ABSTRACT
Background: Huntington disease (HD) is a genetic neurologic disorder. Weight loss is common in HD and is related to progression of the disease, but the cause of weight loss remains unclear.
Objective: The study objective was to compare 24-h energy expenditure (EE) and energy intake in persons with early midstage HD with those of matched control subjects to determine how HD affects energy balance.
Design: EE was assessed in 13 subjects with early-stage HD and in 9 control subjects via indirect calorimetry in a human respiratory chamber. Energy intake was determined by weighing all food provided and all leftovers from an ad libitum diet. Body composition was measured via air-displacement plethysmography. Stage of disease was estimated on the basis of the Unified Huntington’s Disease Rating Scale and modified Mini-Mental Status examinations. Regression analysis included all 13 HD subjects; t tests were used for the comparisons between matched HD and control subjects.
Results: 24-h EE was 11% higher in the HD subjects than in the control subjects (NS). This difference was due to a higher (P = 0.043) waking metabolic rate, which was related to a significantly greater displacement of the center of mass by HD subjects than by control subjects (P = 0.028). On average, both groups were in positive energy balance and exceeded their energy expenditure by 2510–2929 kJ.
Conclusions: Higher 24-h EE in persons with early midstage HD is due to increased physical activity, both voluntary and involuntary. However, HD subjects are able to maintain positive energy balance when offered adequate amounts of food in a controlled setting. Am J Clin Nutr 2005;81:1335–41.

KEY WORDS Huntington disease, energy expenditure, energy balance, metabolic rate, nutrition, physical activity

INTRODUCTION
Huntington disease (HD) is a genetic neurologic disorder characterized by uncontrollable dance-like physical movements (chorea), dystonia, impairment in gait and eye movement, cognitive impairment, and psychiatric symptoms, eg, depression, apathy, irritability, obsessive-compulsive disorder, and psychosis.
Predictions of increased basal metabolic rate as a cause of weight loss in HD (1, 2) are consistent with a cross-sectional observation of a lower average BMI in presymptomatic carriers of the HD gene and in persons with very early symptoms of HD than in healthy control subjects (3). These studies, however, have not ruled out increased energy expenditure (EE) with HD from voluntary movement, such as fidgeting, which may be related to body mass (4).

At least 3 studies (3, 5, 6) found that HD subjects had lower average BMIs than did control subjects; however, only 2 studies (3, 6) showed statistically significant differences.

Hamilton et al (7) examined weight changes prospectively in 927 HD patients participating in the Huntington Study Group database. They found that, over 3 y of observation, most HD subjects maintained their weight. However, the entire group gained less than the US national average weight gain as per the third National Health and Nutrition Examination Survey (8). In the subset of HD subjects who lost weight during the study period, weight loss was significantly correlated with chorea (P = 0.001)

A direct measurement of resting metabolic rate (RMR) by Shoulson et al (9) found that RMR and the total volume of oxygen consumed were not greater in HD subjects than in age-matched control subjects. The authors concluded that nonresting EE must be elevated in HD, perhaps because of involuntary physical activity (chorea).

The only study to date to have examined 24-h EE and physical activity in a human respiratory chamber is that by Pratley et al (5). They found that mean 24-h EE was significantly higher in HD subjects than in control subjects (P < 0.04), but that there was no significant difference in sleeping metabolic rate (SMR). The authors concluded that the greater EE of the HD subjects was entirely due to greater spontaneous involuntary and voluntary physical activity by the HD subjects, as measured by radar in the chamber. The use of calculated diets in this study, however, may have underestimated the food intake necessary to meet the energy needs of the HD subjects. All subjects spent 3–4 d in the metabolic research unit and were only allowed to eat a calculated diet...
based on a presumed normal metabolic rate (determined by using the Harris-Benedict equation). HD subjects were in negative energy balance (average of −770 kJ/24 h) during the 24-h EE studies and were likely to have been consuming less than their actual energy needs on preceding days as well. Fasting, and to a lesser extent dieting, reduces metabolic rate and therefore 24-h EE. This may have blunted the differences in metabolic rate between HD subjects and normal control subjects, hence producing no significant differences other than the most robust, which were due to physical activity. This problem was addressed in the study reported here by providing all subjects with an ad libitum diet during the 24-h EE measurement. This protocol also addressed the question of whether HD subjects have a greater appetite than do persons without HD, which has not been studied previously.

