

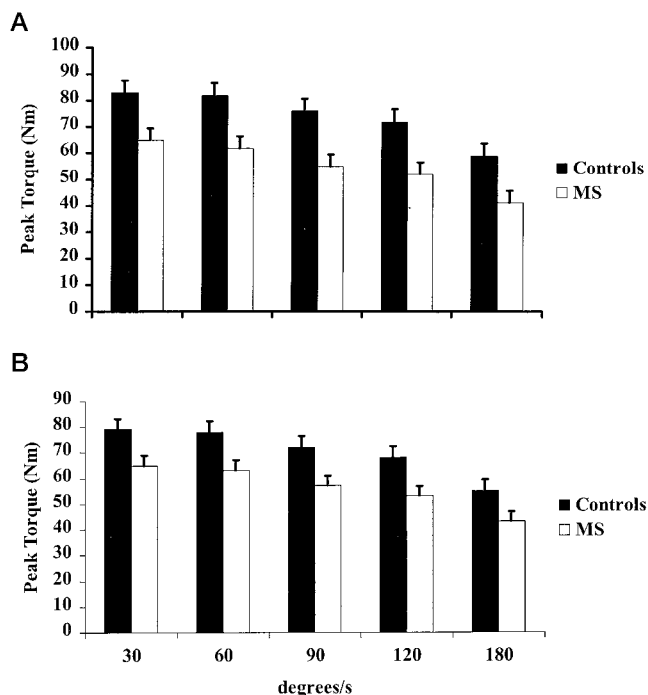


FIGURE 2—A, Peak torque of the dominant knee flexors adjusted for body mass and age. Significant group ($P = 0.007$) and speed effects ($P < 0.0001$) were seen; however, there was no interaction ($P = 0.860$). B, Peak torque of the dominant knee flexors adjusted for fat free mass and age. Significant group ($P = 0.017$) and speed ($P < 0.0001$) effects were observed, but no significant interaction ($P < 0.0001$) was observed.

MS were weaker than controls. Peak torque production was 16.9%, 25.7%, and 20.8% lower in MS than controls for the nondominant extensors, dominant flexors, and nondominant flexors, respectively. Similar findings have been reported by others (8,12,13,15). The reason for this reduced muscle force generating capacity cannot be determined from this investigation. However, Kent-Braun et al. (5) have shown that the muscle fiber cross-sectional area is reduced by 26% relative to that of controls. It is well known that muscle cross-sectional area is highly related to maximal force-generating capacity in healthy subjects (18). Other explanations for the lower force-generating capacity relate to the nervous system defects in MS. It has been reported that when a supramaximal electrical stimulus is imposed on the working muscle during a maximal voluntary contraction, there is a large increase in force in individuals with MS, suggesting a reduced ability to activate the available muscle mass (13). In addition, Rice et al. (13) have reported that

motor neuron firing rates of the working muscle during a maximal isometric contraction are significantly lower in individuals with MS than controls.

Strength of the dominant leg versus the non-dominant leg. Individuals with MS commonly have weakness to a greater extent in one lower limb than the others or on one side of the body than the other. Thus, we compared the difference between MS and controls with regard to torque of the dominant leg versus torque of the nondominant leg (dominant – nondominant; Table 4). The means between groups were numerically greater for MS than controls but not statistically significant. Thus, if there truly was asymmetry in muscle force production between MS and controls, we could not detect it with our methods.

Strength relative to fat free mass. In the present investigation, when strength was adjusted for fat free mass and age, strength in individuals with MS was significantly lower across speeds of contraction in three of the four muscle groups tested when compared with the control individuals. Peak torque was 12.8%, 20.2%, and 21.3% lower for MS than controls for the nondominant extensors, the dominant flexors, and the nondominant flexors, respectively. This is an extremely important finding. Assuming fat free mass is representative of muscle mass, it appears that individuals with MS are weaker than controls, and this is not accounted for by differences in the amount of muscle mass between groups. Thus, the reduced muscle fiber size (26% lower in MS than controls; 7) may not be as relevant in MS as compared with individuals without the disease with regard to strength. There are at least a few possible explanations for the finding of reduced force production when corrected for fat free mass. First, as discussed above, individuals with MS cannot activate their muscles as well as individuals without the disease. Thus, for a given amount of fat free mass, there is less force in an MS versus a control subject because of reduced muscle activation. Another or an additional potential mechanism is that the muscle of an individual with MS is of lower quality (force generating capacity of a given amount of skeletal muscle mass is less in MS than controls) than that of a person without the disease. Ng and Kent

