

# Energy expenditure, physical activity, and body composition of ambulatory adults with hereditary neuromuscular disease<sup>1-3</sup>

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**ABSTRACT** Persons with neuromuscular disease (NMD) have progressive weakness and wasting of skeletal muscle, reduced fat-free mass, and increased fat mass relative to healthy control subjects. To test the hypothesis that resting energy expenditure (REE), estimated total daily energy expenditure (TEE), and physical activity patterns are altered in ambulatory adults with NMD, 26 adult men and women with slowly progressive NMD and 19 able-bodied control subjects similar in age and weight were evaluated. REE was measured after an overnight fast by indirect calorimetry, TEE by heart rate monitoring, and body composition by air-displacement plethysmography. REE was not significantly different between NMD and control subjects; however, TEE was significantly reduced in NMD subjects compared with control subjects, respectively (women:  $7.8 \pm 1.5$  compared with  $10.5 \pm 2.8$ ; men:  $10.2 \pm 3.6$  compared with  $12.7 \pm 2.6$  MJ/d;  $P \leq 0.01$ ), indicating that NMD subjects expended less energy in physical activity than did control subjects. NMD subjects also tended toward an increased energy cost of physical activity, particularly at higher activity levels ( $P = 0.06$ ). Multiple regression analysis indicated that for all subjects combined, adiposity was positively associated with age and TEE and negatively associated with time spent in the active heart rate range and fat-free mass ( $P \leq 0.0001$ ). This relation did not differ between NMD and control subjects, nor did it differ between men and women. We hypothesize that because of their reduced physical activity and increased adiposity, persons with NMD may be at risk for developing secondary conditions such as cardiovascular disease, hypertension, and diabetes. *Am J Clin Nutr* 1998;67:1162-9.

**KEY WORDS** Energy expenditure, body composition, disability, energy cost, physical activity, neuromuscular disease, humans, fat-free mass

## INTRODUCTION

Hereditary neuromuscular disease (NMD) describes a diverse group of diseases characterized by progressive weakness and wasting of skeletal muscle (1). Both muscle fiber size and number may be affected to different extents depending on the specific disease and rate of progression, and the disease can originate at the level of either the muscle fiber or the motor neuron (2). Associated with all forms of NMD are impairments of strength, mobility, and physical work capacity, although the

degree and severity of these impairments vary greatly, even among persons in the same family (3-9). Persons with this disease may eventually use wheelchairs for mobility at some time in their adult lives despite the slowly progressive course of many NMDs.

A recent review on physical activity and disability stressed the insufficiency of information on physical activity patterns in disabled persons (10). The Surgeon General's report on physical activity and health echoes the need for this type of research because of the many benefits that physical activity confers, including assistance with weight control, reduced risk of morbidity and premature mortality, and improved psychologic well-being (11). Body-composition measurements in NMD subjects by various methods indicate reduced fat-free mass (FFM) and increased adiposity in these subjects relative to able-bodied control subjects of comparable ages and body weights (3, 5-7, 12-15). Consistent with these observations, it is often assumed that persons with NMD are relatively sedentary; however, the extent to which reduced strength and endurance and alterations in body composition are associated with modifications in daily activity patterns and free-living energy expenditure in NMD subjects has not been reported.

Skeletal muscle accounts for  $\approx 20$ -30% of resting energy expenditure (REE) (16). Because of their reduced muscle mass (17), NMD subjects might be expected to have a relatively low REE. Previous researchers noted a lower basal metabolic rate (BMR) in patients with myotonic dystrophy than in healthy control subjects (14, 18-21), which was not due to thyroid dysfunction (22). However, Jozefowicz et al (18) reported an elevated ratio of BMR to total body potassium in men with myotonic dystrophy, suggesting increased rather than decreased metabolically active tissue in this type of NMD. The authors noted that this

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apparent hypermetabolism may not in fact have been due to skeletal muscle itself, but may have been due to other tissues that together contribute to a higher proportion of overall metabolism (23). Studies in other adult forms of NMD have yielded mixed results. Welle et al (24) reported that the BMR of one patient with limb-girdle muscular dystrophy and one with fascioscapulo-humeral muscular dystrophy was lower than that of control subjects, whereas Okada et al (25) reported that the BMR of 22 patients with limb-girdle muscular dystrophy did not differ markedly from their BMR predicted with use of an age-appropriate equation.

