Longitudinal Risk Factors for Persistent Fatigue in Adolescents

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**Objective:** To examine whether sedentary behavior, obesity, smoking, and depression are risk factors for persistent fatigue in adolescents.

**Design:** Longitudinal population-based survey.

**Setting:** Twenty-eight randomly selected schools in east London, England, in 2001 and 2003.

**Participants:** A total of 1880 adolescents (49% male; 81% nonwhite British) aged 11 to 12 years and 13 to 14 years in 2000.

**Intervention:** Confidential questionnaires completed in class.

**Main Outcome Measures:** Persistent fatigue (extreme tiredness twice weekly or more often in the previous month at both surveys), sedentary behavior, physical activity, depressive symptoms, body mass index, and smoking.

**Results:** Severe fatigue was reported in 11% of participants aged 11 to 14 years and 17% of participants aged 13 to 16 years. Eighty-four participants (4%) reported persistent fatigue. Across both surveys, only 3 pupils reported chronic fatigue syndrome. In multivariate logistic regression, risk of persistent fatigue was independently associated with being sedentary for more than 4 hours per day (odds ratio = 1.6; 95% confidence interval, 1.1-2.3; \( P = .01 \)), being physically active (odds ratio = 1.5; 95% confidence interval, 1.1-2.3; \( P = .004 \)), and depressive symptoms (odds ratio = 2.0; 95% confidence interval, 1.5-2.7; \( P < .001 \)) in the first survey, after adjustment for age, sex, and socioeconomic status. Obesity and smoking were not associated with fatigue.

**Conclusions:** Persistent fatigue is common. Being highly sedentary or highly active independently increased the risk of persistent fatigue, suggesting that divergence in either direction from healthy levels of activity increases the risk for persistent fatigue. Mental health is important in the etiology of persistent fatigue. To help define effective preventive strategies, further work is needed on the mechanisms by which these factors contribute to fatigue.

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Fatigue is a common symptom in modern adolescent populations; contemporary data suggest that severe morning fatigue at least once per week is reported in early adolescence by 40% to 60% of European adolescents and 30.6% of US girls. A detailed recent Dutch study found that 20.5% of adolescent girls and 6.5% of boys report severe fatigue at a clinical level in the previous fortnight. While fatigue itself may be a normal feature of the increased growth and educational demands of adolescence, persistent fatigue syndromes are an increasing concern and one of the major causes of long-term school absence. In a recent United Kingdom (UK) population-based sample of individuals aged 11 to 15 years, 0.6% reported severe fatigue lasting longer than 6 months and 0.19% had chronic fatigue syndrome (CFS) as defined operationally by the Centers for Disease Control and Prevention criteria. Despite the prevalence of fatigue and persistent fatigue states in young people, little is known of factors associated with severe symptomatic fatigue and persistent fatigue in adolescents. In cross-sectional studies, severe symptomatic fatigue in young people has been reported to be associated with other somatic symptoms, sleep problems, depression and anxiety, and alcohol and tobacco use. However, to our knowledge, these associations have not been examined in longitudinal studies and may represent outcomes of fatigue rather than risk factors. Being sedentary in childhood has recently been identified as a potential risk factor for chronic fatigue in adult life. There is cross-sectional evidence in adults...
that severe symptomatic fatigue is associated with physical inactivity. However, the associations between physical exercise, sedentary behaviors, psychological problems, and severe or persistent fatigue have been little studied in young people. A better understanding of such factors might inform preventive strategies to reduce the incidence of persistent fatigue states in adolescence.

The extent to which risk factors for symptomatic fatigue may also be associated with operationally defined fatigue syndromes such as CFS in adolescents is also unclear. Studies in adults suggest that there is considerable overlap between chronic symptomatic fatigue and CFS and that persistent symptomatic fatigue may be a precursor of CFS. A recent study in Dutch adolescents similarly suggested that there is a continuum of symptoms of fatigue from healthy adolescents to those with CFS. Additionally, the potential for overlap between symptomatic fatigue and CFS has recently been increased by a move away from using operational criteria to define CFS in Europe; the Royal College of Paediatrics and Child Health in the UK has suggested CFS be defined simply as 3 or more months of medically unexplained debilitating fatigue.