SUBJECTS AND METHODS

Subjects

The participants (8 men and 5 women) had early-to-midstage (stage I and stage II) HD and were followed at the Huntington’s Disease Center of Excellence at the New York State Psychiatric Institute; 9 healthy, age-matched control subjects (5 men and 4 women) were recruited through advertisements. TFC, a global functional measurement designed specifically for HD (10), and scores for chorea and dystonia were derived from the Unified Huntington’s Disease Rating Scale (UHDRS) (11), which was administered to every patient at this clinic.

TFC scores (10) range from 13 (no functional impairment) to 0 (severe impairment). TFC scores have been further divided into stages that correlate with disease severity. Stage I represents scores from 11 to 13, stage II scores from 7 to 10, stage III scores from 3 to 6, stage IV scores from 1 and 2, and stage V scores of 0.

HD subject inclusion criteria were as follows: 1) unequivocal evidence of HD on examination based on the presence of movement disorder, 2) a positive family history of HD or documentation of the presence of the HD mutation by genetic testing, 3) a TFC score ≥6 (patients with this level of function are able to function independently and therefore would not have difficulty living in the metabolic chamber), 4) a limited history of serious choking episodes (<2 times/mo), 5) the ability to eat without assistance, 6) a modified Mini-Mental status (12) of >35, and 7) a nonsmoking or light-smoking status (ie, able to abstain for >24 h).

HD subject exclusion criteria were as follows: 1) any medical condition that would affect dietary intake, ie, malabsorption syndrome, gastric ulcers, colitis, esophageal strictures, severe dysphagia, edentulous, or presence of a gastrostomy tube for enteral feeding; 2) any concurrent major psychiatric illness that affects function; 3) a Beck Depression Score (13) >7; and 4) heavy smoking or the inability to abstain from smoking for >24 h.

Selection criteria for the control subjects were as follows: 1) no personal or family history of HD; 2) in general good health and able to perform the activities required by the study (remaining in the human respiratory chamber for 24 h without direct assistance); 3) nonsmoking or light smoking status (able to abstain for >24 h); 4) similarity to one of the HD subjects by age, sex, race-ethnicity, height, and weight. (See Table 1 for descriptive data for HD subjects and control subjects). On the basis of these criteria, we were able to recruit 9 control subjects who matched 9 of the HD patients (Table 2).

The study protocol was reviewed and approved by the Institutional Review Boards of Columbia Presbyterian Medical Center, St Luke’s–Roosevelt Hospital Center, and Teacher’s College, Columbia University; all subjects gave verbal and written informed consent. The subjects received a small honorarium for their participation.

Energy expenditure

Twenty-four hour EE was measured by indirect calorimetry in the human respiratory chamber at the New York Obesity Research Center at St. Luke’s-Roosevelt Hospital Center. The respiratory chamber is an air-tight room (22 000 L volume) equipped with a bed, chair, desk, television, videocassette recorder, radio, telephone, bicycle, sink, and toilet. The temperature of the room is maintained at 23 ± 0.2 °C. A fan draws mixed air (sample air) out of the chamber while fresh air (reference air) is forced into the chamber by the resulting negative pressure. A flow meter measures the flow rate; aliquots of entering reference air as well as of exiting sample air are collected continuously. The

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Characteristics of the subjects with Huntington disease (HD)7</th>
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<tbody>
<tr>
<td></td>
<td>HD subjects (n = 8 M, 5 F)</td>
</tr>
<tr>
<td>Age (y)</td>
<td>49.0 ± 11.1</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>87.1 ± 25.6</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>172.1 ± 11.0</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29.6 ± 8.9</td>
</tr>
<tr>
<td>Chorea</td>
<td>11.4 ± 6.1</td>
</tr>
<tr>
<td>Dystonia</td>
<td>5.7 ± 3.8</td>
</tr>
<tr>
<td>Total functional capacity</td>
<td>9.5 ± 2.6</td>
</tr>
</tbody>
</table>

7 All values are x ± SD. TFC, total functional capacity; FFM, fat-free mass; TEE, total energy expenditure; SMR, sleeping metabolic rate; WMR, waking metabolic rate; DP, displacement of the center of mass (movement); NA, not applicable.