The purpose of this study was to test the hypothesis that REE, estimated total daily energy expenditure (TEE), and physical activity patterns are altered in ambulatory adults with NMD compared with able-bodied control subjects of similar ages and body weights. A secondary purpose was to determine the feasibility of measuring body composition in this disabled population by using the newly developed method of whole-body air-displacement plethysmography (26). This method was evaluated in healthy subjects and found to compare favorably with hydrostatic weighing (27). In contrast with hydrostatic weighing, however, the air-displacement method does not require significant physical exertion or mobility, suggesting that this method may be appropriate for use in this disabled population. Last, the relation between energy expenditure and body composition was explored in NMD and control subjects.

## SUBJECTS AND METHODS

### Subjects

Patients followed at the NMD clinic at the University of California, Davis, Medical Center were invited to participate in this study. Twenty-six ambulatory adults with slowly progressive NMD volunteered. Diagnoses included nine of myotonic dystrophy, nine of hereditary motor and sensory neuropathy (type I), three of limb-girdle muscular dystrophy, three of fascioscapulo-humeral muscular dystrophy, one of Becker muscular dystrophy, and one of spinal muscular atrophy. NMD patients were compared with an able-bodied control group of similar ages and weights ( $n = 19$ ). Several of the NMD and control subjects participated in regular recreational physical activity. The study was approved by the Human Subjects Review Committee at the University of California, Davis. All subjects gave verbal and written informed consent before participating.

### Study design

Subjects underwent two test sessions  $\approx 1$  wk apart in the Human Performance Laboratory in the Department of Exercise Science at the University of California, Davis. They were instructed to not participate in strenuous physical activity for 24 h and to fast for 12 h before their appointment time. Subjects were driven to the laboratory in the morning; the exact appointment time was scheduled at the subject's convenience because many had to travel from nearby cities. They were instructed to keep their activity to a minimum the morning before their arrival time. In the first session, REE was measured and the relation between heart rate and oxygen consumption ( $\dot{V}O_2$ ) was determined. In the second session, REE was again determined and a fasting venous blood sample was taken. This was followed by body-composition measurement. Between the two laboratory

sessions, subjects recorded their dietary intakes and wore a heart rate monitor on 3 successive days, including 2 weekdays and 1 weekend day. Detailed data on macronutrient intake and blood lipids will be reported elsewhere. Premenopausal women were tested between days 5 and 12 of the menstrual cycle (follicular phase).

### Body composition

Body composition was determined by whole-body densitometry with an air-displacement plethysmograph (BOD POD Body Composition System; Life Measurement Instruments, Concord, CA) according to the manufacturer's instructions. Subjects were in a fasting state and wore a spandex swimsuit and swim cap. Body weight was measured to the nearest 1 g on the accompanying scale. Raw body volume was determined during two measurements of 20 s each while the subject sat quietly. A third measurement was conducted if the two measurements did not agree within 2.0%. Raw body volume was corrected for thoracic gas volume and a body surface area artifact, which were both also determined with the air-displacement plethysmograph. Body density was calculated (mass/volume) and converted to body fat percentage by using the formula of Siri (28). Calculations were performed with BOD POD software, version 1.14 (Life Measurement Instruments).

### Energy expenditure

TEE was estimated by heart rate monitoring as described previously (29). In the laboratory, a heart rate- $\dot{V}O_2$  relation was established for individual subjects by the following means. Heart rate and  $\dot{V}O_2$  were measured during sedentary activities (while subjects were supine, sitting, and standing) and while subjects walked on a treadmill. Control subjects walked at 1.6, 3.2, and 4.8 km/h. NMD subjects, according to their ability, were tested at either 1.6, 2.5, and 3.2 km/h or 1.1, 1.8, and 2.4 km/h. Heart rate was recorded every 15 s with a portable heart rate monitor (Polar Vantage XL, Port Washington, NY).

$\dot{V}O_2$  and  $\dot{V}CO_2$  (carbon dioxide production) were measured by open circuit indirect calorimetry using a metabolic cart (Sensormedics 2900 Metabolic System; Sensormedics, Yorba Linda, CA). A ventilated hood was used while subjects were supine and a ventilated face mask was used while subjects were sitting and standing. A face mask (Series 7920; Hans Rudolph, Kansas City, MO) was used while subjects were walking. The temperature of the room was maintained between 22 and 24 °C. Subjects rested for  $\approx 20$  min before the measurements were taken. Resting  $\dot{V}O_2$  was measured for  $\geq 15$  min, until 5 min of steady state was reached. Each subsequent activity was carried out for 5–10 min, until steady state was reached for 5 min. Resting  $\dot{V}O_2$  and  $\dot{V}CO_2$  were converted to REE by use of de Weir's formula (30) and normalized for a 24-h period by multiplying by 1440 min/d.

