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Evaluation of muscle strength and manual dexterity in patients with Charcot-Marie-Tooth disease

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ABSTRACT

Study design: Matched pair study.
Introduction: Differences in hand-muscle strength/dexterity between dominant (DH) and non-dominant (NDH) hand in Charcot-Marie-Tooth disease (CMT) are not wellunderstood.
Purpose of the study: To compare muscle strength/dexterity between DH and NDH and to correlate manual dexterity, strength and sensory function.
Patients and methods: Thirty CMT patients were studied using functional muscle testing (FMT) and strength (dynamometry), dexterity (the Nine Hole Peg Test [NHPT]), and Jebsen–Taylor Hand Function [JTT]), and sensory function (the Nottingham Sensory Assessment [NSA]).
Results: Scores were worse for DH than NDH on FMT ($p = 0.043$) and NHPT ($p = 0.014$) but not on JTT ($p = 0.098$), handgrip strength ($p = 0.710$) or tripod pinch ($p = 0.645$). NSA did not correlate significantly with any tests (p′s0.05).
Conclusions: In CMT disease, DH appears more impaired than NDH in terms of function and dexterity. Greater muscle weakness in DH may also emerge as CMT progresses.
Level of evidence: 3b.

Introduction

Hereditary motor and sensory neuropathies form a heterogeneous group of genetically determined, degenerative diseases affecting peripheral nerves with a prevalence rate of 1:2500.[1] The disorder is known as Charcot-Marie-Tooth (CMT) disease, after the authors who first described it.[2] More than 50 genetic causes of inherited neuropathies have so far been identified.[3] CMT disease may be autosomal dominant or recessively inherited, but an X-linked form is also known.[1,4] The myelin or the axon is affected by gene mutations encoding their proteins, and CMT is accordingly subdivided into demyelinating CMT1 and axonal CMT2 forms.[5] It is possible to distinguish between the two types using nerve-conduction studies.

Despite genetic heterogeneity, there is a common clinical phenotype.[6] CMT patients often present with bilateral distal muscle weakness and wasting of the lower extremities, pes cavus deformity, and distal sensory loss, with abnormal stepping gait as a result. Spinal deformities are more common in CMT patients than in the general population.[6,7] CMT symptoms usually develop in first two decades of life with the disease subsequently progressing over life.[6] The upper extremities usually become involved later, however, reduced hand function limiting prehension may occur early in the progression of the disease, resulting in reliance on compensatory grasp patterns.[8] A distal to proximal progression of muscle weakness, wasting, and sensory loss occurs, ultimately resulting in a "claw hand" with disturbed dexterity. Albeit CMT patients rarely experience hand pain, limitations in upper limb functioning is perceived by the majority of patients with CMT to be strongly related

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to restricted participation at work, family role or leisure activities.[9] Greater involvement of the dominant hand as a result of overwork has been reported by some authors,[10,11] while others question its existence.[12–14] Understanding the progression of CMT with respect to the strength, dexterity and function of the DH vs. NDH has important clinical implications. If enough evidence exists that the NDH becomes superior to the DH with respect to strength, dexterity, or function (or all) as the disease progresses, clinical approach may shift to encourage training and use of the NDH over the DH.

Few studies address the relationship between muscle strength, sensory deficit and manual dexterity,[15–18] however, no consensus exists on how to evaluate hand function in CMT patients. The aim of our study was to compare muscle strength and dexterity in all CMT patient volunteers using a matched pair design, where the matched pair was represented by the DH and NDH of the same patient. Previously, Vinci[19] and Videler[13] suggested that overwork weakness appears in more severely affected CMT patients. To test this notion, we also classified patients into three categories of muscle weakness according to the published CMTNS criteria[20] and used our measure of handgrip strength to explore DH vs. NDH differences in handgrip strength based on severity. In addition, we present correlations of hand muscle strength and sensory function with manual dexterity.

Methods

Participants

Thirty patients, of whom 13 were male, aged 21–68 (mean age 40.2 ± 10.29) were recruited from the local Clinic of Rehabilitation and Sports Medicine. Exclusion criteria was any disease other than CMT that may cause hand weakness and impaired motor dexterity and sensitivity. Written informed consent was obtained from all participants. CMT diagnosis was confirmed by electromyography (EMG) and DNA analysis, or by EMG alone (in absence of confirmed genotype markers). Twenty-five patients were classified as CMT1 (demyelinating type) and 5 patients as CMT2 (axonal type); 29 patients declared right-hand dominance, 1 was left-hand dominant. According to Charcot-Marie-Tooth Neuropathy Score (CMTNS),[20] 6 patients fell into Group I, 14 into group II, and 10 into Group III.

