Body Mass Index in Essential Tremor

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Background: The pathogenesis of essential tremor (ET) is unknown, but it could be neurodegenerative. Weight loss has been observed in patients with neurodegenerative diseases.

Objectives: To compare body mass index (BMI) (calculated as weight in kilograms divided by the square of height in meters) in ET cases and controls and to determine whether BMI is correlated with tremor severity and duration.

Methods: Patients with ET were ascertained from the Neurological Institute of New York, New York, NY. Control subjects were recruited from 2 studies at the same institution. Height and weight were measured and BMI was calculated. Dietary data were collected using a Willett Semi-Quantitative Food-Frequency Questionnaire. Tremor severity was assessed using a clinical scale and the Klove Matthews Motor Steadiness Battery.

Results: The 78 cases and 242 controls were of similar age. Mean (SD) BMI in cases vs controls was 26.5 (5.0) vs 28.2 (4.8) (P = .008). This difference remained significant in an unconditional linear regression analysis that adjusted for age, sex, ethnicity, and years of education (P = .02). Mean daily caloric intake was similar in cases and controls. In cases, BMI was negatively correlated with both measures of tremor severity (r = −0.22; P = .05 and r = −0.24; P = .03) and with tremor duration (r = −0.22; P = .05).

Conclusions: The BMI was lower in ET cases than in controls, and lower BMI was associated with disease of greater severity and longer duration. Caloric intake did not differ between groups, suggesting that lower BMI is not due to a reduction in calories. Lower BMI may be due to increased energy expenditure in ET.

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Several neurodegenerative diseases are accompanied by progressive weight loss,1-5 with hypothesized causes including decreased caloric intake and increased caloric expenditures. Weight loss can be problematic, particularly in elderly populations, where it has been linked with an increased risk of adverse outcomes such as hip fractures and mortality.6,7 The pathogenesis of essential tremor (ET) is not known, but it could be neurodegenerative. First, it is clinically progressive; there is an increase in tremor severity with age and disease duration.8,9 Second, some patients eventually develop signs of more widespread cerebellar involvement,10-13 basal ganglia involvement,13 and deficits in several cognitive domains,14,15 suggesting that there may be progressive spread of the underlying pathologic condition.

Patients with ET also experience tremor-related functional disability.16-19 Eating and drinking can be difficult,18 and severely affected end-stage patients may be unable to feed themselves independently.20 This could result in weight loss as well.

We hypothesized that patients with ET might exhibit weight loss unrelated to caloric intake. In this cross-sectional study, we compared body mass index (BMI) (calculated as weight in kilograms divided by the square of height in meters) and daily caloric intake in ET cases and similarly aged control subjects and studied the association between BMI and the severity and duration of tremor.

RESULTS

There were 78 cases and 242 controls (67 in the study of environmental risk factors for ET and 175 in the study of the genetic epidemiology of PD) of similar age (Table). None lived in nursing homes. Slightly more than half of the cases were women compared with 43.8% of the controls, and 89.7% of the cases were white.
compared with 81.0% of the controls, a difference that approached significance ($P = .07$). On average, cases had had 3 years of college education compared with 2 years in controls. The mean Cumulative Illness Rating Scale score was similar in cases and controls.

The BMI was normally distributed (Kolmogorov-Smirnov test, $z = 1.14; P = .15$). The BMI in men vs women was 28.1 (4.5) vs 27.5 (5.3) ($t = 1.14; P = .36$) and in whites vs nonwhites was 27.6 (4.8) vs 28.7 (5.5) ($t = 1.51; P = .13$). There was no correlation between BMI and years of education ($r = -0.06; P = .28$). There was no correlation between BMI and age ($r = 0.08; P = .17$), but in individuals older than 65 years, there was a negative correlation ($r = -0.18; P = .01$).

The BMI in cases vs controls was 26.5 (5.0) vs 28.2 (4.8) ($t = 2.67; P = .008$), representing on average a 6.0% reduction in BMI in cases. In an unconditional linear regression analysis that adjusted for age, sex, ethnicity (white vs nonwhite), and years of education, there was an association between BMI (dependent variable) and participant type (case vs control; $P = .02$). We also stratified by sex. The BMI in male cases vs controls was 26.2 (3.4) vs 28.7 (4.6) ($t = 3.60; P = .001$), which on average was an 8.7% reduction. The BMI in female cases vs controls was 26.9 (6.1) vs 27.7 (5.0) ($t = 0.86; P = .39$), which on average was a 2.9% reduction. Sex did not interact with participant type in determining BMI (analysis of covariance, $F = 1.62; P = .20$). Two cases (2.6%) and 7 controls (2.9%) had a BMI less than 20.0, suggesting that malnutrition was not a concern in most participants.