The average REE measured on the second day was calculated and if the between-day CV exceeded 5% a third REE measurement was scheduled for another day. This occurred for nine subjects. The average of the two closest REEs was used, and the resultant between-day CVs for REE were 3.1% for control subjects and 2.3% for NMD subjects.

Subjects wore heart rate monitors during waking hours. During this time heart rate was recorded and stored at 1-min intervals. Each individual's sedentary and active regression equations were determined from the laboratory measurements, and  $\dot{V}O_2$  at each heart rate (from outside the laboratory) was calculated by using

the heart rate– $\dot{V}O_2$  relation for each subject. A “flex” heart rate was defined as the average of the highest sedentary heart rate and the lowest walking heart rate, plus 10 (31). Heart rates falling below the flex heart rate were converted to  $\dot{V}O_2$  by using the sedentary regression equation; heart rates greater than or equal to the flex heart rate were converted to  $\dot{V}O_2$  by using the active regression equation.  $\dot{V}O_2$  throughout the day was converted to energy expenditure with the conversion factor of 20.19 kJ/L  $O_2$  (30).

Subjects kept detailed activity records for the time during waking hours when a heart rate monitor was not worn ( $\bar{x} \pm SD$ : 65  $\pm$  49 min) and for all activity that was self-reported as exercise. Energy expenditure while subjects were not wearing the heart rate monitor was estimated by the factorial method, which uses the average energy cost of physical activities multiplied by an individual’s REE (32), weighted for the time spent in each activity (33). TEE was calculated by summing energy expenditure during heart rate monitoring and other activities. Energy expenditure during sleep was assumed to be equal to 90% of REE (32). Energy expenditure in physical activity (ACTEE) was determined by subtracting REE from estimated TEE. The physical activity level during exercise was calculated as energy expended in exercise normalized for a 24-h period (1440 min) and divided by REE. Five NMD subjects were unable to walk on the treadmill without losing their balance and were also unable to ride a cycle ergometer for more than just a few minutes. Therefore, they were not able to undergo heart rate and  $\dot{V}O_2$  measurements above the flex heart rate. These subjects kept detailed activity records throughout the day by talking into a tape recorder and the factorial method was used to estimate TEE throughout the whole day.

#### Data analysis

Data were analyzed with SYSTAT statistical software, version 5.02 for Windows (SPSS Inc, Chicago). Variables were log-transformed before being analyzed if they did not meet the condition of normality. For all analyses, statistical significance was accepted at a  $P$  value  $\leq 0.05$  for main effects and  $\leq 0.10$  for interactions.

Energy expenditure and body-composition variables were compared by diagnosis (NMD or control) and sex by using two-factor univariate and multivariate analysis of covariance (ANCOVA), controlling for appropriate covariates where needed (eg, REE for FFM). Potential differences in REE among NMD subtypes compared with REE control subjects were evaluated with linear regression analysis and computation of residual values. Specifically, REE was regressed on FFM by sex for control subjects; studentized residuals of the relation between REE and FFM for each NMD subject relative to the control regression line were then computed. NMD subjects with residual values within  $\pm 2.0$  of the regression line for control subjects were considered to not be significantly different from control subjects.

The relation between energy expenditure and body composition was evaluated by stepwise multiple regression analysis. The outcome variable was percentage body fat; variables included in the analysis as possible predictors were REE, estimated TEE, ACTEE, and time spent above the flex heart rate (herein referred to as minutes active). Covariates of body weight, FFM, fat mass, body mass index (BMI), and age were also included, and diagnosis and sex were entered as dummy variables (men = 0, women = 1; NMD = 0, control = 1). To determine whether the relations

differed for NMD compared with control subjects and for men compared with women, all variables were examined as main effects and as two-way interactions with diagnosis and sex.

## RESULTS

### Subjects

The subjects’ physical and occupational characteristics are reported in **Table 1**. The NMD subjects had been living an average of 16  $\pm$  12 y since their diseases were diagnosed. All were ambulatory, but six women and seven men used devices to assist them in walking, such as a cane or ankle-foot orthoses. There were no significant differences between NMD and control subjects in age, weight, height, and BMI, but both male and female NMD subjects had a significantly higher percentage of body fat and significantly lower FFM than did male and female control subjects ( $P \leq 0.01$ ). Fat mass did not differ significantly between the NMD and control subjects. There were no significant interactions between sex and diagnosis for any of the body-composition variables examined.