Muscle strength and fatigue during isokinetic exercise in individuals with multiple sclerosis

CHARLES P. LAMBERT, ROBERT L. ARCHER, and WILLIAM J. EVANS

Nutrition, Metabolism, and Exercise Laboratory, Department of Geriatrics, and Department of Neurology, University of Arkansas for Medical Sciences, Little Rock, AR 72205

ABSTRACT

LAMBERT, C. P., R. L. ARCHER, and W. J. EVANS. Muscle strength and fatigue during isokinetic exercise in individuals with multiple sclerosis. *Med. Sci. Sports Exerc.*, Vol. 33, No. 10, 2001, pp. 1613–1619. **Purpose:** To compare muscle strength and muscle fatigue of the knee extensors and flexors in individuals with multiple sclerosis (MS) and non-MS control subjects and to evaluate the reliability of muscle strength and muscle fatigue testing in these individuals. **Methods:** Thirty individuals (13 women and 2 men for both MS and control groups), age (mean $\pm$ SD) 38.8 ± 10 for MS and 33.1 ± 7.6 yr for controls, participated in this investigation. Peak torque was measured on two occasions separated by approximately 7 d at 30, 60, 90, 120, 180°s^{-1} with 2 min of recovery between each bout. The nondominant leg was tested followed by the dominant leg after 10 min of recovery. Subjects then performed three bouts of 30 flexions and extensions of the dominant leg at 180°s^{-1} with 1 min of recovery between bouts. **Results:** The reliability of muscle torque was very high for individuals with MS (only 1 of 20 measurements with an ICC below 0.900). Total work was also highly reliable for MS, but the Fatigue Index (work during the last 15 contractions/work during the first 15 contractions) $\times 100$ was not. Peak torque adjusted for age, body mass, and fat free mass (measured by whole body plethysmography; the Bod Pod; Life Measurement Instruments, Concord, CA) was significantly greater for controls than for MS for three of four lower body muscle groups tested. For the muscle fatigue test (3 bouts of 30 knee extensions and flexions at 180°s^{-1}), the Fatigue Index was greater (less fatigue) for the knee extensors for controls than MS for the third bout. For flexion, the Fatigue Index was greater for controls than MS over the three bouts (group effect). Total work was significantly greater for controls than MS for the flexors (group effect) and approached significance for the extensors. **Conclusions:** Individuals with MS were weaker than controls when data were adjusted for age, body mass, and fat free mass. This latter finding (force relative to age and fat free mass) suggests that there is a reduced ability to activate muscle mass in MS and/or the muscle mass of individuals with MS is of lower quality (i.e., reduced force/unit muscle mass) than controls. **Key Words:** WEAKNESS, DYNAMIC MUSCLE CONTRACTION, DEMYELINATING DISEASE

Individuals with multiple sclerosis (MS) have been reported to have reduced muscle strength compared with non-MS controls during dynamic exercise (1,12). Armstrong et al. (1) reported that peak torque measurements at 70, 190, and 230°s^{-1} for knee extensors and flexors was significantly lower in individuals with MS than non-MS control subjects (Kurtzke EDSS (6) ≤ 5 ; EDSS stands for Expanded Disability Status Scale and is a measure of disease severity with an emphasis on mobility. A score of 0 represents individuals with a normal neurologic exam, whereas a score of 10 is death due to MS). In addition, Ponichtera et al. (12) reported that concentric peak torque was significantly greater for knee extension at 30, 60, and 90°s^{-1} for able bodied individuals when compared with the MS group (Kurtzke EDSS 1–4). Thus, at both slow and fast

speeds, individuals with MS have been shown to be weaker than non-MS controls. With regard to isometric force production, Schwid et al. (15) reported that individuals with MS were significantly weaker in only one of four upper body measurements but were significantly weaker in all eight lower body measurements. Rice et al. (13) reported that the maximum voluntary isometric contractile force of the quadriceps in individuals with MS was 30–70% lower than controls. Rice et al. (13) also reported that individuals with MS had a decreased ability to activate their muscles when compared with individuals without disease. Thus, at least part of the weakness in MS appears to be the result of an inability to activate the muscle that they have.

Systemic fatigue or lassitude is a common problem for individuals with MS. Fatigue, which reduces muscle performance, has been shown to occur to a greater extent in individuals with MS than controls in some (8,15) but not all studies (4,10). Increased fatigue localized to skeletal muscle has been determined using electrical stimulation experiments. Lenman et al. (8) used trains of stimuli of 40 Hz that

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TABLE 1. Descriptive statistics for study participants.