We used longitudinal data from a population-based sample of UK adolescents to examine the hypotheses that higher levels of sedentary behavior, obesity, smoking, and depression increase the risk for later persistent fatigue.

METHODS

The Research With East London Adolescents Community Health Survey study is a longitudinal school-based survey of a representative sample of young people in east London, England. In 2001, 30 of the 42 secondary schools in east London were randomly selected and balanced to ensure representation of single- and mixed-sex schools. In the 28 schools that agreed to participate in phase 1 (2001), 2 representative mixed-ability classes were selected from each of year 7 and year 9 and data were collected from 2790 young people aged 11 to 14 years (84% response rate). Phase 2 resurveyed classes involved in phase 1 in 2003 when the young people were aged 13 to 16 years (years 9 and 11). The total sample size for phase 2 was 2675 participants (78% response rate), of whom 2004 had participated in phase 1. Ethical approval was obtained from the North East London Research Ethics Committee. Written consent was obtained from all of the pupils.

Data were collected by confidential questionnaires completed in class. Questionnaires have been shown to be the most reliable method of collecting activity data from large adolescent samples. Questions on fatigue were modified from the World Health Organization Health Behaviour in School-aged Children activity questions that have been shown to be valid and reliable in individuals aged 12 to 15 years. The frequency question asked, “Outside school hours, how often do you usually exercise in your free time, so much that you get out of breath or sweat?” with responses from once a month or less to every day. The duration question asked, “Outside school hours, how many hours do you usually exercise in your free time, so much that you get out of breath or sweat?” with responses ranging from 0 to 7 or more hours per week. Following the recommendations by Booth et al, we defined adolescents as active if they exercised more than twice a week for an hour or more, with the remainder defined as inactive.

The quantification of inactivity has received little attention. We used a modified version of the Health Behaviour in School-aged Children study activity duration question to obtain data on sedentary behaviors, asking, “Outside school hours, on average, how many hours a day do you usually watch TV or videos, play video games, or play on the computer?” We categorized sedentary behavior as less than 2 hours, 2 to 4 hours, and more than 4 hours per day.

Depressive symptoms were assessed using the reliable Short Moods and Feelings Questionnaire with thresholds for high scorers from validation studies. Long-standing illness was assessed using a question from the Health Survey for England, and smoking and assessed using the standard Office for National Statistics questions. Height (Leicester portable stadiometer; CMS Camden Ltd, London) and weight (Tanita Body Fat 300 electronic scales; Tanita Corp, Tokyo, Japan) were measured by trained researchers, and body mass index (calculated as weight in kilograms divided by height in meters squared) z scores were calculated from the UK growth reference. Body mass index z scores were categorized as underweight (≤−1.00), normal (−0.99 to 0.99), overweight (1.00 to 1.99), and obese (≥2.00), corresponding to body mass index ≥98th percentile.

Ethnicity was reported using an adaptation of the UK Census 2001 questions; 73% of the phase 1 sample was nonwhite. For socioeconomic data, household crowding (>1.5 persons per room) and country of birth were reported by young people, with eligibility for free school meals obtained from Local Education Authorities. Analyses were weighted to take account of unequal probabilities of selection. As the sample selection used a stratified cluster design with pupils clustered within schools, standard errors and 95% confidence intervals (CIs) for means and proportions were calculated using the survey commands in Stata version 8 statistical software (Stata Corp, College Station, Texas). Logistic regression was used to examine associations between potential predictor variables in phase 1 and each of severe fatigue in phase 2 and persistent fatigue. Associations were first adjusted for socioeconomic status, sex, and school year. Multivariate models were then developed, including all predictor factors together with socioeconomic status, sex, and school year. We also included country of birth in the models because of the ethnic diversity of our sample.

RESULTS

Data on fatigue in both phases were available for 1880 participants (49% male; 90% of the total longitudinal sample), who form the subject of all of the report analyses. The distribution of ethnicity in this population was white British in 19%, white other in 5%, Bangladeshi in 27%, Asian Indian in 10%, Pakistani in 7%, black Caribbean in 6%, black African in 10%, black British in 5%, mixed ethnicity in 7%, and Chinese, Vietnamese, or other in 5%, very similar to that in the entire longitudinal sample.