### Energy expenditure, physical activity, and reported exercise

Estimated TEE and its components are shown in **Table 2**. There were no significant differences in REE between the NMD and control groups, although men had a significantly higher REE than women ( $P = 0.001$ ). However, when REE was adjusted for FFM by ANCOVA, this difference was no longer significant ( $P = 0.07$ ). The resting respiratory quotient averaged 0.82  $\pm$  0.1 and did not differ between the groups.

To further examine potential differences in REE among patients with the various NMD subtypes and control subjects, REE was plotted as a function of FFM, as shown in **Figure 1**. The regression line of the relation between REE and FFM is shown for the control subjects. Among the women, only one NMD subject (with hereditary and sensory motor neuropathy) differed markedly from the control subjects in the relation between REE and FFM (from analysis of residual values). Among the men, three NMD subjects (one with myotonic dystrophy, one with limb-girdle muscular dystrophy, and one with Becker muscular dystrophy) had a different relation between REE and FFM than did control subjects. Each of these four NMD subjects (one woman and three men) had relatively high REEs in relation to FFM compared with the control subjects and the remaining NMD subjects.

Estimated TEE was significantly lower in the NMD group than in the control group ( $P = 0.001$ ), and significantly lower in women than in men ( $P = 0.007$ ) (Table 2). There was no significant interaction between diagnosis and sex. When estimated TEE was adjusted for FFM, these differences no longer existed. ACTEE was significantly lower in NMD subjects than in control subjects ( $P \leq 0.001$ ) and significantly lower in women than in men ( $P = 0.05$ ). This sex difference disappeared when ACTEE was adjusted for FFM. When ACTEE was expressed as a percentage of estimated TEE, NMD women spent 29  $\pm$  6% of their estimated TEE in physical activity, whereas control women spent 44  $\pm$  9% ( $P \leq 0.001$ ). Likewise, NMD men spent 35  $\pm$  12% of their estimated TEE in physical activity, compared with 44  $\pm$  8% for control men ( $P < 0.0001$ ). Male and female NMD subjects had a significantly lower number of minutes active (less time spent above the flex heart rate) than did male and female control subjects ( $P = 0.001$ ).

Data on reported exercise are also shown in Table 2. Nine of 26 NMD subjects (35%) and 15 of 19 control subjects (79%)



**TABLE 1**  
Selected physical and demographic characteristics of the subjects<sup>1</sup>

	Women		Men	
	NMD (n = 11)	Control (n = 8)	NMD (n = 15)	Control (n = 11)
Physical characteristics				
Age (y)	48.1 ± 14.8 <sup>2</sup>	45.1 ± 11.8	43.4 ± 14.7	44.2 ± 14.7
Weight (kg)	71.5 ± 21.2	72.6 ± 18.9	78.3 ± 18.6	80.3 ± 10.0
Height (cm)	164.6 ± 3.8 <sup>3</sup>	162.9 ± 4.1 <sup>3</sup>	175.3 ± 8.6	181.0 ± 5.9
BMI (kg/m <sup>2</sup> )	26.3 ± 7.3	27.3 ± 6.8	25.3 ± 4.7	24.6 ± 3.6
Body fat (% weight)	41.6 ± 8.7 <sup>3,4</sup>	35.7 ± 10.2 <sup>3</sup>	29.7 ± 9.1 <sup>4</sup>	20.7 ± 6.0
FM (kg)	31.1 ± 14.6 <sup>3</sup>	27.2 ± 14.8 <sup>3</sup>	24.2 ± 11.2	16.7 ± 6.2
FFM (kg)	40.3 ± 7.3 <sup>3,4</sup>	45.4 ± 7.4 <sup>3</sup>	54.1 ± 10.5 <sup>4</sup>	63.3 ± 5.5
Employment				
Total employed (n)	5	7	6	7
Sedentary job	4	5	3	3
Nonsedentary job	1	2	3	4
Work duration (h/wk)	40 ± 7	38 ± 4	33 ± 13	36 ± 5
Full-time student (n)	0	0	1	3
Other (n) <sup>5</sup>	6	1	8	1

<sup>1</sup> NMD, neuromuscular disease; FM, fat mass; FFM, fat-free mass.<sup>2</sup>  $\bar{x} \pm$  SD.<sup>3</sup> Significantly different from men,  $P \leq 0.001$  (ANOVA).<sup>4</sup> Significantly different from control subjects,  $P < 0.01$  (ANOVA).<sup>5</sup> Retired, unemployed, or receiving public assistance.

exercised during the study period. NMD subjects reported spending less time exercising and therefore also spent less energy during exercise than did control subjects ( $P < 0.02$ ). NMD subjects reporting exercise worked at a light level, whereas control subjects worked at a moderate level ( $P \leq 0.03$ ).