	MS	Control
Age (yr)	38.8 ± 10.0	33.1 ± 7.6
Height (cm)	165.7 ± 7.8	166.4 ± 10.9
Mass (kg)	67.7 ± 11.2	65.3 ± 10.4
Percent body fat	31.8 ± 11.5	27.0 ± 7.8
EDSS	3.5 ± 0.3	Range (1.5–6.0)

Values are mean ± SD (*N* = 15 per group).

lasted 250 ms and were delivered every second for 3 min and found that the fatigue index (ratio of the tension during the last 5 contractions to the tension during the first 5 contractions × 100) was 82 ± 9% for the control group and 45 ± 10.9% for the MS group. In addition, Kent-Braun et al. (3) reported that the half-time of phosphocreatine resynthesis after depletion to similar levels between groups was 2.3 min for MS and 1.2 min for controls, suggesting reduced muscle oxidative capacity in MS. The implication of lower oxidative capacity was later substantiated by lower succinate dehydrogenase and higher alpha-glycerol-phosphate levels in the muscle of individuals with MS than controls (5). The data of Lenman et al. (8) and Kent-Braun et al. (3) (noted above) were obtained during electrical stimulation in the individuals with MS. Earlier but not greater muscle fatigue in MS than controls has been documented in voluntary isometric exercise (4) although the mechanism for this fatigue appears to be different than when electrical stimulation is being used. The increases in the hydrogen ion and inorganic phosphate concentrations were significantly less in MS than controls at fatigue and neuromuscular junction and muscle membrane impairment was similar between groups. These authors concluded that failure of muscle activation (central activation failure and impaired excitation contraction coupling) were the probable causes of fatigue during voluntary isometric contraction in MS.

The purpose of this investigation was to further compare muscle strength and muscle fatigue during isokinetic exercise in individuals with MS and non-MS control subjects, as muscle fatigue measurements during dynamic exercise are not well documented in MS. In addition, we evaluated the reliability of muscle strength and muscle fatigue in individuals with MS and non-MS controls.

METHODS

Subjects. Fifteen individuals with MS with a Kurtzke EDSS score ≤ 6 (mean ± SD: 3.5 ± 0.3 range: 1.5–6.0; median: 3.5; 2 men and 13 women) and 15 control subjects (2 men and 13 women) participated in this investigation

after giving their written consent. Three MS and two controls were recreationally active (<2 exercise sessions/week). One MS and one control exercised 3 times/week. This investigation was approved by the University of Arkansas for Medical Sciences institutional review board.

Preliminary testing. After subjects signed the consent form and completed a medical history questionnaire, a venous blood sample was obtained for routine clinical chemistry analyses (electrolytes, creatine kinase, and blood lipids) and a complete blood count. A urine sample for urinalysis, a resting 12-lead electrocardiogram, a physical exam, and a health history were obtained. The blood samples, urine samples, and resting 12-lead electrocardiogram were obtained to ensure subjects were medically stable and not at undue risk by their participation in this study. After review and approval of this information by an advanced nurse practitioner, all of the subjects were deemed medically stable and capable of successfully completing the study protocol. Subjects maintained their medication constant during the course of the study and no exacerbations of disease occurred during the study.

Experimental trials. Two experimental trials were performed after the familiarization trial. The two experimental trials and the familiarization trial were identical except that body density was determined during the familiarization trial. The time between the familiarization trial and the first experimental trial, and between the first experimental trial and the second experimental trial was approximately 7 d. Body density was determined using whole body plethysmography (Life Measurement Instruments; Concord, CA; 9), and % body fat and fat free mass were determined using the equation of Siri (16). Percent body fat was determined for descriptive statistics and fat free mass was determined to normalize peak torque to fat free mass as fat free mass is an indirect indicator of muscle mass.

Strength testing. After arriving at the laboratory, subjects were positioned in the Cybex Norm dynamometer so that the lateral condyle of the knee was aligned with the axis of rotation of the dynamometer and the angle at the hip was 90°. After determining the range of motion and the gravity correction for the mass of the limb, subjects performed 10 submaximal warm-up contractions at 0.52 rad·s⁻¹ (30°·s⁻¹) followed by 2 min of

TABLE 3. Reliability of total work and the endurance ratio for knee flexion (Flex) and extension (Ext) of the dominant leg.

