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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

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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 seconds(s) for each 1lb loss ($p=0.001$). Likewise T25FW changed by 0.19s for each 1lb 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 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.

Search Terms

Multiple Sclerosis; Outcome Measures; Neurological Disability; Rehabilitation

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.¹ 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.^{2–4} 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).⁵ 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.

Methods

Participants

Participants were recruited by Johns Hopkins MS Center physicians from November 2004–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).⁶ 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.

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.⁵ For this test, each subject was required to determine which of two rods is vibrating using a two-alternative forced choice procedure over multiple trials⁷

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.⁵ 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.⁵

Ambulation was assessed using the T25FW.⁷⁻¹⁰ 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.

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 baseline (i.e., weakest, least sensation) and subsequently divided the population for each measure into three groups (i.e., lowest, middle, and highest 33%). To determine change over time within each tertile a mixed effects regression model with interaction terms was used, that also accounted for age, gender, disease subtype, and symptom duration.

To determine the variables that best predict T25FW we used a mixed effects regression model. Table 2 shows the results when the variables were unadjusted as well as a comprehensive model adjusting for all variables (quantitative strength and sensation, disease subtype, symptom duration, age, and gender). First, quantitative measures were plotted against T25FW using a linear regression model. Because the relationship between the strength data and T25FW was not linear, linear splines were used to model these data. We used lowess smoothing plots to assess this non-linear relationship, and to select knots for the linear splines. For ankle strength, we divided the group into less than or greater than 20 pounds of strength. However, for hip strength the relationship was better characterized by three line segments with changes in slope at 20, and 40 pounds. The difference between sides for strength and sensation within the regression model was also evaluated.

To compare impairment change with FSS change individuals were divided into those who showed a 20% change in quantitative measure from baseline to year 2 (on at least one side) and a one-point change on sensory or pyramidal FSS scores over a two-year period. A 20% change constituted a change in quantitative measures, based on work by Schwid et al.¹¹ Individuals were divided into 4 groups: 1) no change in both, 2) no change in FSS, change in quantitative measure, 3) change in FSS, no change in quantitative measure, 4) change in both.

Results

Study population

MS participants were a mean age of 44.3 ± 10.8 years (mean $\pm$ SD) (range: 20–67), disease duration of 6.7 ± 8.9 years (range: 0.5–42), and 66% were females. Disability varied from EDSS 0–7.5 (Table 1). Participants included 83 with RRMS, 31 with SPMS, and 22 with PPMS with a mean longitudinal follow up of 2.1 ± 1.2 years. The mean age for individuals with RRMS was 38.3 ± 10.7 years, 61 female; with SPMS, 51.9 ± 7.4 years, 18 female; with PPMS, 50.1 ± 9.8 years, 12 female.

Changes over time

Table 1 shows baseline and year 2 data of the EDSS, HF strength, ADF strength and vibration sensation measures. Figure 1a shows HF strength data for each individual visit over a two-year period. Overall there was a significant decrease in hip strength across all subtypes (-1.26 lbs/yr, $p < 0.001$); disease subtype, disease duration, and sex contributed significantly to this decline ($p = 0.001$, $p = 0.030$, $p = 0.001$; respectively), while age was not associated ($p = 0.600$). The PPMS group showed the most significant loss of hip strength, 2.1 pounds per year (CI = -3.49 : -0.72 , $p = 0.003$). The RRMS group also showed significant changes in hip strength with an average loss of 1.24 lbs/year (CI = -1.92 : -0.56 , $p < 0.001$). The SPMS group showed a smaller loss in hip strength of 0.67 lbs/year (CI = -1.90 : 0.56 , $p = 0.280$). When evaluating the overall difference in hip strength between the MS subtypes, the SPMS group on average was 18.62 lbs/yr weaker than the RRMS group, and the PPMS group was 11.26 lbs/year weaker than the RRMS group.

Figure 1b shows ADF strength data for each individual visit over a two-year period. There were significant changes in overall ankle strength across disease subtypes; ankle strength improved 2.6 lbs/yr ($p<0.001$). Disease subtype and sex were significantly associated ($p=0.002$), but disease duration and age were not ($p=0.300$). The RRMS group showed the most significant change, 3.3 lbs/yr (CI=2.29:4.29, $p<0.001$). For the SPMS group, ankle strength improved 1.99 lbs/yr (CI=.22:3.76, $p<0.050$). The PPMS group showed a smaller change of 0.40 lbs/yr (CI=-1.75:2.56, $p=0.713$). When evaluating the overall difference in ankle strength amongst the MS subtypes, the SPMS group was 19.4 lbs/year weaker than the RRMS group and the PPMS group 10.9 lbs/year weaker than the RRMS group.