### Energy cost of physical activity

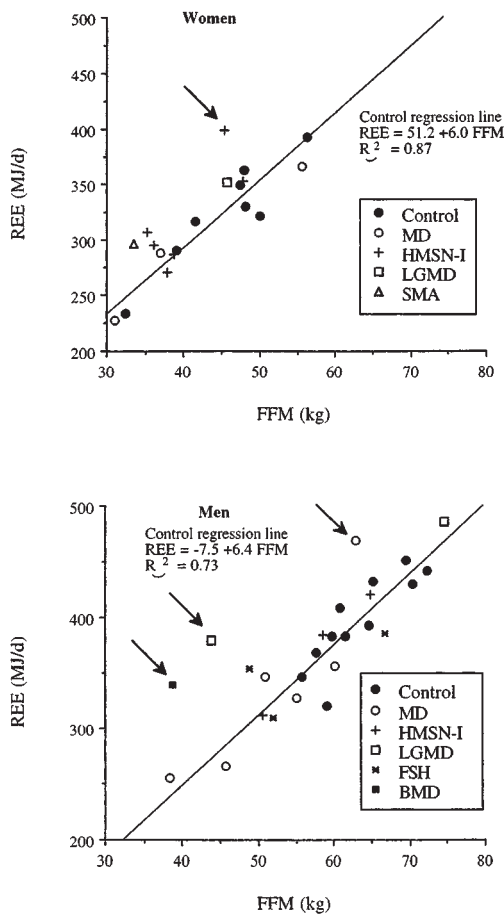
The average heart rate- $\dot{V}O_2$  relations for NMD and control subjects are shown in **Figure 2**. The NMD group had an increased energy cost of physical activity, as judged by comparison of the

slopes of the regression lines. Heart rate was higher at a given  $\dot{V}O_2$  for the NMD group than for control subjects in both the sedentary and active heart rate ranges. For the sedentary heart rate range, MANOVA showed that the heart rate- $\dot{V}O_2$  relation was not significantly different between NMD and control subjects ( $P = 0.27$ ); in the active heart rate range the difference tended toward significance ( $P = 0.06$ ). The flex heart rate was significantly higher in NMD subjects than in control subjects, respectively (women:  $95 \pm 11$  compared with  $83 \pm 10$  beats/min; men:  $85 \pm 13$  compared with  $74 \pm 7$  beats/min;  $P = 0.002$ ).

**TABLE 2**  
Energy expenditure, physical activity, and reported exercise<sup>1</sup>

	Women		Men	
	NMD (n = 11)	Control (n = 8)	NMD (n = 15)	Control (n = 11)
Energy expenditure				
REE				
(MJ/d)	5.48 ± 0.87 <sup>2,3</sup>	5.69 ± 0.84 <sup>3</sup>	6.29 ± 1.31	6.93 ± 0.72
Adjusted for FFM	6.51 ± 0.64	6.25 ± 0.54	6.04 ± 0.53	5.83 ± 0.65
TEE				
(MJ/d)	7.79 ± 1.45 <sup>3,4</sup>	10.50 ± 2.81 <sup>3</sup>	10.23 ± 3.59 <sup>4</sup>	12.74 ± 2.56
Adjusted for FFM	10.28 ± 2.47	11.87 ± 2.09	9.63 ± 2.10	10.07 ± 2.54
ACTEE				
(MJ/d)	2.31 ± 0.81 <sup>3,4</sup>	4.81 ± 2.16 <sup>3</sup>	3.95 ± 2.68 <sup>4</sup>	5.82 ± 2.18
Adjusted for FFM	3.77 ± 2.15 <sup>4</sup>	5.62 ± 1.83	3.59 ± 1.83 <sup>4</sup>	4.24 ± 2.21
Physical activity				
Minutes active (min/d)	74 ± 45 <sup>4</sup>	206 ± 110	126 ± 106 <sup>4</sup>	248 ± 127
Reported exercise				
Total reporting exercise (n)	3	7	6	8
Duration (min/d)	5 ± 9 <sup>4</sup>	25 ± 22	10 ± 20 <sup>4</sup>	65 ± 66
EXEE (MJ/d)	0.05 ± 0.10 <sup>4</sup>	0.55 ± 0.62	0.18 ± 0.39 <sup>4</sup>	1.44 ± 1.46
PAL	2.9 ± 1.4 <sup>4</sup>	4.9 ± 1.3	3.7 ± 1.4 <sup>4</sup>	5.0 ± 1.8