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<table>
<thead>
<tr>
<th>Table 2</th>
<th>Comparison of characteristics between subjects with Huntington disease (HD) and matched control subjects7</th>
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<tbody>
<tr>
<td></td>
<td>HD subjects (n = 5 M, 4 F) Control subjects (n = 5 M, 4 F)</td>
</tr>
<tr>
<td>Age (y)</td>
<td>48.0 ± 12.0                                    46.5 ± 11.6</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>81.4 ± 17.1                                    79.7 ± 21.3</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>172.4 ± 12.6                                   167.3 ± 12.4</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.6 ± 5.9                                     28.3 ± 6.4</td>
</tr>
<tr>
<td>Chorea</td>
<td>11.9 ± 7.0                                    NA</td>
</tr>
<tr>
<td>Dystonia</td>
<td>5.6 ± 3.4                                     NA</td>
</tr>
<tr>
<td>TFC</td>
<td>9.9 ± 2.3                                     NA</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>32.5 ± 13.0                                   34.5 ± 12.0</td>
</tr>
<tr>
<td>FFM (kg)</td>
<td>54.5 ± 14.0                                   51.4 ± 15.0</td>
</tr>
<tr>
<td>TEE (kJ)</td>
<td>2826.7 ± 547.3                                2422.6 ± 599.4</td>
</tr>
<tr>
<td>SMR (kJ/min)</td>
<td>1.47 ± 0.28                                   1.32 ± 0.36</td>
</tr>
<tr>
<td>WMR (kJ/min)</td>
<td>2.28 ± 0.46                                   1.86 ± 0.46</td>
</tr>
<tr>
<td>Overall DP (m/min)</td>
<td>4.99 ± 2.27                                  1.31 ± 1.05</td>
</tr>
<tr>
<td>Waking DP (m/min)</td>
<td>6.01 ± 2.55                                   1.65 ± 1.38</td>
</tr>
<tr>
<td>Sleeping DP (m/min)</td>
<td>0.93 ± 0.45                                  0.82 ± 0.46</td>
</tr>
</tbody>
</table>

7 All values are x ± SD. TFC, total functional capacity; FFM, fat-free mass; TEE, total energy expenditure; SMR, sleeping metabolic rate; WMR, waking metabolic rate; DP, displacement of the center of mass (movement); NA, not applicable.

2 Significantly different from HD subjects, P < 0.05.
air samples are dried and analyzed by differential oxygen (Magnos 4G) and carbon dioxide (Magnos 3G) analyzers (Hartman-Braun, Frankfurt, Germany). Actual oxygen consumption and carbon dioxide production were calculated as the difference between the composition of the entering and exiting air. The results were corrected for barometric pressure, flow rate, and humidity. Data were recorded every 10 s and were averaged over 2-min intervals (14).

force platform

The subjects’ displacement of the center of mass (DP) due to physical activities in the chamber was measured by a force platform (274 × 198 cm) that rests on 4 force transducers that measure forces in the vertical direction. The subjects remained on the force platform for the entire time they were in the chamber. The 4 transducers measure the ground reaction forces generated by the subject for each movement. These measurements are then used to calculate the subject’s position and DP, which are averaged over 2-min intervals that coincide with EE assessments. (See Appendix A for equations.)
The force platform was calibrated by an Omega LCCB-500 force transducer (Omega Engineering Inc, Stamford, CT). After the platform was divided into 256 sub-regions (16 × 16) of 0.0212-m² each, this force transducer was placed directly under the feet of a subject who performed activities inside the room. The actual force $F'$ measured by the transducer under the feet and the force $F$ measured by the direct sum of the 4 platform transducers were in good agreement. The average error ($F' - F/F'$) was 2%.
The average error of displacement was 2.71 cm in the $x$ direction and was 2.62 cm in the $y$ direction. The maximum error was 6.2 cm (absolute distance) from the actual position. The size of the platform was 274 × 198 cm, so the relative errors for $x$ and $y$ were 0.99% and 1.32%, respectively. By comparing actual positions of human volunteers on the calorimeter floor with computer-predicted positions, we determined that the platform system could acutely determine the position of the subject on the floor (14).