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Table 1 shows the distribution of severe fatigue in the sample in both phases. Severe fatigue increased from 219 participants (11%; 95% CI, 10%-13%) in phase 1 to 305 participants (17%; 95% CI, 15%-18%) in phase 2 (P = .001). Eighty-four (38%) of the students reporting severe fatigue at phase 1 also reported severe fatigue at phase 2, thus, 4% of the students reported persistent fatigue. Ethnicity was not associated with frequency of fatigue in either phase. Chronic fatigue syndrome was reported by 2 subjects (0.07%) in phase 1, neither of whom participated in phase 2, and by an additional subject in phase 2.

Among the participants, 367 (20%; 95% CI, 18%-22%) were born outside the UK. Those born outside the UK had a trend toward lower prevalence of severe fatigue in phase 1 (15%; 95% CI, 11%-21%) compared with those born in the UK (20%; 95% CI, 19%-23%) (P = .08) and a lower prevalence in phase 2 (those born outside the UK: 15%; 95% CI, 12%-20%; those born in the UK: 21%; 95% CI, 19%-23%) (P = .03). Those born outside the UK also had a trend toward lower prevalence of persistent fatigue (3%; 95% CI, 2%-5%) compared with those born in the UK (5%; 95% CI, 4%-6%) (P = .07).

Sedentary behavior and activity were associated in both phases. In phase 1, 23% (95% CI, 21%-26%) of active young people were sedentary for more than 4 hours per day compared with 30% (95% CI, 27%-33%) of inactive young people (P = .007). In phase 2, 23% (95% CI, 20%-26%) of active young people and 33% (95% CI, 30%-36%) of inactive young people were sedentary for more than 4 hours per day (P < .001).

SEVERE FATIGUE

Table 2 shows the distribution of fatigue in both phases in relation to potential risk factors in phase 1. Table 3 shows associations between phase 1 factors and severe fatigue in phase 2. The sample size for the multivariate model adjusted for all factors was 1597 owing to missing data for some variables, particularly for body mass index. In the multivariate model adjusted for all factors, increased risk of severe fatigue in phase 2 was independently associated with sedentary behavior for more than 4 hours per day, being physically active, depressive symptoms, and having a long-standing condition at phase 1. Female sex was also associated with an increased risk, whereas birth outside the UK was associated with reduced risk. There was no significant interaction between sedentary behavior and physical activity. Odds ratios in the multivariate model were not materially changed when the frequency of severe fatigue in phase 1 was added to the model (data not shown).

PERSISTENT FATIGUE

Table 4 shows associations between phase 1 factors and persistent fatigue. Similar to findings for severe fatigue, sedentary behavior for more than 4 hours per day, being physically active, depressive symptoms, and having a long-standing illness at phase 1 were associated with an increased risk of persistent fatigue. There was no significant interaction between sedentary behavior and physical activity in the model. The association of sedentary behavior with fatigue was similar in both active and inactive subjects. Sex was not an effect modifier of the association between sedentary behavior and fatigue.

STRENGTHS AND LIMITATIONS

We gathered data from a large, ethnically diverse, population-based sample of adolescents using validated questions. Analyses were controlled for factors potentially associated with the presence or reporting of fatigue. The models for severe fatigue and persistent fatigue were similar and robust.
exercise were each independently predictive of persistent fatigue. Severe fatigue increased significantly with age. 24% of girls aged 12 to 17 years had fatigue weekly or more often. Severe fatigue increased significantly with age. Our estimate that 25% of participants reported severe fatigue. Our findings suggest that sedentary behavior and exercise may influence the development of fatigue in different ways. Inactivity may predispose to fatigue through a symptom of depression or chronic illness; however, our models for persistent fatigue included both chronic illness and a validated measure of depression. Sedentary behaviors and physical activity were highly correlated. To account for this, we entered each of them separately into the models and tested for any interaction.