Figure 1c shows data from vibration sensation testing for each subject visit over a two-year period. Overall, there was a trend towards a significant increase (i.e., worsening) in toe vibration thresholds (0.09 vu/yr, $p=0.3$). The RRMS group showed the greatest trend in vibration threshold with an increase of 0.20 vu per year (CI=-.01:0.41, $p=0.065$). Comparably, the SPMS group showed a loss of sensation of 0.27 vu per year (CI=-.61:0.08, $p=0.13$). The PPMS group showed a much smaller change of 0.17 vu per year (CI=-.27: .61, $p=0.45$). Overall, the SPMS group had the highest (i.e., worst) vibration sensation threshold; 4.27 vu/yr worse than RRMS group. Similarly, the PPMS group vibration thresholds were 1.30 vu/yr higher than RRMS group.

Tertile analysis

Figure 2 shows data for each subject over a two-year period, separated into tertiles, for HF, ADF and vibration sensation. For Figure 2a, individuals whose HF was the weakest at baseline (i.e., in lowest tertile) on average lost 1.18 pounds of HF strength per year (CI=-2.12:-0.23, $p<0.02$). Individuals in the middle tertile lost only 0.98 lbs/yr (CI=-1.90:-0.05, $p<0.05$). By contrast, individuals who started out the strongest at baseline lost 2.61 lbs/year (CI=-3.47:-1.74, $p<0.0001$) of HF strength.

Figure 2b show ADF strength data. Individuals with the weakest ankle strength at baseline gained 2.32 lbs/year (CI=0.82:3.81, $p<0.01$). Individuals in the middle tertile at baseline gained 4.59 lbs/yr (CI=3.28:5.92, $p<0.001$). By contrast, individuals who started out the strongest at baseline (i.e., top tertile) show a change of only 0.57 lbs/year (CI=-0.71:1.86, $p=0.38$).

Figure 2c shows toe vibration sensation thresholds. Individuals with the most normal vibration thresholds (i.e., in the lowest tertile) showed small changes of 0.06 vu/yr (CI=-0.21:0.33, $p<0.1$). However, individuals in the middle tertile at baseline showed a significant worsening of vibration sensation thresholds of 0.42 vu/yr (CI=0.14:0.70, $p<0.01$). Individuals with the highest (i.e., worst) vibration thresholds at baseline showed non-significant changes of 0.01 vu/yr (CI=-0.30:0.27, $p<0.1$).

Predicting change in walking speed

The average T25FW at baseline required 6.34s (3.97 feet/s), and increased to 7.45s (3.36 feet/s) at year 2. Individuals with MS walked considerably slower than the published norms for fast walking velocity in adults age 40–49 (3.10s for men and 3.95s for women).¹³ Table

2 shows results from the mixed effects regression model with the variables that best predict changes in the T25FW.

In the complete model ankle and hip strength are the only factors that significantly affect T25FW (right column, Table 2). For each pound of change in ADF, a change of 0.2s in T25FW would be expected. This is true for individuals who at baseline have stronger ADF, > 20lbs ($p=0.001$), or weaker ADF, <20 pounds ($p=0.002$). With the more limited model, adjusting only for ankle strength, results show a similar strong effect of ankle strength over contextual variables ($p<0.001$).

When considering hip strength in the complete model, a change in HF was significant only in the weakest group, with HF <20 pounds at baseline ($p=0.001$). For individuals with HF <40 pounds, the T25FW would only be expected to change 0.13s for each pound of HF strength ($p=0.030$). By contrast, individuals who have closer to normal HF strength, >40 pounds, T25FW was not significantly affected ($p=0.430$). With the more limited model, adjusting only for HF, not ADF or vibration sensation, results show that the strongest effect is for individuals whose HF was <20 pounds ($p<0.0001$).

There was not a significant impact on T25FW when considering other measures.

Relating quantitative sensorimotor measures and their respective FSS

Table 3 highlights the relationship between the number of individuals that showed a change (i.e., >20% from baseline), or no change, in sensory and motor measures versus sensory or pyramidal FSS scores (one point change). The most important finding of this analysis was the subgroup of individuals who experienced no change in FSS, with a change in quantitative measure (highlighted). For these subgroups, 32% of participants show a change in ankle strength of >20%, 9% show a change in hip strength of >20% not accompanied by a change in pyramidal FSS, and 42% show a change in vibration sensation of >20% not accompanied by a change in sensory FSS.