body composition

After 24-h EE was measured, body composition was assessed to determine fat-free mass (FFM) and percentage body fat for each subject by using air-displacement plethysmography (BOD POD; Life Measurement Instruments, Concord, CA). This instrument has been validated in a variety of populations (15-19). This air-displacement method is fast, is safe, requires minimal subject effort, and is especially suitable for subjects with HD who would likely have difficulty with the traditional underwater weighing method.
The subjects were tested while wearing only underwear and a swim cap. Body weight was measured to the nearest 0.1 kg on the accompanying scale. Raw body volume was determined from 2 measurements of 20-s each while the subject sat quietly. A third measurement was conducted if the 2 measurements did not agree within 2.0%. Raw body volume was corrected for thoracic gas volume with the air-displacement plethysmograph. Calculations were performed with BOD POD software.

Dietary intake

Dietary intake was measured by weighing all food provided ad libitum and all leftovers from meals eaten in the metabolic chamber. Although one might expect a certain amount of “opportunistic eating” in sedentary individuals provided an ad libitum diet, there is no a priori reason to believe that persons with HD would be more likely to overeat than would matched control subjects.
The first of three 24-h dietary recalls was obtained for the day before the 24-h EE measurement was made. Two additional 24-h dietary recalls were obtained for each subject on 2 subsequent nonconsecutive days that did not include the day in the chamber. All food intake data were analyzed by a registered dietitian (AMG) with the use of nutrient analysis software (NUTRITIONIST V; First Databank, San Bruno, CA).

Other metabolic measures

Twenty-four–hour urine samples were obtained from each subject, and protein oxidation was calculated from urinary nitrogen measured by a modified Kjeldahl procedure (20). Lipid and carbohydrate oxidation rates were then calculated with the use of the nonprotein respiratory quotient (RQ) (21).

Nonfasting blood samples were obtained from each subject for the measurement of leptin, insulin, and glucose. The CAG repeat length in the IT15 gene (4p.16) was determined for all HD subjects via extraction from leukocytes using standard procedures, (22) which was followed by polymerase chain reaction amplification of the relevant gene and fixation by Southern blot (23). Anonymous genetic testing for research purposes was carried out by either Dianon Systems Inc or the Massachusetts General Hospital. The results were available for research purposes only and were not provided to the subjects. This is standard practice for persons who have not requested genetic testing and who have not been offered genetic counseling.

Debriefing of subjects

At the conclusion of the study, all subjects were provided with copies of their study test results and the diet analysis, except for the results of genetic testing as mentioned above. Presymptomatic genetic testing is done only at designated centers, preferably under the guidance of a genetic counselor. However, an exception is made to allow anonymous genetic testing for research purposes. The subjects were given ample opportunity to discuss all of their other study results.

Data analysis

Linear regression was used for the analysis of 24-h TEE, SMR, and waking metabolic rate (WMR) with 2 independent variables, FFM and chorea score for all 22 subjects (13 HD subjects, 9 control subjects). For the purpose of this analysis, the control subjects were assumed to have chorea and dystonia scores of 0 and a TFC of 13, which indicated no functional impairment.