<sup>1</sup> NMD, neuromuscular disease; REE, resting energy expenditure; FFM, fat-free mass; TEE, estimated total daily energy expenditure; ACTEE, energy expenditure in physical activity; EXEE, energy expenditure in reported exercise; PAL, physical activity level of reported exercise.<sup>2</sup>  $\bar{x} \pm$  SD.<sup>3</sup> Significantly different from men,  $P \leq 0.05$  (ANOVA).<sup>4</sup> Significantly different from control subjects,  $P \leq 0.03$  (ANOVA).



**FIGURE 1.** Relation between resting energy expenditure (REE) and fat-free mass (FFM) in control subjects and among subjects with different neuromuscular disease (NMD) subtypes. The regression lines shown are for control subjects. Among NMD subjects, one woman and three men (designated by arrows) differed markedly from control subjects with respect to the relation between REE and FFM on the basis of analysis of studentized residual values. MD, myotonic dystrophy; HMSN-I, hereditary and sensory motor neuropathy; LGMD, limb-girdle muscular dystrophy; SMA, spinal muscular atrophy; FSH, fascioscapulohumeral dystrophy; BMD, Becker muscular dystrophy.

### Relation between energy expenditure and body composition

Sixty-three percent of the variation in percentage body fat was explained by a model that included several independent predictors. Age ( $P = 0.02$ ), sex (men = 0, women = 1;  $P = 0.02$ ), and TEE ( $P \leq 0.0001$ ) were positive predictors, whereas minutes active ( $P \leq 0.0001$ ) and FFM ( $P = 0.002$ ) were negative predictors. The regression equation was as follows:

$$\text{Percentage body fat} = -203.1 + 0.2\text{age} + 8.1\text{sex} + 36.5\log_{10}(\text{TEE}) - 7.4\log_{10}(\text{minutes active}) - 0.7\text{FFM} (I)$$

with  $R^2 = 0.63$  ( $P \leq 0.0001$ ). None of the interaction terms with diagnosis or sex were significant. Adiposity in relation to minutes active is shown in **Figure 3**.

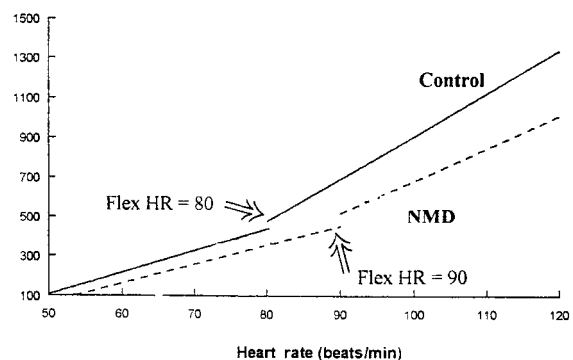
### DISCUSSION

In this study, we observed that NMD subjects did not differ in REE, but did have a lower estimated TEE, exercised at a lower

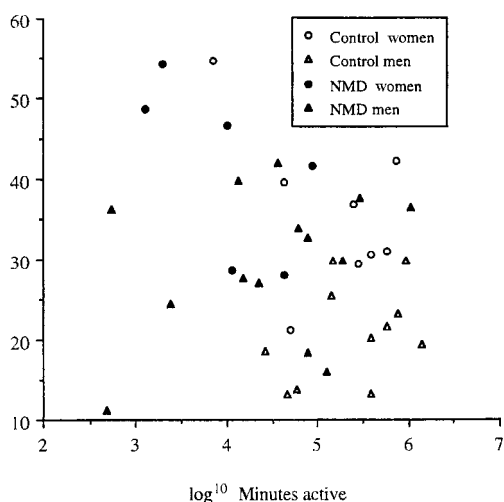
intensity, and had a higher energy cost of physical activity than able-bodied subjects of the same sex who were similar in age and weight. Furthermore, in both NMD and control subjects, increased adiposity was independently and negatively related to time spent in physical activity (as indicated by the number of minutes in a day spent above the flex heart rate). However, all of the NMD subjects in this study were relatively mobile and these findings may not be applicable to more severely disabled, non-ambulatory NMD patients.