Discussion

Overall, our data show that quantitative measures of strength and sensation detect specific impairments in MS and these relate to global disability measures and ambulation. Quantitative measures of strength significantly changed over time; when accounting for MS subtype the RRMS group had the most significant change in ADF and the PPMS group for HF strength. Individuals starting out with the strongest HF showed the largest decline in strength. Quantitative vibration sensation showed trends for detecting change over time; the RRMS group demonstrated the strongest trend towards change. Individuals with only mild sensory changes (the middle 33%) showed the largest decline in vibratory sensation over time. Walking speed was most affected by weak HF. Lastly, a subgroup of patients had a change in their quantitative measures that was not detected in the respective FSS of the EDSS. This highlights the need to use quantitative measures that can detect subtle clinical changes.

Strength measures have been shown to have importance to walking, balance¹⁴ and overall disability^{15,16} in MS, however the methods used to assess weakness are quite variable. Some studies measure the perception of strength¹⁷, or use a 5-point rating scale¹⁸, isokinetic devices^{12,19} or hand held dynamometry^{5,20}. What has not been addressed is the extent that impairments such as strength change over time, whether a baseline measure gives clues as to the rate of change, and the impact of sensory and motor impairments on walking function in individuals with MS. This study addresses these issues. The data show that individuals that started out with strong HF muscles (the top 33%) lost the most strength relative to the other groups. When accounting for MS subtype, HF muscles weakened to a greater extent for individuals with PPMS compared to individuals with RRMS or SPMS. The extent of worsening over two years for the PPMS cohort is more than twice that of the SPMS cohort (see Figure 1a, 1b). Since there is a lack of outcome measures that are sensitive enough to detect changes over time in PPMS⁵, the use of dynamometry to monitor HF strength over time in this MS subtype may prove to be useful for detecting even subtle changes that are not picked up by rating scales (see table 3).

ADF strength improved over time. While this was not expected, we suggest that this increase could be attributed to the use of functional electrical stimulation, the decreased reliability in testing ADF versus HF strength⁵, and/or exercise/physical therapy that individuals may have been participating in during the year. To test this we did a chart review to evaluate the individuals who showed more than a 5 pound increase in strength (~1 standard deviation of healthy ankle strength (Newsome et al 2011)), since that is outside of the noise of the instrument. We show that 48 out of the 136 of individuals (35.3%) increased their strength in two years. Of these 48, 11 (22.9% of the 48) reported an increase in physical activity or started physical therapy (which may have included use of electrical stimulation to the ankle dorsiflexor muscles) over the two-year span. Fifteen (31.3% of the 48) started a new immunomodulatory medication over the two-year period. These two variables alone influence more than 50% of the individuals who show increases in ankle strength. Though the chart review is not specific to factors that only influence the ankle dorsiflexor muscle strength it highlights the reality that multiple factors could be influencing the increase we report. We posit that the limited reliability of the ankle joint may be the most important factor explaining this increase in ankle strength, and should be more closely evaluated in future studies. Regardless, variations in ankle dynamics are known to be important in walking²¹ and use of the dynamometer may provide a quantitative means to detect these variations which could improve our understanding of the fluctuation of gait function in MS. Interestingly, individuals who started out with moderately weak ADF strength (~43 pounds) gained the most strength over two years (see figure 2). It would be interesting to know, not only the factors that may accompany this increase but also if this increase is related to clinically meaningful improvements in walking performance.

Vibration sensation is known to be impaired in many individuals with MS⁵, and is frequently implicated as a reason for impaired balance and higher risk for falls²². Overall, the vibration sensation data from this study show that individuals who are on the upper margin of “normal sensation” (the middle third of our cohort) at baseline have the most significant worsening compared to individuals who, at baseline, had poorer sensation or are within normal values. Thus, use of the Vibratron II device allows for detection of even

subtle changes from “normal” that may not be apparent when using a tuning fork. The strongest trend in this cohort is for changes in vibration sensation within the RRMS group, although the SPMS group had the poorest sensation at baseline. This finding in combination with the tertile analysis results suggest that quantitative vibration testing may be best utilized in assessing early to mid MS disease duration.