To minimize differences between cases and controls in ethnicity, sex, and education, we restricted the sample to whites. These 70 cases and 196 controls were similar in age (67.8 [16.2] vs 67.1 [11.5] years, $t = 0.34; P = .74$), sex (50.0% vs 41.3% women, $\chi^2 = 1.58; P = .21$), and years of education (15.3 [3.0] vs 15.1 [3.0] years, $t = 0.32; P = .75$). The BMI in cases vs controls was 26.1 (4.6) vs 28.2 (4.7) ($t = 3.17; P = .002$), which on average was an 7.3% reduction. In an unconditional linear regression analysis that adjusted for age, sex, and years of education, BMI was associated with participant type (case vs control, $P = .003$). We also stratified by sex. The BMI in male cases vs controls was 26.2 (3.5) vs 28.8 (4.7)
Videotaped Tremor Examination

A trained examiner videotaped a tremor examination that included 1 test to elicit postural tremor and 5 tests to elicit kinetic tremor in each arm.24-26 Each videotaped tremor examination was reviewed by 1 of 2 neurologists (E.D.L. and K.M.) with experience in movement disorders who had reviewed a training videotape for the rating of ET.27 Each neurologist rated the tremor using a scale from 0 to 3 and assigned a total tremor score (range, 0-36).24-27 Based on the videotaped tremor examination, the diagnosis of ET or not was confirmed using published diagnostic criteria24-27 that require each case to have at least a moderate-amplitude tremor during 3 activities or a head tremor.

ADDITIONAL EVALUATION OF ET CASES AND CONTROLS ENROLLED IN THE STUDY OF ENVIRONMENTAL RISK FACTORS FOR ET

Willett Semi-Quantitative Food Frequency Questionnaire

This 20-minute food frequency questionnaire29 includes questions about the frequency of current consumption of 61 foods and on the use of vitamins and mineral supplements. Food-frequency data may be used to compute mean daily caloric intake. The questionnaire has shown good reliability and validity related to recent nutrient intake.29,30

Klove Matthews Motor Steadiness Battery

This battery includes a groove-type steadiness tester (model 32010; Lafayette Instrument, Lafayette, Ind), which consists of 2 adjustable steel plates that form the sides of a progressively narrowing groove, and a 9-hole steadiness tester (model 32011; Lafayette Instrument), which consists of a vertical metal plate with 9 holes of gradually diminishing size.30 Any contact between a handheld metal-tipped stylus and the steel wall of the groove or hole completed a circuit and was recorded by a battery-operated silent impulse counter (model 38023; Lafayette Instrument). The impulse counter recorded the number of contacts between the stylus and the wall. After a practice trial, the subject moved the stylus through the groove once and held the stylus for 15 seconds in 3 of 9 holes. The total number of contacts was summed, yielding a Klove Matthews test score.

Cumulative Illness Rating Scale

This scale was used to document and rate the severity of co-existing illnesses. The severity of illness in each of 14 body systems (eg, cardiac, renal, and pulmonary) was rated from 0 to 3. The Cumulative Illness Rating Scale score can range from 0 (no illness) to 42 (severe comorbidity in all 14 systems).31 The scale has been validated in geriatric populations.32

STATISTICAL ANALYSIS

Ethnicity was recoded as white (non-Hispanic white) and nonwhite (including non-Hispanic black, Hispanic, and other). All statistical analyses were performed using a statistical software package (SPSS version 9.0; SPSS Inc, Chicago, Ill). To test whether the BMI was normally distributed, a 1-sample Kolmogorov-Smirnov test was performed. In this test, failure to reject the null hypothesis ($P > .05$) was consistent with a normal distribution. $\chi^2$ and 2-tailed $t$ tests were used. Pearson correlation coefficients were used to assess correlations between continuous variables. Unconditional linear regression analyses were performed in which the dependent variable was BMI and the independent variables in different models included participant type (case vs control), age, sex, ethnicity (white vs nonwhite), years of education, and duration quintile. Analysis of covariance was used to test whether there was interaction between sex and participant type in determining BMI. With 78 cases and 242 controls and $\alpha = .05$, the study had 80% power to detect a 6% difference in BMI between cases and controls. Data are given as mean (SD).