Assessments

All measurements were performed by the same researcher in the following sequence.

Muscle strength evaluated by functional muscle testing (FMT)

Janda's *functional muscle testing*[21] was utilized to assess hand and forearm muscle strength. The test includes 26 measurements for each hand, as shown in Fig. 1. The Medical Research Council (MRC) Scale was used for muscle grading, each ranging from 0 to 5. We averaged scores across these 26 measurements and measured FMT with this continuous variable.

Muscle strength evaluated by dynamometry

Handgrip strength was assessed using hand-held dynamometry (Citec, C.I.T. Technics, Haren, The Netherlands) following standardized testing procedure.[22] *Tripod pinch strength* was assessed as shown in Fig. 2. Three attempts were recorded (in Newtons) for each the handgrip strength and the tripod pinch strength tests. As done previously,[11] the three trials were averaged to create scores for analysis.

Dexterity

The *Nine Hole Peg Test (NHPT)*, which involves taking pegs one-by-one from a container, placing them into holes on a board, and then replacing them back into the container. As recommended by standardized testing procedures,[23] the test was performed by the DH followed by NDH and normalized based on sex and age. In addition, *the Jebsen–Taylor Test (JTT)*[24] was performed by NDH followed by DH and normalized based on sex and age. JTT is a well-established, widely used test of hand function and dexterity consisting of seven tasks which are representative of hand activities performed during activities of daily living.

Sensory function

Nottingham Sensory Assessment (NSA)[25] was used. The NSA is used mainly to identify sensory deficits, i.e. proprioceptive, stereognostic and epicritic sensory modalities in hemiparetic patients, showing good psychometric properties.[25] For this study, only hand, wrist and elbow segments were tested. British coins suggested for stereognostic testing by NSA authors were replaced by local currency coins of similar size and shape. For further analysis, all points scored within this test were added up for DH and for NDH. The maximum score was 97 points, implying normal stereognostic function at the area of hand, wrist and elbow.

To reduce any influence of fatigue, 5-min breaks were given between tests.

Statistical analysis

Normality of score distribution was assessed using the Kolgomorov–Smirnov test. The test revealed that scores for the tripod pinch test, and JTT test were not normally distributed. Therefore, the differences between the DH and NDH were analyzed using the non-parametric Wilcoxon signed-rank test for paired samples. Student's paired-sample *t*-test was used otherwise.

Based on Vinci[19] and Videler,[13] who posit that overwork weakness appears in more severely affected CMT patients, we used CMTNS criteria[20] to classify patients based on the extent of impairment into stage I ($n = 6$), stage II ($n = 14$), and stage III ($n = 10$), and applied this classification to handgrip dynamometry. Given the small sample size, we consider these results only exploratory.

In addition, we examined correlations between the administered tests of strength, dexterity, and sensory function. Spearman rank correlation coefficients, which are less susceptible to bias due to outliers than Pearson correlation, were used with non-normally distributed variables. A p-value <0.05 determined significance. Following Svensson at al[18] we interpreted the strength of the correlation according to Munro[26]: <0.25 little if any correlation, 0.26–0.49 low correlation, 0.50–0.69 moderate correlation, 0.70–0.89 high correlation, >0.90 very high correlation. All analyses were performed using the SAS software version 9 (The SAS Institute, Cary, NC). Significance was set at a two-tailed 0.05 level.

Results

Comparison of muscle strength and function between DH and NDH (see Table 1)

With respect to muscle strength, the NDH was significantly stronger than the DH in FMT. Handgrip dynamometry and the tripod pinch test yielded no differences in strength between the NDH and the DH.

We subcategorized patients into groups according to CMTNS stages I–III (not in Table 2). Handgrip strength was greater for NDH than DH in Group II ($p = 0.002$) and Group III ($p = 0.037$), but not in Group I ($p = 0.249$).

With respect to motor dexterity, the scores were significantly better for the NDH than the DH on NHPT, and the difference in JTT scores approached significance.