Paired t tests were performed to compare DP, TEE, SMR, and WMR values between 9 HD subjects and 9 matched control subjects. The DP over 24 h, and while awake and asleep, were described by average speed in m/min. The data were analyzed with SPSS-PC statistical software, version 10.0 for WINDOWS (SPSS Inc, Chicago, IL). Significance was defined as a $P$ value $<0.05$. 
RESULTS

Correlation between age at diagnosis and CAG repeat length in 13 HD subjects

Age at diagnosis of HD was used as an approximate estimation of age at onset and duration of disease because accurate prediagnosis information was not available for all subjects. In the 13 HD subjects, this was highly correlated with CAG repeat length ($r^2 = 0.629, P < 0.03$), as seen in previous studies (24). The CAG repeat length ranged from 41 to 48 for these subjects. Persons without HD have a CAG repeat length of 6–35, whereas persons with HD have CAG repeat sizes of 36–121. Thus, the HD subjects participating in the current study were typical in terms of their CAG repeats and therefore could be considered representative of the larger population of persons with HD. There was also a strong correlation between UHDRS (11) chorea scores and duration of disease, as defined by date of diagnosis ($r = 0.737, P < 0.001$).

Because of the limited range of CAG repeats, other correlations, such as those to TEE, were not significant. Individual CAG repeat lengths are not reported here to protect the privacy of the study subjects.

Energy expenditure and metabolic rate in all 22 subjects

To examine how the disease affects EE, linear regression was performed with the use of data from all 22 subjects. TEE, SMR, and WMR were the 3 dependent variables, and FFM and chorea score were the 2 independent variables for the linear regression. Dystonia and TFC were evaluated, but they did not significantly affect TEE in regression models.

For TEE,

$$\text{TEE} = 30.8 \times \text{FFM} + 17.5 \times \text{CS} + 832.2 \quad (1)$$

where $P < 0.001$ for the coefficient of FFM, and $P = 0.122$ for the coefficient of chorea score. FFM contributed significantly to TEE, whereas TEE was not significantly affected by chorea score.

For SMR,

$$\text{SMR} = 0.0178 \times \text{FFM} + 0.0034 \times \text{CS} + 0.408$$

where $P < 0.001$ for the coefficient of FFM, and $P = 0.59$ for the coefficient of chorea score. FFM was the main contributor to SMR, and chorea score had no effect on SMR.

For WMR,

$$\text{WMR} = 0.0223 \times \text{FFM} + 0.0215 \times \text{CS} + 0.7138$$

where $P < 0.001$ for the coefficient of FFM, and $P < 0.05$ for the coefficient of chorea score. Both FFM and chorea score contributed significantly to WMR.

These findings indicate that FFM is the primary determinant of TEE, and that chorea scores also contribute significantly to EE while a person is awake but not while asleep.

There were no significant differences between the HD subjects ($n = 13$) and the control subjects ($n = 9$) in substrate utilization, RQ, 24-h nitrogen excretion, nonprotein RQ, serum glucose, serum insulin, or serum leptin (data not shown). As would be expected, leptin was highly correlated with % body fat, ($r^2 = 0.8728, P < 0.001$) as was glucose ($r^2 = 0.6395, P < 0.002$). Adjusted RQs did not differ between groups ($P = 0.11$), which indicated that fat and carbohydrate utilization were not significantly different between HD and control subjects under sedentary conditions. A lack of difference in RQ between HD subjects and control subjects would indicate that substrate utilization is essentially normal in persons with stage 1 and stage 2 HD under conditions of mild negative energy balance, as seen in the study by Pratley et al (5), and of positive energy balance, as seen in the current study.

Energy expenditure and metabolic rate for 18 matched subjects

The 4 HD subjects without matched control subjects did not differ significantly from the 9 HD subjects with control subjects for sex, age, height, and body weight. Further analysis was undertaken with the 9 matched pairs of HD subjects and control subjects. The average TEE of the HD subjects was ≈11% higher than that of the matched control subjects, but the difference was not significant (HD subjects: 11 828 ± 2288 kJ; control subjects: 10 284 ± 2389 kJ; $P = 0.09$ by $t$ test). A similar pattern was found for SMR. SMR was ≈9% higher in the HD subjects than in the control subjects, but this difference was not significant (HD subjects: 6.11 ± 1.17 kJ/min; control subjects: 5.60 ± 1.42 kJ/min; $P = 0.20$ by $t$ test). However, there was a significant difference in WMR between HD subjects and control subjects; WMR was ≈20% higher in the HD subjects than in the control subjects (HD subjects: 9.54 ± 1.92 kJ/min; control subjects: 7.91 ± 1.84 kJ/min; $P < 0.05$ by $t$ test) (Figure 1).