Previous cross sectional data from our group and others show that strength is more important to walking than vibratory sensation loss.^{5,23,24} Many individuals in our cohort were weaker than published norms for healthy adults. Results from the mixed effects regression showed that for individuals who have limited HF strength at baseline (i.e., <20 lbs) a loss of even 5 lbs of strength results in a gain of one second on the T25FW test. This shows a strong relationship between strength and walking speed, but also shows a practical way of predicting what a change in T25FW speed may indicate within a specific disability subgroup. Identifying clinical markers of disability has been historically difficult in MS given the heterogeneity of the population. Simple tests such as the T25FW may be useful in predicting fall risk, or who can benefit from strategic rehabilitation treatments and drug therapies.

As with all studies there are several limitations. Clinically meaningful changes in the quantitative measurements of strength and sensation have yet to be determined for individuals with MS, making it challenging to determine thresholds of loss that influence walking speed. A longer follow-up may have garnered further information about meaningful changes in these measures and their relationship with issues such as fall risk. A second limitation is that use of quantitative measures does not alleviate a problem of ceiling and floor effects, but does specify these limitations. All devices capture only a range of disability, and these features need to be better understood. A third limitation is that all participants were on prescribed pharmacologic interventions.

Conclusions

In summary, the results of this 2-year natural history study demonstrate the slow but steady progression of sensory and motor impairments in MS. The quantitative devices used in this study detected changes in impairments in MS subjects that correlated to walking speed. Proximal lower extremity weakness contributed the most to slowing walking speed especially in the weakest individuals. Vibratory sensation shows the greatest trend toward detecting subtle changes early in the disease course, and the individuals with mildest changes at their first visit show the largest changes over two years. The quantitative measures used in this study can help improve our ability to detect disability in MS and has the potential to be useful as outcome measures in future rehabilitative and neuro-reparative trials.

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Figure 1.

Scatterplot of strength and sensation, over multiple visits, in individuals with MS. **A.** Hip Flexion strength in pounds (lbs); **B.** Ankle dorsiflexor strength, in pounds (lbs); **C.** Vibratory sensation at the great toe, in vibration units (vu). RRMS = Relapsing-Remitting MS; SPMS = Secondary Progressive MS; PPMS = Primary Progressive MS; Black circles are individuals with RRMS; Light gray squares are individuals with SPMS; Gray diamonds are individuals with PPMS. Normative values for 40–49 years for ankle dorsiflexion strength: for women is 59.3 ± 7.4 lbs, for men is 75.8 ± 11.0 lbs; Hip Flexion: for women is 47.2 ± 11.1 lbs, for men is 69.6 ± 12.0 lbs. The threshold for vibratory sensation that is within normal limits is 2.56 vu^{25} . The lines indicate the best fit for each MS subtype

Figure 2.

Scatterplot of strength and sensation measures for individuals with MS, data is divided into tertiles, from the baseline measure. **A.** Hip Flexion strength in pounds (lbs); **B.** Ankle dorsiflexor strength in pounds (lbs); **C.** Vibratory sensation at the great toe, in vibration units (vu). Light gray squares are individuals in the bottom 33%; gray diamonds are individuals in the middle 33%; black circles are individuals in the top 33%. RRMS = Relapsing-Remitting MS; SPMS = Secondary Progressive MS; PPMS = Primary Progressive MS.

Table 1

Characteristics of individuals with multiple sclerosis

		RRMS	SPMS	PPMS	Total
Disease Duration at Baseline (yrs)		7.2±6.4	18.1±10.9	10.0±9.7	6.7±8.9
EDSS	Baseline	2.5±1.7	5.3±1.8	4.5±1.8	3.4±2.1
	Year 2	2.5±1.8	5.7±1.7	4.6±2.0	3.4±2.2
Worse Hip, lbs [mean±SD]	Baseline N	41.97±12.80 (83)	14.92±16.61 (31)	27.52±17.06 (22)	33.47±18.31 (136)
	Year 2 N	38.95±12.66 (65)	15.71±17.18 (19)	21.62±16.38 (13)	32.07±17.19 (97)
Worse Ank DF, lbs [mean±SD]	Baseline N	43.96±14.05 (83)	19.02±18.21 (31)	32.14±18.81 (22)	36.36±18.87 (136)
	Year 2 N	50.10±17.35 (65)	23.16±18.23 (19)	33.50±19.36 (13)	42.60±20.83 (97)
Worse Vib Sensation, vu [mean±SD]	Baseline N	3.44±2.82 (83)	9.82±6.32 (31)	5.69±3.03 (22)	5.26±4.69 (136)
	Year 2 N	4.16±4.25 (65)	8.65±4.46 (19)	5.99±2.59 (13)	5.28±4.45 (97)