Many of the conclusions reached in the current study rely on the adequacy of our control group. Control subjects were selected carefully so that on average they would be similar in age and weight to the NMD subjects, but not unusually physically active. In terms of body composition, both the NMD and control groups were above the desired level of fatness; the subjects in this study could be classified in the grade 1 category of obesity (BMI, in  $\text{kg}/\text{m}^2$ : 25–30), with the exception of the control men who had a BMI of 24.6 (34). Regarding physical activity, our control group represented the upper level of the range of activity factors typically found in the United States, which is 1.5–1.7. This is based on a calculated activity factor (TEE/predicted REE) for the control group of 1.7, derived by using predicted REE from equations from the World Health Organization (35). The activity factor classified the control group as being moderately active (33). Using this criterion, the NMD group was in the very light activity category, with activity factors of 1.3 and 1.4 for the women and men, respectively.

The reduced estimated TEE seen in the NMD subjects was primarily because of a lower ACTEE in NMD subjects than in control subjects. However, ACTEE remained lower in NMD subjects even after FFM differences were adjusted for. The lower number of minutes spent above the flex heart rate for NMD subjects suggests that the lower ACTEE was due to less time spent in physical activity. In addition, the NMD subjects had a higher energy cost of physical activity, as indicated by the lower slope of the heart rate– $\dot{V}O_2$  relation. It is possible that the lower amount of time spent in physical activity by NMD subjects can be attributed to the higher energy cost. An alternative explana-



**FIGURE 2.** Relation between heart rate (HR) and oxygen consumption in the sedentary and active HR ranges for subjects with neuromuscular disease (NMD) and control subjects. Regression equations were as follows: for NMD subjects,  $y = 9.6x - 413.3$  in the sedentary HR range and  $y = 16.4x - 955.2$  in the active HR range; for control subjects,  $y = 11.0x - 442.7$  in the sedentary HR range and  $y = 21.6x - 1251.1$  in the active HR range. The difference between the regression equations in the active HR range for NMD compared with control subjects tended toward significance,  $P = 0.06$  (MANOVA).



**FIGURE 3.** Adiposity in relation to minutes active (time spent above the flex heart rate) in subjects with neuromuscular disease (NMD) and control subjects. The relation was significant when other explanatory variables in the regression model (age, sex, total energy expenditure, and fat-free mass) were controlled for. Partial  $R = -0.49$ ;  $P = 0.002$ .

tion is that persons with NMD avoid physical activity because of the widespread belief that too much stress on the muscles will accelerate the disease process—a phenomenon known as overwork weakness. This belief is largely based on anecdotal evidence, however, and is not substantiated by scientific research. We reported previously that persons with slowly progressive NMD could spend 30 min/d up to 4 d/wk in moderate aerobic walking at 50% of their peak  $\dot{V}O_2$  without any negative effects (36).

Time spent above the flex heart rate was negatively associated with adiposity in both NMD and control subjects. Several investigators have found a negative relation between fatness and energy expenditure in physical activity in able-bodied persons (37–39). Whether the increased body fatness is a cause or a consequence of low physical activity is unknown. However, there is increasing evidence from longitudinal studies that low physical activity leads to increased fatness in the long term (39). It is conceivable, however, that at least for persons with NMD, fatness is a result not only of their lower physical activity but also of a reduction in metabolically active muscle mass over time. Diet also undoubtedly plays a role in the development of obesity in persons with NMD, but this is difficult to ascertain because of the tendency for individuals to underreport energy intake (40, 41).


Little to no information exists on the exercise habits of persons with NMD (10). In this study, reported exercise was lower in duration and intensity in NMD subjects than in control subjects. The few NMD subjects who exercised did so at a light level whereas control subjects exercised at a moderate level (33). However, it has become clear that for able-bodied persons exercise need not be performed at vigorous levels to be beneficial; even moderate levels of exercise confer reduced risk of morbidity and mortality (11). More research is needed on a representative sample of NMD subjects to determine their usual exercise habits and whether they can indeed benefit from light levels of exercise.