Physical activity for 18 matched subjects

Data from these 18 matched subjects were used in the further analysis of physical activity. The overall average DP was significantly greater in the HD subjects than in the control subjects (HD subjects: 3.44 ± 1.58 m/min; control subjects: 0.860 ± 0.697 m/min; $P < 0.001$ by $t$ test), which is consistent with the finding of a greater amount of both voluntary and involuntary physical activity in the HD subjects.

The average DP while awake was also significantly greater in the HD subjects than in the control subjects (HD subjects: 6.03 ±
This measurement showed a difference between intakes reported by stage 1 and stage 2 HD subjects. The subjects with more advanced HD (stage 2) had a greater variability in intake than did stage 1 HD subjects (SDs of 2405 and 3899 kJ/d; \( P = 0.06 \)).

Energy balance

For the 9 matched control subjects, energy balance (observed intake – TEE) was not significantly different from that of the HD subjects. (HD subjects: 2581 ± 5368 kJ; control subjects: 3021 ± 4330 kJ; \( P = 0.85 \)). Because they were provided an ad libitum diet, most subjects in both groups were in positive energy balance.

DISCUSSION

Energy expenditure and metabolic rate

The findings of this study are consistent with those of previous studies, which showed that RMR (9) and SMR (5) were not significantly different between the HD subjects and the matched control subjects. Although the 9% greater SMR in the HD subjects than in the control subjects in this study was not statistically significant, it was consistent with the possibility of an overall defect in oxidative metabolism, as suggested by 2 studies in which the phosphocreatine:creatine ratios were measured in subjects with HD (25, 26). In the present study, SMR was only 0.12 kJ/min (<209 kJ/d) higher in the HD subjects than in the control subjects (\( P = 0.20 \), which is not greater than previously reported (5, 9). Therefore, although oxidative defects cannot be excluded, it seems unlikely that differences in SMR and RMR alone account for weight loss in persons with early-to-midstage HD. There are no available data on the TEE of persons with known mitochondrial dysfunction (eg, Leigh Syndrome, MELAS) measured with comparable methods. Therefore, it was not possible to directly compare the magnitude of a difference in measured metabolic rate in HD subjects with the biochemical differences found in studies of patients with HD.

Physical activity differences

The DP of the HD subjects was approximately double that of the control subjects (\( P < 0.001 \)) and was a significant factor in estimating WMR with a regression model (\( P < 0.03 \)). This difference is consistent with reports of increased EE (27) and increased displacement of mass (28, 29) with central nervous system gait disorders compared with orthopedic injuries.

Energy intake and balance

“Opportunistic eating” was especially evident in the younger men, in both the HD and control subjects. Of note, if the HD subject with the highest observed intake was removed from the analysis, the remaining HD subjects actually had a lower average observed intake than did the control subjects. This finding indicates that most of the HD subjects did not have a greater appetite or engage in opportunistic eating to a greater extent than did the control subjects. The finding of overall higher EEs in the HD and control subjects in the current study than in the study by Pratley et al (5) may be partially explained by the thermic effect of food in subjects with large positive energy balances in both the HD and control groups.
On the basis of the repeated 24-h dietary recalls, stage 2 HD (more impaired) subjects had a substantially higher variability in intake than did stage 1 HD subjects (SDs of 2405 and 3899 kJ/d; \( P = 0.06 \)). Although the difference in variability was not statistically significant, the trend may help to explain the etiology of weight loss in some HD patients. In general, the variability in intake over the three 24-h dietary recalls increased as TFC decreased. This finding is in line with the decline in TFC observed with progression of the disease (30), which may help explain why some HD patients lose weight even though they report high energy intakes to their physicians and clinic staff. The higher energy intakes reported on some days may not be enough to offset the lower energy intakes reported on other days. This increasing variability in energy intake may have been due to an increase in physical disabilities, the inconsistent availability of assistance with meals, or changes in mental status.