Measure	MS		Control	
	Ext	Flex	Ext	Flex
Total work	0.938	0.796	0.915	0.801
Endurance ratio	0.357	0.510	0.575	0.375

to represent a relatively broad range of speeds and to encompass both slow and fast speeds. The first two repetitions were performed so that subjects could familiarize themselves with the speed of movement, and the last three were to assess peak torque (Nm), which was recorded for each speed. Contraction speeds were not randomized so that the exact protocol was performed by all subjects for both of the experimental trials. In addition, this assured that the same protocol was performed before the muscle fatigue testing (see below) such that changes in the order of velocities could not have an effect on the muscle fatigue test. Also, the 2-min rest period between velocities should have been adequate for full recovery preceding the subsequent force measurement. After completion of testing of the nondominant leg, subjects were positioned into place for strength testing of the dominant leg. Strength testing was carried out in the same manner as for the nondominant leg. Subjects then recovered for exactly 10 min after strength testing of the dominant leg before testing of muscle fatigue.

Muscle fatigue testing. Muscle fatigue of the dominant leg was determined by having the subject perform three bouts of 30 concentric knee extensions and flexions at $180^{\circ}\cdot\text{s}^{-1}$, each separated by 1 min of seated static recovery. The Fatigue Index for each bout was calculated as the (work performed during the last 15 contractions divided by the work performed in the first 15 contractions) $\times 100$. The total amount of work performed during the 30 contractions was also determined. All trials for strength and fatigue testing were performed at the same time of day and by the same investigator.

Statistical analyses. The intraclass correlation coefficient (ICC) was calculated for each speed of contraction across the two experimental trials for muscle strength of both the dominant and nondominant legs. In addition, the ICC was calculated for the Fatigue Index and for the total work performed during each of the three 30 repetition bouts across the two experimental trials. For comparison of strength between groups, a two-way ANCOVA was performed with group and contraction speed as the independent variables and age and body mass as the covariates (age and body mass were used as covariates as they likely have an effect on muscle strength). In addition, to adjust the data for fat free mass, a two-way ANCOVA was conducted with group and speed as the independent variables and age and fat free mass as the covariates. For total work, an ANCOVA was used adjusting for age and body mass. For the Fatigue Index, data were corrected for age using an ANCOVA. Significance was accepted at a probability ≤ 0.05 .

RESULTS

No significant differences were observed for age, height, weight, or percent body fat between the MS and control groups (Table 1).

The ICCs for peak torque production of the dominant and nondominant legs are presented in Table 2. The ICCs for the Fatigue Index and total work are presented in Table 3.

No significant differences between groups were observed when comparing the force produced for the dominant leg to that produced by the nondominant leg (force of dominant leg – force of nondominant leg; Table 4).

Peak torque of the dominant extensors adjusted for age and body mass is presented in Figure 1A. No significant difference was observed between groups or the interaction of group and speed ($P = 0.058$ for group; $P < 0.0001$ for speed; $P = 0.844$ for the interaction). Significant differences were observed between groups for nondominant extension (Table 5; $P = 0.014$ for group; $P < 0.0001$ for speed; $P = 0.656$ for the interaction), dominant flexion (Fig. 2; $P = 0.007$ for group; $P < 0.0001$ for speed; $P = 0.860$ for the interaction), and nondominant flexion (Table 6; $P = 0.048$ for group). In addition, there was a significant speed effect for peak torque with torque declining as contraction speed increased ($P < 0.0001$). No interactions were observed ($P = 0.947$).

Peak torque data adjusted for age and fat free mass are presented in Figure 1B, Figure 2B, and Tables 5 and 6. No significant group or interaction effects were observed for extension of the dominant knee ($P = 0.214$ for group; $P < 0.0001$ for speed; $P = 0.173$ for the interaction). Significant group effects were observed for extension of the nondominant knee (Table 5; $P = 0$

