremity related activities in subjects with Hereditary Motor and Sensory Neuropathy (HMSN).

**Method:** Cross-sectional study of 20 HMSN subjects. Manual dexterity was assessed using the Jebsen test of hand function. Perceived limitations were assessed using the Rehabilitation Activities Profile (RAP) and the Disabilities of Arm, Shoulder and Hand questionnaire (DASH).

**Results:** Impaired manual dexterity was found in four out of seven Jebsen subtests. Turning over cards, lifting large light and large heavy objects were most impaired, as reflected by median z-scores of 5.7, 12.0 and 16.9, respectively. Perceived limitations, as reflected by median and percentile (P25; P75) sum-scores, were 7.5 (3; 11.7) for the RAP domains of personal care (scale 0 - 69) and 6.0 (1.25; 15.5) for the domains of occupation (scale 0 - 42). The median (P25; P75) DASH score (scale 0 - 100) was 13.3 (2.7; 48.1). Jebsen test scores were significantly associated with RAP and DASH scores.

**Conclusions:** Manual dexterity of HMSN subjects, especially requiring the manipulation of flat and of large objects, was impaired and associated with the amount of perceived limitations in upper extremity function. Major limitations were perceived in activities related to upper extremity function by 25% of HMSN subjects. Measurement of manual dexterity and perceived limitations should be incorporated into the evaluation and treatment of HMSN subjects.
INTRODUCTION

Hereditary motor and sensory neuropathy (HMSN), also known as Charcot-Marie-Tooth disease (CMT), represents a heterogeneous group of degenerative peripheral neuropathies\(^1,2\). With prevalence ranging from 14 to 282 per million it is the most common group of peripheral neuropathies encountered in clinical practice\(^3\). Two major phenotypes have been distinguished: HMSN type I, the demyelinating and most frequent form, and type II, the axonal form\(^4,6\). Both types of HMSN are characterized by a generally symmetrical slowly progressive muscle weakness, atrophy, and sensory impairment of the extremities. Compared to the lower extremities, the upper extremities are often involved later in the progress of the disease, and are usually less severely affected. In the hand, the intrinsic muscles are primarily affected. Characteristically resulting in a (mild) clawing position of the fingers, loss of opposition (Figure 1), and a weak pinch\(^1,2,7\).

Available literature on upper extremity manifestations in HMSN has focussed predominantly on impaired body functions\(^1,2,7,8\). No attention has yet been paid to the functional restrictions due to these impairments, suggesting that it is not of great importance. This is surprising, since loss of functional abilities is probably the major concern to the patients involved. Therefore, this study focuses on the functional assessment of the upper extremity in HMSN subjects.

With the assessment of manual dexterity, insight can be obtained in the subject’s ability to move the hands easily and skilfully and to work with the hands in turning and placing motions\(^9\). For goal-oriented therapy, instruction and advice to subjects with HMSN, it is necessary to also understand their perceived limitations in upper extremity related activities. Insight in both manual dexterity and perceived limitations is an essential step towards preserving or restoring daily life functioning and well-being.

Figure 1
Subject with HMSN with loss of opposition while performing one of the subtests of the Jebsen test of hand function (stacking checkers).
The aim of this study is: (1) to explore impairments in manual dexterity of subjects with HMSN, (2) to explore their perceived limitations in upper extremity-related activities, and (3) to investigate the associations between manual dexterity and perceived limitations.

PARTICIPANTS & METHODS

A convenience sample of 20 subjects with HMSN participated. Subjects were recruited from the outpatient rehabilitation clinic of the Academic Medical Center in Amsterdam and from members of the Dutch Patients’ association for Neuromuscular Diseases ('Vereniging Spierziekten Nederland'). Inclusion criteria were: (1) diagnosis of HMSN or CMT, confirmed by electrophysiologic, histopathologic, or DNA study; and (2) age between 18 and 70 years. Patients were selected on the basis of diagnosis and not on any involvement of the upper extremity. Subjects were excluded if there were any disabling disorders in their medical history that might influence hand function or if they had difficulty understanding Dutch. Informed consent was obtained in accordance with a protocol approved by the university hospital Medical Ethics Committee.