Limitations

There were several limitations of this study that must be kept in mind when interpreting the results and applying them to persons with HD. The selection criteria for the study may have biased the results toward the healthiest people with HD. The study participants were independently functioning, weight-stable persons with stage 1 or stage 2 HD. They also had an average BMI that was significantly higher than that reported for HD patients in other studies (5, 7). These factors may have yielded a more “normal” metabolic picture than would be seen in subjects with more advanced disease or who are losing weight rapidly.

The relatively small number of subjects precluded the possibility of a more finely delineated analysis of factors contributing to TEE in this population. It is possible that other factors, such as dystonia, may play a role that was not detectable by these measures. Also, the lack of a set protocol of physical activity for the subjects while they were in the human respiratory chamber made it impossible to compare the energy costs of specific activities, other than a comparison of waking and sleeping activities.

Conclusions

The results of this study showed that persons with early-to-midstage HD have overall daily energy requirements that are \( \approx 11\% \) higher than those of control subjects. This difference was due to the difference (20%) in WMR (\( P < 0.05 \)) with increased amounts of both voluntary and involuntary physical activities. Meeting these additional energy requirements was apparently not difficult for the HD subjects under the controlled conditions of the study because the subjects were provided with an excess of food consistent with their food preferences. However, under free-living conditions as measured by repeated 24-h dietary recalls, intakes varied much more in the HD subjects than in the control subjects. The variability in energy intake also increased with the progression of the disease, as measured by TFC. Both of these factors are likely related to the weight loss observed with HD and should be taken into account in nutritional evaluations of persons with HD. Further studies of patients with late-stage HD are warranted.

AMG helped develop and design the study, collect and analyze the data, and write the manuscript. (This work formed part of her doctoral dissertation.) KZ helped collect and analyze the data and write the manuscript. KM provided significant clinical consultation on HD, helped design and develop the study and recruit the HD subjects, and reviewed the manuscript. CBM provided clinical consultation on HD and helped recruit the HD subjects. PW helped collect the data, analyze the preliminary data, and review the manuscript. CNB was the principal investigator and was responsible for the study design, development, and oversight and helped prepare the manuscript. None of the authors had any financial or personal interest (including advisory board affiliations) in the organization sponsoring this research.

REFERENCES

APPENDIX A

Equations for calculating position of subject and displacement of center of mass:

Position of subject:

\[ x(n) = \frac{1}{2} \left( 1 - \frac{F_{A2}(n) - F_{D2}(n)}{F_{A2}(n) + F_{D2}(n)} \right), \quad \text{or} \quad x(n) = \frac{1}{2} \left( 1 - \frac{F_{B2}(n) - F_{C2}(n)}{F_{B2}(n) + F_{C2}(n)} \right) \]

\[ y(n) = \frac{1}{2} \left( h - \frac{F_{A1}(n) - F_{B1}(n)}{F_{A1}(n) + F_{B1}(n)} \right), \quad \text{or} \quad y(n) = \frac{1}{2} \left( h - \frac{F_{D1}(n) - F_{C1}(n)}{F_{D1}(n) + F_{C1}(n)} \right) \]

\[ (A1) \]

\[ (A2) \]

Delta displacement of center of mass:

\[ \Delta S_{mn} = \sqrt{\left( x(n) - x(n-1) \right)^2 + \left( y(n) - y(n-1) \right)^2} \]

\[ (A3) \]

where \( F_{A2}, F_{B2}, F_{C2}, \) and \( F_{D2} \) are outputs of 4 transducers; \( l \) is the length of the floor; \( h \) is the width of the floor; \( m \) is body mass; \( n \) is the ninth sample; and \( \Delta S_{mn} \) is a function of the change in position of the subject.