Quantification of upper limb dysfunction   in the activities of the daily living in people with Multiple Sclerosis

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Background

Importance: Impairment in upper limb (UL) function has been reported as important, prevalent and possibly an early clinical indicator for disease progression in people with Multiple Sclerosis (PwMS), thus as a relevant outcome in clinical trials.

Objective: To deeply endophenotype UL involvement in PwMS throughout each domain of the International Classification of Functioning, Disability and Health guidelines; and to (i) offer for each measure cut-off values anchored to UL impairment in activities of the daily living (ADL), and (ii) determine the most accurate set of measures needed to capture the complexity of UL impairment.

Methods

Design: 400 PwMS were randomly selected among those routinely followed at the Comprehensive Multiple Sclerosis Center to participate at a one-time research visit, 257 completed the assessments. The visit was conducted by research therapists trained to maximise inter-rater reliability.

Assessment : 257 PwMS underwent an extensive UL assessment using standardized measures of grip strength and endurance, coordination, vibratory and tactile sensation, dexterity, capacity and functionality. In order to determine the most accurate set of measures needed to capture the complexity of UL impairment, seven standardized tests were selected:

Isometric Grip Strength	**Jamar ® handheld dynamometer**; Mean peak isometric grip strength (kg) between three maximal isometric trials	*Fine Dexterity*	**Nine-Hole Peg Test (NHPT)**; average time to complete the two trials
Grip Endurance	**Martin vigorimeter**; amount of time that the 50% of maximum strength was maintained	*Gross Manual Dexterity*	**Box and Block Test (BBT)**; Participants had to transport as many blocks (2.5 x 2.5 x 2.5 cm) as possible, one at a time using one hand, from one compartment to another in one minute. The number of accurate blocks was averaged over two trials per hand.
Vibration Sensation	**Vibratron II device** (Physitemp Instruments, Inc., Clifton, NJ); average vibration unit between last perceived and first not-perceived intensity	*Coordination*	**Finger-Nose Test (FNT)**; Participants alternately touched their nose and the examiner's finger (45 cm apart) as quickly and accurately as possible for 20 seconds, the Number of accurate repetitions during one trial on each limb is recorded
Tactile Sensation	**Five Semmes–Weinstein monofilaments** (SWMT); The filament with the lowest pressure rating accurately felt 3/3 times was recorded as the score. Each fingertip was scored separately for each hand		

Limitation in ADL was defined using two anchors reflecting:

1) **Objective perspective - the TEMPA** (Test d'Evaluation de la performance des Membres Supérieurs des Personnes Âgées). TEMPA consists of the time to complete nine everyday activities (eg open a jar, write on an envelope and stick a stamp on it, pick up and move small objects)

2) **Subjective perspective - the DASH** (Disabilities of the Arm, Shoulder and Hand), a questionnaire rating (1-no difficulty to 5-unable) the ability to perform 21 UL specific tasks

Results

Population characteristics: heterogeneous cohort of PwMS encompassing the whole spectrum of disease from mild/no disability (34%) to moderate (43%), severe (22%), and severe non-ambulant disability (21%). The mean age was 48.7 ± 11.6 years, with a mean disease duration of 12.40 ± 8.8 years.

Prevalence of UL involvement: UL dysfunction was highly prevalent in all the modalities tested, even in participants with no/mild disability. In PwMS with no/mild disability, approximately 10% had impaired body functions such as grip strength and endurance, FNT, and vibration sensation, while hypoesthesia was present in up to 80-90% of patients. Abnormality in activities such as fine dexterity and TEMPA were even more frequent, being present in up to 80% of participants with no/minimal disability. Limitation in UL activities was detected even when single modality testing was normal. The greater sensibility of activities compared with body functions likely reflects that activities require complex integration of motor, cerebellar, sensory and cognitive functions.