Manual dexterity

Manual dexterity was evaluated with the Jebsen test of hand function\(^{10}\). This short (15 min), easily administered capacity test assesses seven different unilateral hand functions that are frequently used in daily activities. It is widely applied for evaluating manual dexterity\(^{11,12}\), and is currently recommended for the assessment of manual dexterity in HMSN patients in The Netherlands\(^{13}\). The time needed to complete each sub-test (writing, turning over cards, picking up small objects, simulated feeding, stacking checkers and lifting up large light and heavy objects) is recorded. The results for each sub-test can be compared to reference values\(^{10,14,15}\). Lower Jebsen test scores indicate greater manual capacity. The reported test-retest reliability coefficients for the Jebsen test range from 0.60 to 0.99\(^{10,12}\).

Perceived limitations in activities

Perceived limitations in activities related to upper extremity function were assessed with two instruments: the Rehabilitation Activities Profile (RAP)\(^{16}\) and the official Dutch language version of the Disabilities of Arm, Shoulder and Hand (DASH-DLV) questionnaire\(^{17}\). The RAP quantifies the severity of the limitations in activities on a 4-point Likert scale. This semi-structured interview assesses various activities in 5 domains:
communication, mobility, personal care, occupation and relationships. For each activity the response options range from 0 (= no difficulty) to 3 (inability). Sum-scores are calculated for each domain. Inter-rater and intra-rater agreement of the RAP has been found to be good to very good\textsuperscript{18}. Only the domains of personal care (23 activities) and occupation (14 activities) were assessed, since activities of the upper extremity are best represented within these two domains.

The DASH questionnaire is a brief, self-administered questionnaire to assess a patient’s perception of impairments and limitations in activities, associated with various conditions affecting the upper limb. This 30-item questionnaire includes 21 items on physical function, 6 items on symptoms, and 3 items on social or role function. The response to each individual item is scored on a 5-point Likert scale. The DASH assessments were scored according to the test instructions, and a sum-score was calculated, ranging from 0 to 100: a score of 0 indicating no impairments and limitations, and a score of 100 indicating maximal impairment and difficulty\textsuperscript{19}. Veehof et al.\textsuperscript{17} showed that the Dutch version of the DASH questionnaire is a reliable and valid instrument for assessing activity limitations and impairments in upper limb disorders in patients in The Netherlands.

Protocol

A standard sequence of testing was adhered to. First, we recorded the medical history and subjective neuromuscular symptoms. Subsequently, upper extremity function was evaluated with the Jebsen test of hand function, the RAP, and the DASH-DLV. Because none of the subjects were familiar with the Jebsen test, the test was explained and demonstrated. Only the dominant hand was tested. All assessments took place during a single visit, and the subjects were given the opportunity to rest between the assessments until they felt fully recovered.

Statistical analysis

Median sum-scores (25\textsuperscript{th} and 75\textsuperscript{th} percentiles) were calculated for the Jebsen test, the RAP and the DASH. For each Jebsen subtest, raw time scores were compared with the appropriate age- and sex-matched norm, and were transformed into \(z\)-scores on the distribution of the norm value. Univariate linear regression analysis was applied to investigate associations between the overall sum-scores of the Jebsen test, the sum scores of the DASH and the RAP domains of personal care and occupation. The level of significance was set at 0.05 for all analyses. Data-analyses were performed with the SPSS 11.5.1 software package (SPSS Inc., Chicago, Illinois, USA).
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### Table 1: Jebsen test of hand function scores

<table>
<thead>
<tr>
<th>Test</th>
<th>Writing</th>
<th>Turning over cards</th>
<th>Picking up small obj.</th>
<th>Simulating feeding</th>
<th>Stacking checkers</th>
<th>Lifting light obj.</th>
<th>Lifting heavy obj.</th>
<th>Sum scores</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Time scores (s)</strong></td>
<td>4.9</td>
<td>9.8</td>
<td>4.6</td>
<td>4.2</td>
<td>4.5</td>
<td>7.8</td>
<td>11.9</td>
<td>50.2</td>
</tr>
<tr>
<td></td>
<td>(4.0; 15.0)</td>
<td>(8.5; 15.0)</td>
<td>(3.4; 6.8)</td>
<td>(3.3; 6.7)</td>
<td>(3.8; 7.4)</td>
<td>(6.7; 17.8)</td>
<td>(9.7; 14.1)</td>
<td>(4.6; 72.1)</td>
</tr>
<tr>
<td><strong>z-scores</strong></td>
<td>-2.1</td>
<td>5.7</td>
<td>-1.2</td>
<td>-2.4</td>
<td>1.8</td>
<td>12.0</td>
<td>16.9</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(-3.6; -0.6)</td>
<td>(3.3; 11.7)</td>
<td>(-2.5; 1.1)</td>
<td>(-3.1; 0)</td>
<td>(0.8; 5.5)</td>
<td>(7.9; 35.4)</td>
<td>(14.1; 21.2)</td>
<td></td>
</tr>
</tbody>
</table>

