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Quantitative sensory and motor measures detect change over time and correlate with walking speed in individuals with multiple sclerosis

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Abstract
Background: Impairments of sensation, strength, and walking are common in multiple sclerosis (MS). The relationship among these abnormalities and how they change over time remains unclear.
Objective: To determine the extent that quantitative lower extremity sensory and motor measures detect abnormalities over time, relate to global disability, and to walking speed in individuals with MS.
Methods: This prospective, longitudinal analysis evaluated 136 MS subjects. Measures included measures of leg strength, sensation, the Expanded Disability Status Scale(EDSS) and timed 25-foot walk test (T25FW). Mixed effects regression models were used.
Results: Our cohort's mean age is 44.3±10.8 years (mean±SD), EDSS score range 0–7.5, 66% were females, and follow-up time was 2.1±1.2 years. Strength significantly changed over time; the RRMS group demonstrated the greatest changes in ADF (3.3 lbs/yr) while the PPMS group showed significant HF changes (−2.1 lbs/yr). Walking speed was affected most by HF, especially in the weakest individuals (HF<20 lbs); T25FW increased by 0.20 s for each 1 lb loss ($p=0.001$). Likewise T25FW changed by 0.19 s for each 1 lb change in ADF ($p<0.01$).
Conclusion: Quantitative measures detected changes in sensation and strength over time, despite a stable respective functional systems scores of the EDSS. Quantitative measurement

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tools may improve the sensitivity of disability measures in MS and further investigation of these tools as outcomes in future clinical trials of rehabilitative and neuroreparative interventions is warranted.

1. Introduction

Multiple sclerosis (MS) is a primary demyelinating disease of the central nervous system that often results in accumulation of neurological disability. Rating scales such as the Expanded Disability Status Scale Score (EDSS) are often used to evaluate global disability (Kurtzke, 1983). However, rating scales provide limited information about specific impairments and their relationship to functional disability, resulting in treatment interventions that are broad and typically tested on a "trial-by-trial" basis (Schwid et al., 1997, 2000; Cohen et al., 2000). Following the natural history of changes in strength and sensation in a large group of individuals with MS is useful to determine differences in the impairment among MS subtypes and for understanding the extent that these impairments affect disability over time. Development of quantitative outcome measures could then be used to more precisely measure their effects on disability and lead to more focused rehabilitation interventions.

Quantitative devices to measure strength and sensation have been previously shown to detect impairments in MS versus healthy controls, in addition these measures correlated with the EDSS and the Timed 25-foot walk (T25FW) (Newsome et al., 2011). However, it is not known to what extent these tools can detect change over time and how they relate to global disability measures and ambulation. The purpose of this study was to determine the extent that quantitative measures of lower extremity strength and sensation detect abnormalities over two years, as well as how they relate to global disability measures and walking speed in individuals MS.

2. Methods

2.1. Participants

Participants were recruited by Johns Hopkins MS Center physicians from November 2004 to May 2011. Participants were excluded if they had an MS relapse within three months of testing or reported a history of peripheral neuropathy or any other orthopedic, neurologic, or cognitive condition that might interfere with study procedures. All participants provided signed, informed consent in accordance with Institutional Review Board regulations at Johns Hopkins University and Kennedy Krieger Institute.

To address the study objectives, 136 individuals with clinically definite MS as defined by the 2005 McDonald criteria were examined (Table 1) (Polman et al., 2005). A retrospective chart review and interviews with participants were done to obtain disease subtype by a physician trained in MS disease categorization (SDN). Within each session, quantitative lower extremity strength and sensation was measured, and overall disease status (i.e., EDSS and T25FW) were assessed. Thirty-nine individuals were lost to follow-up due to time constraints and scheduling difficulties.

2.2. Quantitative and functional impairment measures

Vibration sensation thresholds (vibration units [vu]) for the right and left great toes in 262 of 272 toes were quantified using the Vibratron II device (Physitemp, Huron, NJ). Follow up for five individuals were not collected due to time constraints. Quantitative vibration testing has previously been shown to be valid and reproducible in MS (Newsome et al., 2011). For this test, each subject was required to determine which of two rods is vibrating using a two-alternative forced choice procedure over multiple trials (Arezzo, 1985).

A Microfet2 hand-held dynamometer (Hoggan Health Industries, WestJordan, UT) was used to measure lower extremity strength (force in pounds [lbs]). Quantitative strength testing has previously been shown to be valid and reproducible in MS (Newsome et al., 2011). The average of two maximum ankle dorsiflexion (ADF) and hip flexion (HF) efforts were collected for each leg. We tested 256 of 272 legs for ADF measures and 268 of 272 legs for HF measures. Follow-up for seven individuals for ADF measures and two individuals for HF measures were not collected due to time constraints (i.e., scheduling difficulties). ADF and HF strength were chosen because they: 1) can be reliably quantified, 2) are common sites of weakness in MS, and 3) describe proximal and distal weakness, which are important for walking (Newsome et al., 2011).

Ambulation was assessed using the T25FW (Arezzo, 1985; Hobart et al., 2013; Goldman et al., 2013; Kieseier and Pozzilli, 2012). The EDSS was used as a measure of overall disease status; the sensory and pyramidal functional subscores (FSS) were then compared to the quantitative data.

2.3. Statistical analysis

Statistical analyses were completed using Stata 11 (StataCorpLP, College Station, TX). All reported p-Values are two-tailed and considered statistically significant if $p<0.05$.

A mixed effects regression model was used to determine change in quantitative strength and sensation over time. This regression model accounted for age, gender, disease subtype, and symptom duration.

A secondary analysis was used to determine whether starting at different levels of disability affected the rate of change in the quantitative measures tested over time. We used the worse side of the quantitative measures from