Predicting UL dysfunction in the activities of the daily living – ADL: We tested the accuracy and predictive value of measures of grip strength and endurance, coordination, tactile and vibratory sensation, gross and fine dexterity on the limitations in the ADL using two independent anchors reflecting an objective (TEMPA) and a subjective perspective (DASH). Despite TEMPA and DASH highly differed one another in terms of method of administration, sensitivity in our cohort and in the construct they tested, both independently identified BBT, NHPT and FNT as the most accurate variables, with good to excellent values of area under the curve (Figure 1).

Time to complete the TEMPA was significantly predicted by each variable at univariate regression analysis: NHPT (adj. R2 0.772, P<0.001), BBT (adj. R2 0.707, P<0.001) and, FTN (adj. R2 0.532, P<0.001) showed a strong predictive value, while grip strength and endurance, vibratron and, SWMT had very weak predictive values (adj. R2 < 0.2). The DASH score was also significantly predicted by each tested variable at univariate analysis: NHPT (adj. R2 0.375, P<0.001), BBT (adj. R2 0.373, P<0.001), and FTN (adj. R2 0.359, P<0.001) showed a weak to moderate predictive value, while grip strength and endurance, vibratron and, SWMT had very weak predictive values (adj. R2 < 0.2) (Figure 2).
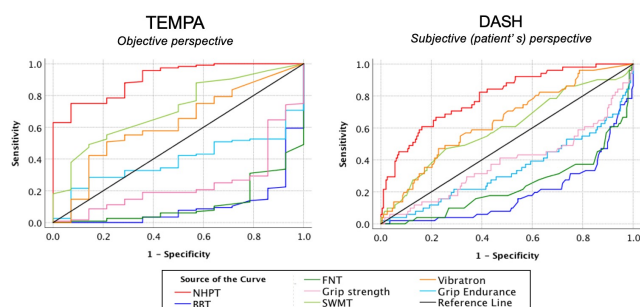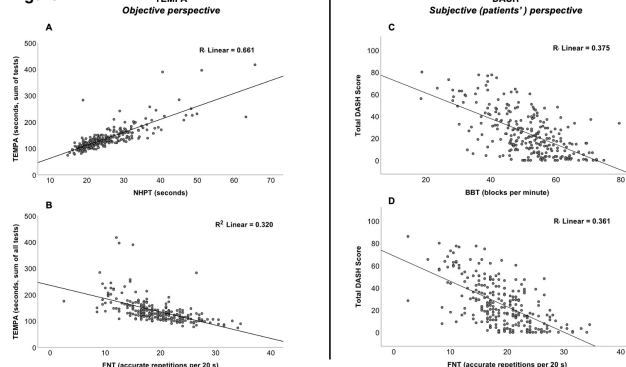
Figure 1

Figure 2

Discussion

Recent evidence from clinical trials on people with progressive MS suggests that UL function is a more sensitive and clinically relevant outcome measure than lower limb function. This is supported by our cohort as even those PwMS who were "asymptomatic" or at least unaware of their limitations, had significant UL dysfunction even in early disease stages (DASH was abnormal in 2% of mild disease, whilst 20% of the mild disability cohort already had difficulties with the NHPT). Thus, it is important to incorporate both performance and capacity measures in the evaluation of UL function to obtain a thorough understanding of the limitations of PwMS so that healthcare services may be adapted to their needs.

Our data suggest the incorporation of the BBT and FNT alongside the NHPT are needed to fully characterize UL dysfunction in the ADL. In both the ROC Curve and univariate regression analyses, BBT, FNT and NHPT were the most accurate variables in detecting the presence of abnormalities in UL ADL. The fact that these variables were also independently selected using two different anchor variables (the DASH self-administered questionnaire and the timed TEMPA test) further strengthens the accuracy of BBT and FNT in detecting objective (TEMPA) and subjective (DASH) UL limitations in ADL. The BBT taking 2 minutes with low additional costs, and FNT taking 40 seconds with no additional costs or special equipment attesting to their accessibility. BBT and FNT are time-efficient and cost-effective measures that could complement the NHPT to capture all elements of UL disability.