Time scores and z-scores of HMSN subjects are expressed as median scores. The 25th and 75th percentile values of the time scores are given between parentheses. 

A z-score indicates the number of standard deviations from average normal performance given the subjects age and gender.

### RESULTS

#### Participants
Twenty subjects with HMSN (9 males and 11 females) were assessed. Thirteen subjects were diagnosed as type I, 7 as type II. The mean age on examination was 40 ±13 years (range of 18-65), and all subjects were right-handed. From the reported neuromuscular symptoms it appeared that the majority of the subjects experienced subjective loss of hand function. Diminished touch was experienced by 40 subjects, loss of hand strength by 13 subjects, tremors by 12 subjects and cramps and pain by 11 subjects. Other subjective findings were loss of motion/deformities (n= 5), loss of manual dexterity (n= 3) and sympathetic dysfunction (n= 3). Only one subject reported no involvement of the hand.

#### Manual dexterity
Median time scores, z-scores and the overall sum-score for the Jebsen test are presented in table 1. For three out of seven sub-tests (writing, picking up small objects and simulated feeding) the median z-scores indicated performance within the Jebsen sub-test norm values. The median z-score to perform the subtest turning over cards was 5.7. A z-score of 5.7 is equivalent to a value 5.7 standard deviations above the mean, indicating that subjects needed much more time than average normal performance. Z-scores for the sub-tests, turning over cards and lifting up large light and heavy objects showed an even larger deviation from normal performance.
Perceived limitations in upper extremity-related activities

The median (P_{25}; P_{75}) sum-score for the RAP domain of personal care was 7.5 (3; 11.7) on a scale range from 0 to 69. The domain of occupation showed a median sum-score of 6.0 (1.25; 15.5), on a scale of 0 to 42. Within the domain of personal care the HMSN subjects perceived most disabilities in dressing and undressing, and especially with fastenings (buttons, zippers, shoelaces) and jewellery. Within the domain of occupation, most disabilities were perceived during household activities such as making the bed, cleaning and doing the laundry. The median (P_{25}; P_{75}) DASH sum-score was 13.3 (2.7; 48.1).

Associations

Both domains of the RAP, and the DASH scores were significantly associated with the Jebsen test sum-scores (p< 0.05). Correlations were found between the overall time-scores for the Jebsen test and the sum-scores of the DASH (r= 0.61, p= 0.005), the RAP domains of personal care (r= 0.75, p= 0.001) and occupation (r= 0.49, p= 0.027). The results of the regression analysis showed that the Jebsen test explained 56% of the total variance in the RAP personal care score, 24% of the variance in the RAP occupation score, and 37% of the DASH score.

The RAP domain scores for personal care and occupation correlated significantly with the DASH sum-score (r= 0.81 and 0.88, respectively; p< 0.001). The sum-scores of the Jebsen test, the RAP and of the DASH questionnaire did not correlate significantly with age.

DISCUSSION

This explorative study showed that manual dexterity in this sample of HMSN subjects is impaired. On four of the seven Jebsen sub-tests, HMSN subjects needed much more time to complete the task, compared to the age and gender related norm. Furthermore, 25% of these subjects perceived considerable limitations in activities requiring upper extremity function.

Considering the above, it must be emphasized that HMSN subjects were not selected on the criteria of upper extremity involvement, but solely on the basis of diagnosis. Subjects were recruited from our outpatient rehabilitation clinic to which they were referred to, in most cases, because of lower extremity problems. Despite the small number of subjects, the study sample represented the broad clinical spectrum of upper extremity involvement in HMSN, varying from subjects with no limitations, or only mild limitations in manual dexterity to subjects with severe involvement of the upper extremity. However, we realize that some selection bias
may have occurred. It may well be that willingness to participate in the present study is greater in HMSN subjects with upper extremity involvement. Therefore generalizability is limited. Nevertheless, the findings of our study are not in line with the idea that CMT patients have no deformities or functional impairments related to atrophic intrinsic hand muscles\textsuperscript{20}.