Weight loss is a common accompaniment of neurodegenerative diseases.1-4 We found that BMI was 6.0% lower, on average, in ET cases than in control subjects and that lower BMI was associated with disease of greater severity and longer duration. A similar reduction in BMI of 7.2% has been reported in patients with PD compared with controls2 and of approximately 3% to 9% in patients with Alzheimer disease.3 Weight loss has been linked to an increased risk of hip fractures and mortality,5,6,7,33 and it is important for physicians to be aware of the potential for progressive weight loss in their patients with ET so that nutrition can be addressed as part of the treatment plan. Weight loss might be prevented by routinely monitoring indicators of nutritional risk and, if necessary, providing the appropriate intervention. There are several possible explanations for the observed reduction in BMI in ET cases. First, lower BMI could have been due to decreased caloric intake in ET cases. Diminished appetite, impaired olfaction, diffi-
Demographic and Clinical Characteristics of ET Cases and Control Subjects*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>ET Cases (n = 78)</th>
<th>Control Subjects (n = 242)</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>67.6 (15.6)</td>
<td>67.4 (11.7)</td>
<td>t = 0.12; P = .90</td>
</tr>
<tr>
<td><strong>Sex, No. (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>37 (47.4)</td>
<td>136 (56.2)</td>
<td>χ² = 1.82; P = .18</td>
</tr>
<tr>
<td>F</td>
<td>41 (52.6)</td>
<td>106 (43.8)</td>
<td></td>
</tr>
<tr>
<td><strong>Ethnicity, No. (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>70 (89.7)</td>
<td>196 (81.0)</td>
<td></td>
</tr>
<tr>
<td>Nonwhite</td>
<td>8 (10.3)</td>
<td>46 (19.0)</td>
<td></td>
</tr>
<tr>
<td><strong>Education, mean (SD), y</strong></td>
<td>15.1 (3.2)</td>
<td>14.1 (4.1)</td>
<td>t = 2.2; P = .03</td>
</tr>
<tr>
<td><strong>Tremor duration, mean (SD), y</strong></td>
<td>21.6 (18.8)</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td><strong>Total tremor score, mean (SD)</strong></td>
<td>19.4 (7.7)</td>
<td>3.6 (3.1)</td>
<td>t = 17.75; P &lt; .001</td>
</tr>
<tr>
<td>Taking a medication to treat tremor, No. (%)</td>
<td>39 (50)</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Surgery (thalamotomy or DBS) for tremor, No. (%)</strong></td>
<td>1 (1.3)</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td><strong>CIRS score, mean (SD)</strong>†</td>
<td>4.0 (2.8)</td>
<td>3.9 (3.2)</td>
<td>t = 0.22; P = .83</td>
</tr>
<tr>
<td><strong>Height, mean (SD), m</strong></td>
<td>1.67 (0.10)</td>
<td>1.67 (0.10)</td>
<td>t = 0.06; P = .96</td>
</tr>
<tr>
<td><strong>Weight, mean (SD), kg</strong></td>
<td>74.1 (15.5)</td>
<td>78.9 (17.0)</td>
<td>t = 2.24; P = .03</td>
</tr>
<tr>
<td><strong>BMI, mean (SD), kg/m²</strong></td>
<td>26.5 (5.0)</td>
<td>28.2 (4.8)</td>
<td>t = 2.67; P = .008</td>
</tr>
</tbody>
</table>

*ET indicates essential tremor; NA, not applicable; DBS, deep brain stimulation; CIRS, Cumulative Illness Rating Scale; and BMI, body mass index.
†Available for 78 cases and 67 controls.

Lower BMI was more apparent in men with ET, where the difference with controls reached significance. We are unsure of the explanation for this finding. Age, ethnicity, tremor severity, and tremor duration were similar in men and women with ET. Daily caloric intake in men with ET (1532.2 [478.1] cal) did not differ from that of women with ET (1411.3 [329.5] cal, t = 0.90; P = .38).

As noted in the previous paragraph, lower BMI could be a clinical manifestation of the underlying disease. Differences in the expression of ET in men and women have been reported previously, with head and voice tremor more common in women than in men.

This study has limitations. Although we excluded patients with several comorbidities that could have contributed to lower BMI (e.g., PD and dementia), and although we assessed age, sex, ethnicity, and education in cases and control subjects and adjusted or stratified for these in the analyses, other differences between cases and controls that we did not measure could have accounted for differences in BMI. These differences (e.g., depression, impaired olfaction, use of medications that result in loss of appetite, and intentional dieting), however, would have manifested themselves as a reduction in caloric intake, which we did not find in our cases. Although other medical comorbidities could contribute to lower BMI, we did not find a difference in Cumulative Illness Rating Scale score between cases and controls, and neither have differences in comorbidities been demonstrated between ET cases and controls in the literature. Second, this was a cross-sectional study, and the association between BMI and tremor severity and disease duration needs to be examined in a longitudinal study to determine whether the reduction in BMI in ET is progressive or linear with respect to time. Finally, the difference in BMI between female cases and female controls did not reach significance. The study was not powered to detect differences between cases and controls that were less than 6%, and in analyses stratified by sex, the power was lower.

In summary, BMI was lower in ET cases than in control subjects, and lower BMI was associated with disease of longer duration and greater severity. Lower BMI was more apparent in men with ET. Current caloric intake did not differ in cases and controls, suggesting that lower BMI could be due to increased caloric expenditure. Whether this increased expenditure is a manifestation of the underlying disease or of the movements themselves needs to be explored further.

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Author contributions: Study concept and design (Drs Louis, Marder, and Levy); acquisition of data (Dr Louis, Ms Jurewicz, Watner, and Mejia-Santana); analysis and interpretation of data (Drs Louis, Marder, and Levy); drafting of the manuscript (Drs Louis, Marder, and Levy); critical revision of the manuscript for important intellectual content (Drs Louis, Marder, and Levy; Ms Jurewicz, Watner, and Mejia-Santana); statistical expertise (Drs Louis, Marder, and Levy); obtained funding (Dr Louis); administrative, technical, and material support (Dr Louis, Ms Jurewicz, Watner, and Mejia-Santana); study supervision (Dr Louis).

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