REE, although reduced, was not significantly lower in NMD subjects than in control subjects. Our results support the findings of Okada et al (25), who reported that male subjects with limb-girdle muscular dystrophy ( $n = 22$ ) had BMRs similar to the predicted control value. However, others have reported that the BMRs of subjects with myotonic dystrophy (14, 18–21) and of a group of subjects with mixed adult forms of NMD (seven with myotonic dystrophy, one with limb-girdle muscular dystrophy, and one with fascioscapulohumeral dystrophy) (24) were lower than BMR in control subjects. There are several plausible explanations for these conflicting findings. First, with the exception of our study and the study by Okada et al (25), age was not controlled for (either in the study design or the statistical analyses) in these studies. In addition, myotonic dystrophy may be unique and other forms of NMD may not result in reduced BMRs (42). Finally, in the current study, because most of the NMD subjects came from out of town and had to travel 0.5–1.5 h to our laboratory, their REEs may have been overestimated. However, this is unlikely because all subjects were minimally active between waking that morning and the time of REE measurement; in addition, among the NMD subjects, there was a nonsignificant inverse correlation between distance traveled and REE ( $R = -0.29$ ,  $P = 0.16$ ).

Little information exists on REE adjusted for metabolically active tissue in NMD subjects. Jozefowicz et al (18) reported an increased BMR when this was expressed per gram of total body potassium in subjects with myotonic dystrophy compared with nondiseased subjects. This is in contrast with findings from the current study in which REE was not significantly different between NMD and control subjects when adjusted for differences in FFM by ANCOVA. The different methods used to adjust REE for metabolically active tissue in the current study and that by Jozefowicz et al (18) may be partially responsible for this disagreement (43). However, in the current study, four subjects with NMD (one woman and three men, each with a different NMD subtype) had relatively high REEs in relation to FFM. The relatively small sample size in our study makes meaningful conclusions with respect to the various NMD subtypes limited. REE is driven primarily by substrate cycling,  $Na^+/K^+$  ATPase activity, and protein turnover (23). Whether these systems are differentially affected in the different forms of NMD is unknown.

Compared with control subjects who were similar in age and weight to the NMD subjects, we found significantly higher percentage body fat and lower FFM in NMD subjects as measured by air-displacement plethysmography. These findings agree with previous studies in which skinfold-thickness measurements (3, 5, 6), total body potassium by isotope dilution and whole-body counting (14, 15, 18), isotope dilution of total body water (13, 15), and dual-energy X-ray absorptiometry (12) were used. Because it demands relatively little effort on the part of subject, air-displacement plethysmography was a feasible method for determining body composition in this population of ambulatory NMD subjects with various degrees of mobility. Therefore, this method is a reasonable alternative for determining body composition in disabled individuals to other methods that may be more expensive, such as dual-energy X-ray absorptiometry and whole-body counting, or more difficult for the subject, such as hydrostatic weighing. However, the validity of the air-displacement method, which relies on the classic two-compartment densitometric approach to determine whole-body density, has not been tested in NMD subjects.

There is some evidence that a departure from the basic assumption of the two-compartment model that the density of the FFM compartment is 1.1 g/mL may occur in NMD. Delwaide et al (15) reported a reduced ratio of total body potassium to protein in those with NMD of a myogenic origin but not a neurogenic origin. Blahd et al (44) found that persons with limb-girdle muscular dystrophy and Duchenne muscular dystrophy had reduced total body water levels, primarily in the intracellular water compartment, although Delwaide et al (15) reported normal total body water values in persons with adult NMD. Further studies using three-compartment and four-compartment models in combination with air displacement should be used to determine the validity of the two-compartment densitometric model in NMD subjects. Validation of field methods for determining body composition in these subjects, such as bioelectrical impedance analysis and skinfold thickness equations, is also needed.

NMD subjects not only have reduced strength and FFM, but, on the basis of the current study, also have a high level of adiposity that is associated with a low level of physical activity. It is unknown whether a high percentage of body fat together with reduced physical activity is associated with an increased risk of morbidity from secondary complications such as heart disease, hypertension, and diabetes in these individuals as in the non-NMD population. However, the excess body fat of the NMD subjects places a burden of excess weight on already weakened muscles and probably additionally impairs mobility. Furthermore, these subjects' low physical activity levels may lead to even greater weakness and atrophy of skeletal muscles, beyond that due to the primary disease process, as a result of disuse. Investigation of prevention and appropriate treatment of obesity in persons with slowly progressive NMD would therefore be beneficial. 

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