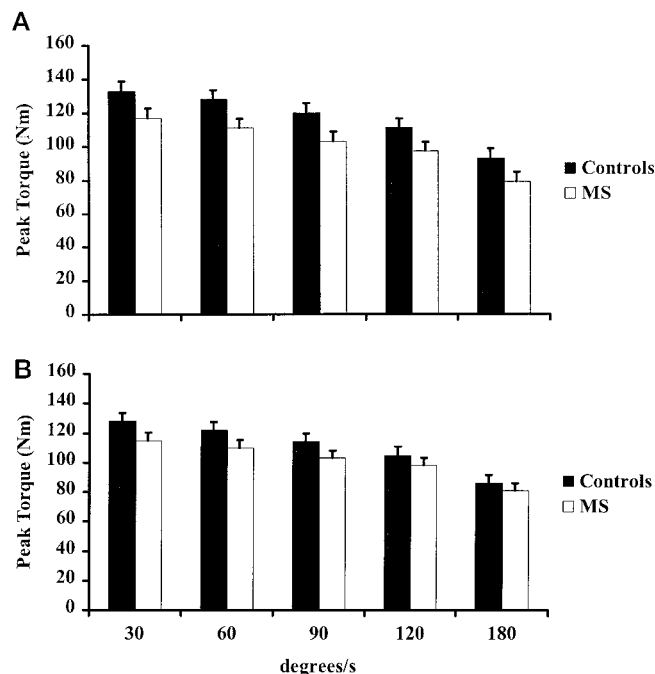


FIGURE 1—A, Peak torque (Nm) of the dominant knee extensors adjusted for body mass and age. No significant group ($P = 0.058$) or interaction effects ($P = 0.844$) were observed; however, there was a significant speed effect ($P < 0.0001$). B, Peak torque (Nm) of the dominant knee extensors adjusted for fat free mass and age. No significant group ($P = 0.214$) or interaction effects ($P = 0.173$) were observed; however, there was a significant speed effect ($P < 0.0001$).

there was a significant bout effect ($P = 0.001$) with the Fatigue Index declining throughout the three trials. No group by trial interaction was observed ($P = 0.363$).

The adjusted means for the work performed during the fatigue trial are presented in Figure 4. For knee extension the difference between the MS and control groups approached (group effect), but did not achieve, statistical significance (Fig. 4A; $P = 0.085$). There was a significant bout effect with total work declining across the three bouts $P < 0.0001$. No group by bout interaction was observed ($P = 0.140$). There was a significant group effect ($P = 0.0003$) for knee flexion (Fig. 4B) with the control group producing more total work than the MS group. In addition, total work declined across the three trials ($P < 0.0001$). No group by trial interaction was observed ($P = 0.169$).

DISCUSSION

Reliability of muscle strength. Weakness and fatigue are common afflictions of individuals with MS. In addition,

individuals with MS have days in which they have a greater degree of weakness and fatigue than other days. This potential day-to-day change in strength and fatigue may make it difficult to assess the effects of different interventions on strength and fatigue due to the potential for low day-to-day reproducibility. With this in mind, we examined the day-to-day or test-retest reliability of muscle strength and muscle fatigue testing in 15 individuals with MS and 15 non-MS control subjects (Table 2). We found that the test-retest reliability of individual with MS was very high with all but 1 of the 20 values being 0.900 or above. According to Vincent (17), ICC values above 0.900 are considered high, between 0.89 and 0.80 moderate, and below 0.80 not of much value in physiologic research. Thus, it appears that researchers should not have reservations regarding the assessment of interventions that may influence muscle force production during concentric isokinetic contractions as performed in individuals with MS in this investigation.

Reliability of muscle fatigue. The reliability of muscle fatigue was determined by evaluating the Fatigue Index (Fig. 3) and the work (Fig. 4) done during each 30-contraction bout. In this investigation, we found that the reliability of the Fatigue Index was low. Burdett and Van Swearingen (2) reported that work ratio (work during the last five contractions/work during the first five contractions all multiplied by 100) determined for the knee extensors at 180°s^{-1} was 0.48, whereas in our investigation, it was 0.357 for extension and 0.510 for flexion in the MS group and 0.575 for extension and 0.3