	Right arm [MRC grade 0-5]		Action	Muscle	Nerve	Left arm [MRC grade 0-5]		
Forearm			Supination	Supinator Biceps	Musculo-cutaneus Radialis			Forearm
			Pronation	Pronator teres Pronator quadratus	Medianus			
Wrist			Flexion, Abduction	Flexor carpi radialis	Medianus			Wrist
			Flexion, Adduction	Flexor carpi ulnaris	Ulnaris			
			Extension, Abduction	Extensor carpi radialis longus et brevis	Radialis			
			Extension, Adduction	Extensor carpi ulnaris	Radialis			
2nd and 5th finger	II.	V.	MP Flexion	Lumbricales II, Lumbricales V	Medianus Ulnaris	II.	V.	2nd and 5th finger
			IP_1 Flexion	Flexor dig. superf.	Medianus			
			IP_2 Flexion	Flexor dig. profundus II V	Medianus Ulnaris			
			Extension	Extensor dig.	Radialis			
			Abduction	Dorsal interossei Abductor digiti quinti	Ulnaris			
			Adduction	Palmar interossei	Ulnaris			
			Opposition V	Opponens digiti quinti	Ulnaris			
Thumb			Opposition	Opponens pollicis	Medianus			Thumb
			MP Flexion	Flexor pollicis brevis	Medianus			
			IP Flexion	Flexor pollicis longus	Ulnaris			
			MP Extension	Extensor pollicis brevis	Medianus			
			IP Extension	Extensor pollicis longus	Radialis			
			Abduction	Abductor pollicis longus brevis	Medianus Radialis			
			Adduction	Adductor pollicis	Ulnaris			

MRC = Medical Research Council

Fig. 1. FMT protocol according to Janda.

Inter-test correlations (see Table 2)

Correlations among muscle strength tests

We identified moderate correlations between handgrip and FMT and high correlations between tripod pinch and FMT.

Muscle strength and manual dexterity tests

There was moderate correlation between FMT and JTT, and between FMT and NHPT for both hands. Tripod pinch showed moderate correlations with JTT and NHPT for the DH, and low correlations for the NDH.

Manual dexterity tests

Significant correlation (high for DH and moderate for NDH) was identified between JTT and NHPT, both of which evaluate hand function quantitatively.

NSA and other tests

There was no significant correlation between NSA and other tests.

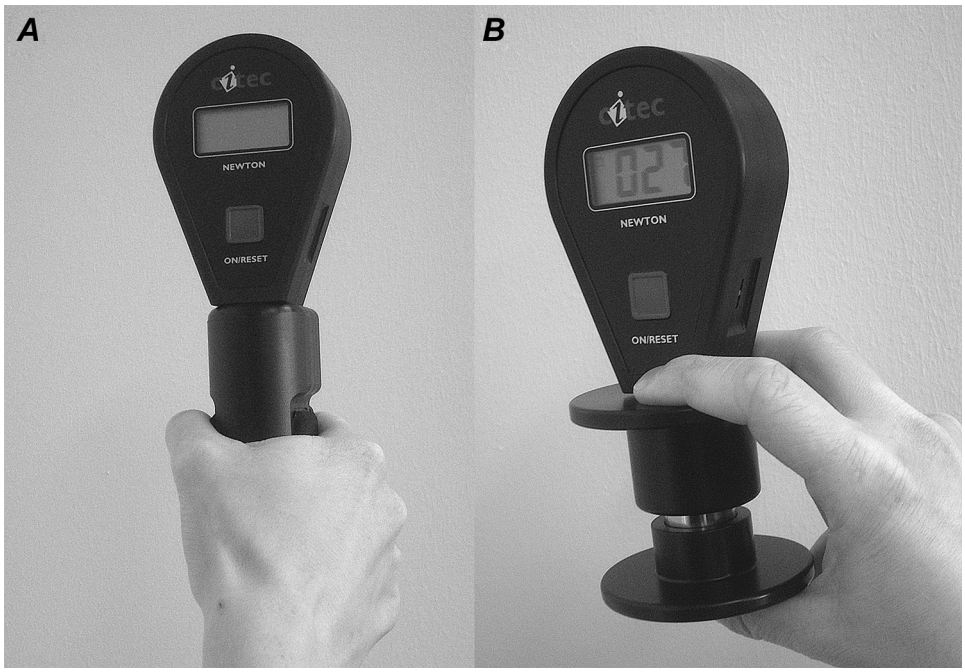

Fig. 2. A: Handgrip dynamometry. B: Tripod pinch dynamometry.

Discussion

Using a convenience sample of all available CMT patients from an entire geographical area, we found observable deficits in the DH compared to the NDH with respect to strength when evaluated by FMT and in dexterity evaluated by NHPT. Further, we found that DH deficits in strength compared to NDH, although not significant overall, show worsening trend in a dose response fashion such that the DH strength deficits get progressively worse with the progression across grades of CMT severity.