For the assessment of limitations in activities we used two different instruments, the RAP and the DASH. The DASH is a questionnaire, and reflects the limitations perceived by the subject, whereas with the RAP, limitations in activities are assessed by the investigator in a semi-structured interview. Furthermore, the DASH evaluates only the activities of the upper extremity, whereas the RAP has a more general focus on activities of daily living. The highly significant correlation found between the outcomes of the RAP and the DASH suggests that, despite the difference in approach, the two instruments overlap.

The Jebsen test of hand function was chosen in order to obtain objective data of standardized tasks that can be compared with norm values. The test items cover the different prehensile patterns required to perform the activities of daily life. Surprisingly, our results show that HMSN subjects needed less time to perform the sub-tests of writing, picking-up small objects and simulated feeding than the prescribed norm. The prehensile patterns for these sub-tests are the three-jaw chuck pinch, the two-point pinch and the lateral pinch and require opposition of the thumb and fine manipulation of the fingers. Due to the affected intrinsic muscles, these functions in particular are expected to be limited when the hands of HMSN subjects are involved. During the assessment of manual dexterity we noted that subjects performed several sub-tests within the time-limits (normative data), but with various compensatory movement patterns. With the Jebsen test these subjects are classified as having normal manual dexterity, because only the time needed to perform the task is recorded, and no qualitative data are obtained. Apparently some HMSN subjects were able to compensate adequately for the prehensile patterns needed for the sub-tests of writing, picking-up small objects and simulated feeding. The same prehensile patterns are needed for turning over cards and stacking checkers, but these sub-tests may be more difficult to execute, due to the required coordination and object manipulation. The extra time needed to complete the sub-tests of lifting large light and heavy objects may be explained by the fact that the hand must first be opened sufficiently to be able to grasp an object. An abduction and opposition movement of the thumb is needed to open the hand, and metacarpal-phalangeal joint flexion is required for an adequate grasp. These functions may be limited in HMSN subjects who have a (mild) clawing position of the hand.
The significant correlations between the limitations scores and the manual dexterity score indicate that, in general, subjects who experience more limitations in upper extremity function perform worse on a capacity test, i.e., the Jebsen test, and vice versa. The correlation between the RAP and the Jebsen test appeared to be the strongest for the domain of personal care. The Jebsen test explained 56% of the variance in RAP personal care score. This may be due to the fact that this domain encompasses more activities that require upper extremity use than the domain of occupation. We expected that the Jebsen test sum-score would have explained a higher percentage of the total variance in the DASH score, because this questionnaire is specifically designed for the evaluation of perceived limitations in activities and symptoms associated with any condition affecting the upper limb. Why less variance in the DASH score was explained by the Jebsen test sum-score remains unclear, given the high correlation between the RAP and the DASH. It is important to realize that capacity measures such as the Jebsen test of hand function, and self-reported measures of perceived activity limitations in daily functioning are complementary, but do not necessarily measure the same construct.

In this explorative study only a limited number of subjects with HMSN were investigated, restricting the generalizability. Studies involving larger, unselected HMSN populations are needed, for a better knowledge of the prevalence, the determinants of manual dexterity and the impact of the loss of dexterity on daily life activities. Such studies will provide the necessary information to develop interventions to preserve or enhance manual dexterity in subjects with HMSN.

**Conclusions**

Manual dexterity of HMSN subjects was impaired for the majority of the Jebsen subtests, and positively related with the amount of perceived limitations in upper extremity function. Subtests requiring the manipulation of flat and of large objects were the most difficult to perform. Furthermore, 25% of the HMSN subjects perceived major limitations in upper extremity-related activities such as making the bed, cleaning, doing the laundry, dressing, and especially with fastenings (buttons, zippers, shoelaces, jewellery). Based on our results, we suggest that, in case of suspect upper extremity involvement, measurement of manual dexterity and perceived limitations should be considered in the evaluation and treatment of HMSN subjects.
REFERENCES