Table 2

Effects of variables on timed 25 foot walk

	unadjusted		ADF		HF		Vibration		Complete	
	coeff.	Conf. Interval	coeff.	Conf. Interval	coeff.	Conf. Interval	coe ff.	Conf. Interval	coeff.	Conf. Interval
ADF <20	-.27	-.39; -.16 (p<0.0001)	-.24	-.36; -.13 (p<0.0001)					-.19	-.31; -.08 (p=0.001)
ADF >20	.26	.14; .38 (p<0.0001)	.23	.11; .35 (p<0.0001)					0.19	0.07; 0.31 (p=0.002)
Diff between sides	-.02	-.05; .02 (p<0.36)	-.02	-.05; .02 (p<0.27)					-.01	-.05; .03 (p=0.59)
HF < 20	-.36	-.49; -.23 (p<0.0001)			-.34	-.7; -.21 (p<0.0001)			-.20	-.28; -.11 (p=0.0001)
HF <40	.08	-.11; .27 (p<0.43)			.08	-.12; .28 (p<0.42)			0.13	0.01; 0.25 (p=0.03)
HF >40	.25	.08; .42 (p<0.005)			.20	.02; .38 (p<0.03)			0.04	-.06; 0.14 (p=0.43)
Diff between sides	-.14	-.22; -.06 (p<0.001)			-.17	-.25; -.08 (p<0.0001)			-.04	-.09; 0.02 (p=0.16)
Vib	.51	.26; .77 (p<0.0001)					.28	-.002; .56 (p=0.05)	-.06	-.23; 0.11 (p=0.48)
Diff between sides	-.45	-.78; -.12 (p=0.008)					-.34	-.67; -.003 (p=0.048)	0.05	-.13; 0.23 (p=0.60)
Age	.18	.08; .28 (p<0.0001)	0.004	-.11; .11 (p<0.94)	0.00004	-.10; .10 (p=0.99)	0.02	-.12; .15 (p=0.81)	0.001	-.10; 0.11 (p=0.98)
Gender	1.56	-.69; 3.80 (p=0.175)	1.05	-.55; 2.64 (p<0.199)	2.35	0.42; 4.27 (p=0.17)	0.84	-.139; 3.07 (p=0.46)	1.2	-.34; 2.81 (p=0.12)
SymDur	.27	.14; .39 (p<0.0001)	.14	.008; .27 (p<0.037)	.09	-.04; .22 (p=0.18)	0.17	0.01; .33 (p=0.04)	0.09	-.23; 0.22 (p=0.14)
RRMS	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
SPMS	5.71	2.79; 8.64 (p<0.0001)	3.10	.21; 5.98 (p<0.035)	-.28	-3.07; 2.52 (p=0.85)	2.69	-.72; 6.09 (p=0.12)	2.15	-.57; 4.88 (p=0.12)
PPMS	3.56	.53; 6.59 (p<0.021)	1.69	-1.33; 4.70 (p<0.27)	0.46	-2.34; 3.26 (p=0.75)	2.32	-1.11; 5.76 (p=0.18)	1.21	-1.59; 4.02 (p=0.39)

ADF = ankle dorsiflexion; HF = hip flexion; Diff = difference; Vib = vibration sensation; SymDur = symptom duration in months; RRMS = relapsing-remitting MS; SPMS = secondary progressive MS; PPMS = primary progressive MS

Conf. Interval (Confidence Interval) are reported as (-95%CI; +95%CI)(p-value)

Table 3

Change in FSS compared with change in quantitative strength and sensation measures

Pyramidal FSS change $\geq$ 1 point				Pyramidal FSS change $\geq$ 1 point				Sensory FSS change $\geq$ 1 point						
A.				B.				C.						
ankle change $\geq$ 20%	No	Yes	Total	hip change $\geq$ 20%	No	Yes	Total	sensory change $\geq$ 20%	No	Yes	Total			
	No	39	40		79	No	93		73	166	No	25	31	56
		18%	19%		37%		41%		32%	73%		10%	12%	22%
	Yes	68	66		134	Yes	20		41	61	Yes	105	89	194
		32%	31%		63%		9%		18%	27%		42%	36%	78%
	Total	107	106		213	Total	113		114	227	Total	130	120	250
		50%	50%		100%		50%		50%	100%		52%	48%	100%