The existence of weakness due to overwork in CMT patients, whereby the DH tends to be weaker than the NDH as a result of the naturally increased burden on the DH, remains a controversial topic.[12–14,18] A direct demonstration of weakness due to overwork has not yet been provided and its mechanisms have not been clearly explained in CMT patients.

Previously, Vinci[19] and Videler[13] suggested that overwork weakness appears in more severely affected CMT patients. To explore this notion, we used CMTNS[20] to classify patients according to the severity of their functional impairment and confirmed greater DH weakness in CMTNS subgroups II and III while in the subgroup I (the mildest clinical impairment) strength difference between the DH and the NDH was not significant. Of course, in this analysis, our interpretation is limited by small numbers of participants in each subgroup. Still, the fact that we found statistical significance in these largely underpowered analyses suggests that this finding may be robust.

Table 1
Strength and function in the dominant versus the non-dominant hand presented in the order in which the tests were administered

Test	DH Mean ± SD	NDH Mean ± SD	*p*-value
FMT [MRC grades]	3.89 ± 0.64	3.96 ± 0.60	0.043
Handgrip strength [in Newton]	61.49 ± 38.87	62.16 ± 13.33	0.710
Tripod pinch[a] [in Newton]	40.30 ± 26.79	42.21 ± 24.49	0.645
NHPT	10.70 ± 9.67	6.99 ± 4.89	0.014
JTT[a]	28.63 ± 23.51	23.56 ± 16.47	0.098

DH = dominant hand, NDH = non-dominant hand, JTT = Jebsen–Taylor Test, NHPT = Nine Hole Peg Test, FMT = Functional Muscle Test.
No units of measurement are given for NHPT and JTT because the values represent data normalized for age and sex.
[a] Non-parametric Wilcoxon signed-rank sum test for paired samples was used due to non-normal score distribution.

Results with FMT deserve additional attention. While FMT results in this study support the overwork weakness theory, the results of dynamometry do not. One possibility is that the examination procedure (objective assessment of strength via dynamometry vs. clinician-based rating on FMT) may play a major role. Dynamometry, while likely more precise, is difficult to use if muscle strength is severely affected as is the case in many CMT patients.[11] On the other hand, FMT, which allows for a relatively thorough evaluation of individual muscle function even in the more impaired CMT patients, may give more comprehensive, and ultimately more accurate, information. However, the fact that the assessment with FMT is time consuming also needs to be considered. Available studies using FMT to evaluate hand strength in CMT test only few intrinsic hand muscles[11,14] but evidence indicates that hand strength depends not only on intrinsic hand muscles, but also on more complex muscle chains with the entire arm-hand system contributing to hand function.[27] Complex neural coupling between the distal and proximal upper extremity musculature affects grip force control during movements.[28] Therefore we tested 26 hand and forearm muscles on each hand to get more complete information about upper extremity muscle strength in CMT population.[19]

With respect to manual dexterity, we found better scores for the NDH than the DH in NHPT and JTT, although the result for JTT did not reach statistical significance, possibly due to low power. When performing JTT and NHPT, patients tended to use substitutive types of grasps that we did not correct during the testing. Videler et al[17] report the same experience when performing JTT and DASH tests, emphasizing that operations requiring thumb opposition are the major determinants of impaired manual dexterity in CMT patients.[15]

The results of these tests are in accordance with the patient's subjective perception of impairment. Many of the participants in our study confirmed that certain tasks they used to do using the DH are now done by the NDH, which they perceive as more skillful. The participants confirming this phenomenon started to do so spontaneously, they were not educated in switching the hands when

Table 2
Correlations between tests of strength, dexterity, and sensory function

Correlation	DH			NDH		
	Correlation coefficient *r*	*p*-value	Significance: interpretation according to Munro[24]	Correlation coefficient *r*	*p*-value	Significance: interpretation according to Munro[24]
Muscle strength tests correlation						
Handgrip with FMT	0.62	<0.001	Moderate	0.59	<0.001	Moderate
Tripod pinch with FMT	0.72	<0.001	High	0.75	<0.001	High
Correlation between muscle strength and manual dexterity						
FMT with JTT	−0.68	<0.001	Moderate	−0.68	<0.001	Moderate
FMT with NHPT	−0.69	<0.001	Moderate	−0.57	0.001	Moderate
Tripod pinch with JTT	−0.54	0.002	Moderate	−0.39	0.031	Low
Tripod pinch with NHPT	−0.67	<0.001	Moderate	−0.48	0.008	Low
Manual dexterity tests correlation						
JTT with NHPT	0.75	<0.001	High	0.67	<0.001	Moderate
Correlation between NSA and other tests						
NSA with FMT	0.39	0.031	Low	0.23	0.229	No
NSA with handgrip	0.32	0.080	No	0.17	0.367	No
NSA with Tripod pinch	0.30	0.104	Low	0.06	0.768	No
NSA with JTT	−0.27	0.155	Low	−0.29	0.121	Low
NSA with NHPT	−0.27	0.149	Low	0.10	0.589	No