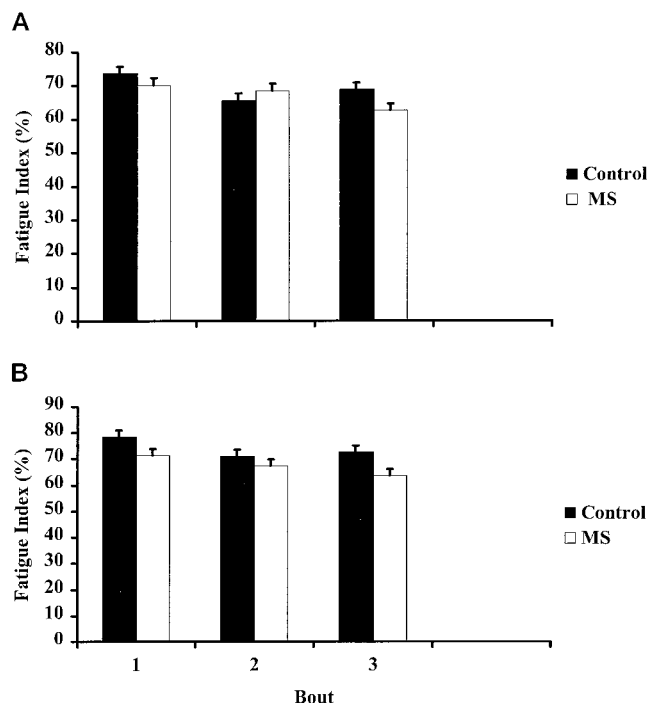


FIGURE 3—A, Fatigue Index [(%; work during the last 15 contractions/work during the first 15 contractions) $\times$ 100] for the dominant knee extensors adjusted for age. No significant group effect ($P = 0.325$) was observed. However, significant bout ($P = 0.002$) and significant interaction effects were observed ($P = 0.032$) with bout 3 being significantly different between MS and controls. B, Fatigue Index (%) for the dominant knee flexors adjusted for age. A significant group effect ($P = 0.033$) and a significant bout effect ($P = 0.001$) were observed. No significant interaction ($P = 0.363$) was observed.

force in half of the subjects studied. Larsson et al. (7) have reported that in humans, the force of single fibers, when corrected for fiber size (specific tension), decreased by 40% as a result of 6 wk of bed rest. It has been suggested that the loss of normalized force may be related to the selective loss of actin (14) without changes in muscle fiber type. The muscle of individuals with MS, with respect to fiber type and fiber size, more closely resembles that of the muscle of individuals with spinal cord injury than the muscle of individuals who have undergone short-term unloading (5). This emphasizes the fact that the changes in the skeletal muscle of individuals with MS are of great magnitude and with regard to specific tension may exceed the changes observed with short-term unloading. The extent to which an inability to activate muscle and the possibility of reduced muscle quality have an effect on muscle force generating capacity remains to be determined in individuals with MS.

Muscle fatigue and total work output. In the present investigation, muscle fatigue was greater in individuals with MS, as evidenced by the Fatigue Index, for the knee flexor muscle group (9.8% lower for MS than controls) of the dominant leg and 9.3% lower for the knee extensor group of that leg for the third bout. In addition, the mean total work output across the three 30-contraction bouts was 34.5% lower ($P = 0.0003$) for knee flexion in MS when compared with controls. Knee extension total work output tended to be lower (13.3%; $P = 0.085$) in the MS group relative to controls. Others have

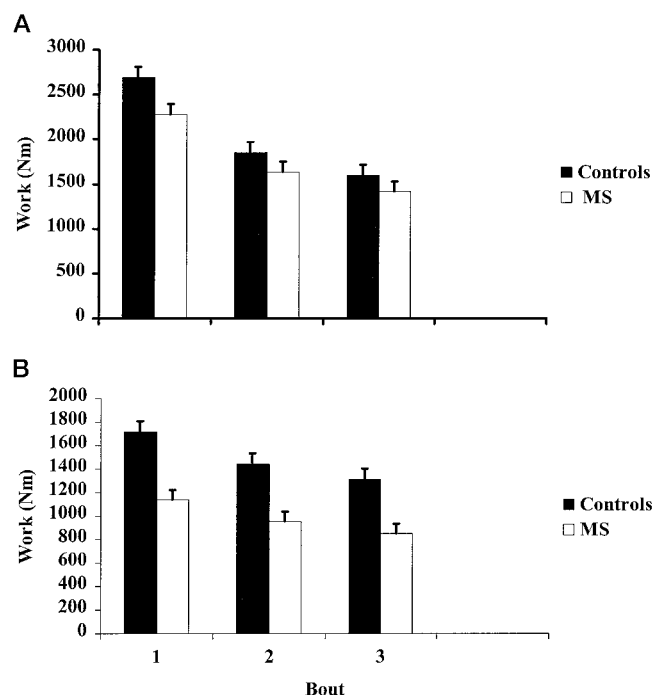


FIGURE 4—A, Work (Nm) performed during the fatigue test for knee extension. No significant group ($P = 0.085$) or interaction effects ($P = 0.140$) were observed. A significant bout effect ($P < 0.0001$) was observed. B, Work (Nm) performed during the fatigue test for knee flexion. A significant group effect ($P = 0.0003$) and bout effect ($P < 0.0001$) were observed;