DH = dominant hand, NDH = non-dominant hand, FMT = Functional Muscle Test, JTT = Jebsen–Taylor Test, NHPT = Nine Hole Peg Test, NSA = Nottingham Sensory Assessment.

doing certain tasks. This supports the hypothesis of greater overwork weakness and more impaired dexterity in the DH especially in more severely affected CMT patients.

Finally, we found significant correlations across most strength and dexterity tests for both hands, while the test of sensory abilities did not correlate with other tests. JTT and NHPT evaluate manual dexterity quantitatively and our results suggest only moderate correlation with FMT and moderate (for the DH) or low (for the NDH) correlation with tripod pinch dynamometry (Table 2). This is not surprising since manual dexterity is determined not only by muscle strength but by several additional factors, such as skillfulness, motivation, carefulness, training, actual psychological condition amongst others which may all play an important role. Here, we cannot confirm the results presented by Videler et al[16] that CMT subjects needed less time to perform some JTT sub-tests, but we do report the same experience that our subjects also performed the tasks with various compensatory movement patterns.

High correlation was identified between JTT and NHPT for the DH and moderate correlation for the NDH (Table 2). Both the NHPT and JTT evaluate manual dexterity quantitatively, but the tasks performed within the tests are different. In practice, just one test seems to be sufficient to evaluate manual dexterity. Since NHPT is quite simple and fast, it can be suggested as a routine test to evaluate manual dexterity in general medical practice. JTT requires both more time and skill in order to correctly instruct the patient and to analyze the results. Therefore, JTT may be suitable especially for occupational therapists to evaluate patients and analyze the effect of treatment.

An important issue is the performance of our sample of patients with CMT relative to normal performance. It is known that patients with CMT disease frequently present with impaired hand dexterity, reduced muscle strength, and possibly impaired sensitivity compared to healthy counterparts. For example, the normal score on FMT is expected to be 5, whereby the individual without impairment would score the maximum score of 5 on all 26 tasks. Participants in our study averaged just more than one unit below the maximum muscle grading, suggesting the ability to respond adequately to resistance but not to maximum resistance. As another example, the normal performance on NHPT would approximately 18 s for the DH and 19 for the NDH,[23] whereas our sample averaged 41 s for the DH and 36 s for the NDH. Finally, unfortunately, norms for dynamometry are published with the Jamar Analogue Hand Dynamometer, whereas we used the CITEC dynamometer. Therefore, a comparison with normal performance is not straightforward.

Nottingham Sensory Assessment (NSA), which we used to measure sensory function, did not correlate with any other test (Table 2). This underscores its uniqueness among the study variables. Fine motor movements are closely related to sensory function[29] and sensorimotor relations allow for adequate estimation of body position in space facilitating refined motor control, which, according to Padua et al[30] is related to both mental and physical aspects of CMT patient's quality of life. Therefore, we consider sensory function evaluation to be a critical part of functional testing and irreplaceable by other functional tests. Also of note in this regard is that only 5 patients from our cohort of 30 reached the full count of 97 points in the NSA; the lowest score (reached by one patient) was 80. This suggests the sensory hand and arm function are at least mildly disturbed in most CMT patients, and these disturbances may not be effectively captured by other tests. Svensson et al[18] used the Shape Texture Identification test and made similar conclusions.

The hand may be affected in CMT patients at all stages, but may be under-recognized in its early stages, potentially delaying therapy.[8] Therefore, a consensus should be reached on how to test hand function in CMT patients. It may be that, in a routine clinical practice, muscle strength and motor dexterity may best be assessed both quantitatively and qualitatively along with somatosensory function.

To evaluate motor dexterity, NHPT appears to be the most valuable and convenient. NHPT is easier and faster to perform than JTT while the evidence of both tests appears to be similar. Based on results of this study, we note that motor dexterity is related to muscle strength (at least partially), and vice versa. However, muscle strength and motor dexterity do not predict quality of somatosensory function and vice versa, and therefore somatosensory function should always be assessed as well.

Also of note is that in CMT patients, fatigue should always be taken into consideration. According to Ramdharry et al,[31] fatigue plays an important role in everyday functional performance of patients with Charcot-Marie-Tooth disease. In this context, sensorimotor testing used in this study, that is the assessment of strength, dexterity, and sensory function, is time consuming and therefore fatiguing for CMT patients, possibly affecting performance to a much greater extent than would be the case in the healthy population. However, we consider such complex analysis to be critical to tailor rehabilitation appropriately to each CMT patient. CMT is not a single diagnosis. While in some

patients poor motor dexterity is a main problem in others it can be weakness, fatigue, limited joint range of movement, pain or other unpleasant sensory phenomena. Only detailed functional analysis allows to plan the most effective functional treatment approach.

There are several limitations to this study. First, the cohort of 30 patients is rather small and consists of both demyelinating CMT type 1 and axonal CMT type 2 patients. Second, genetic classification has not been taken into consideration. However, for the purpose of rehabilitation, clinical classification is more useful than EMG or DNA classification. Third, we used CMTNS[20] clinical scale to characterize the cohort, but the low numbers in the individual subgroups did not allow for valid statistical analysis. Future research should address correlation between severity of impairment characterized by CMTNS and functional clinical tests. Fourth, participants performed tests with a set order with respect to the sequence of tests and testing of the DH vs. NDH according to accepted conventions and/or the test protocol. It is possible, albeit not likely, that this sequence affected results.

Fifth, we used the NSA, which is designed to measure sensory impairment in stroke patients, not in CMT. This test was used because there is no standard scale for a comprehensive sensory assessment of the peripheral neural lesions. The Semmes-Weinstein monofilaments is more routinely used in CMT. However, this test is less comprehensive and targets only superficial sensitivity. On the other hand, NSA can tap also into proprioception, kinesthesia and stereognosis. Dexterity and strength are dependent not only on the superficial indicators captured by the Semmes-Weinstein monofilaments but also on proprioception, kinesthesia, and stereognosis, which we could not measure with this test. Sixth, the length of the testing session may have led to fatigue, affecting performance and potentially magnifying any differences in performance. To reduce this effect, we maintained consistent sequence in terms of test administration. In addition, we found significant differences in the DH and NDH on FMT, which was consistently administered first. Finally, we tried to point to differences in impairment in strength, dexterity, and function. However, it is essentially impossible to completely disentangle the three domains. Therefore, each test, although designed to test one of the three domains, at least partially reflects all three domains.

Conclusion

This study supports the notion that NDH is significantly less functionally impaired than DH, and that the difference may be more apparent in more affected CMT patients, at which point muscle weakness in DH emerges. It appears that the evaluation of sensation and stereognostic function may provide a unique perspective on global impairment in CMT and should therefore be routinely integrated into clinical assessment. Future research should test the utility of sensory function assessment tools such as the NSA in overall evaluation of CMT severity over time.

Appendix. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jht.2015.12.002.

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Quiz: #406

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#1. Charcot-Marie-Tooth disease
   a. is characterized by a cognitive deficit
   b. is a central myelin disease
   c. never affects upper extremities
   d. is a genetically determined hereditary motor and sensory neuropathy presenting with bilateral distal muscle weakness and wasting of the lower and upper extremities

#2. Overwork weakness
   a. cannot occur in patients with CMT disease
   b. often occurs in CMT disease but in lower extremities only
   c. often occurs in CMT disease and involves both lower and upper extremities
   d. results from sedentary lifestyle in individuals with CMT disease

#3. With CMT disease progression the non-dominant hand may become stronger and faster, presenting with better dexterity than the dominant hand because of
   a. overwork weakness affecting the dominant hand more as a result of more physical strain and daily activities burden
   b. asymmetrical sensory impairment that mainly affects the dominant hand
   c. spasticity affecting the dominant hand
   d. all of the above

#4. To test manual dexterity in CMT patients the following test can be used
   a. Nottingham Sensory Assessment
   b. Jebsen-Taylor Test and Nine Hole Peg Test
   c. dynamometry
   d. Ashworth Scale

#5. Nottingham Sensory Assessment
   a. measures hand muscle strength
   b. is a standardized scale for assessing sensory impairment in stroke patients but it can also be a useful tool to evaluate sensory function in CMT individuals
   c. is a standard assessment of cognitive function
   d. is a uni-modal sensory examination

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