**COMPARISON WITH THE LITERATURE**

Our study had a number of limitations. We defined persistent fatigue as reporting severe fatigue in the previous month on 2 occasions 2 years apart. We acknowledge that this may misclassify some subjects as we have no knowledge of fatigue between these occasions. However, this is likely to bias our findings toward underestimation of relationships. Many adolescents with CFS do not attend school regularly; thus, our findings will underestimate the prevalence of persistent fatigue states. Additionally, those who do attend regularly are likely to have less severe fatigue. Our assessment of fatigue was limited and we could not assess the extent to which fatigue disrupted daily life. Fatigue may be a symptom of depression or chronic illness; however, our models for persistent fatigue included both chronic illness and a validated measure of depression. Sedentary behaviors and physical activity were highly correlated. To account for this, we entered each of them separately into the models and tested for any interaction.

**Table 2. Associations of Factors at Phase 1 With Frequency of Extreme Fatigue in Phases 1 and 2**

<table>
<thead>
<tr>
<th>Phase 1 Factors</th>
<th>Frequency of Extreme Fatigue in Phase 1, % (95% CI)b</th>
<th>Frequency of Extreme Fatigue in Phase 2, % (95% CI)b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants, No.</td>
<td>Rarely/ Never</td>
<td>Weekly or Less Often</td>
</tr>
<tr>
<td>Sedentary behavior, h/d</td>
<td>545</td>
<td>64 (59-68)</td>
</tr>
<tr>
<td>&gt; 4</td>
<td>498</td>
<td>51 (46-55)</td>
</tr>
<tr>
<td>Physical activity</td>
<td>Inactive</td>
<td>957</td>
</tr>
<tr>
<td>Active</td>
<td>915</td>
<td>56 (52-59)</td>
</tr>
<tr>
<td>Depressive symptoms</td>
<td>No</td>
<td>1444</td>
</tr>
<tr>
<td>Yes</td>
<td>420</td>
<td>37 (32-42)</td>
</tr>
<tr>
<td>Regular smoker</td>
<td>No</td>
<td>1812</td>
</tr>
<tr>
<td>BMI category</td>
<td>Underweight</td>
<td>926</td>
</tr>
<tr>
<td>Normal</td>
<td>214</td>
<td>55 (51-58)</td>
</tr>
<tr>
<td>Overweight</td>
<td>356</td>
<td>59 (54-64)</td>
</tr>
<tr>
<td>Obese</td>
<td>240</td>
<td>59 (52-65)</td>
</tr>
<tr>
<td>Long-standing illness</td>
<td>No</td>
<td>1355</td>
</tr>
<tr>
<td>Yes</td>
<td>476</td>
<td>54 (49-58)</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CI, confidence interval.

Sample sizes in each predictor category are unweighted.

Weighted proportions (95% CIs) of young people in each demographic or predictor category by frequency of fatigue in phase 1 and phase 2 are shown.

Our study had a number of limitations. We defined persistent fatigue as reporting severe fatigue in the previous month on 2 occasions 2 years apart. We acknowledge that this may misclassify some subjects as we have no knowledge of fatigue between these occasions. However, this is likely to bias our findings toward underestimation of relationships. Many adolescents with CFS do not attend school regularly; thus, our findings will underestimate the prevalence of persistent fatigue states. Additionally, those who do attend regularly are likely to have less severe fatigue. Our assessment of fatigue was limited and we could not assess the extent to which fatigue disrupted daily life. Fatigue may be a symptom of depression or chronic illness; however, our models for persistent fatigue included both chronic illness and a validated measure of depression. Sedentary behaviors and physical activity were highly correlated. To account for this, we entered each of them separately into the models and tested for any interaction.

**COMPARISON WITH THE LITERATURE**

Our estimate that 25% of participants reported severe fatigue weekly or more often at ages 11 to 13 years is similar to that reported by the US National Longitudinal Study of Adolescent Health, which found that 15% of boys and 24% of girls aged 12 to 17 years had fatigue weekly or more often. Severe fatigue increased significantly with age.

We found that high levels of sedentary behavior and exercise were each independently predictive of persistent fatigue. We are unaware of published population data on the association of fatigue with sedentary behavior in adolescents. Our findings are consistent with those by Viner and Hotopf that being sedentary in late childhood increases the risk of later CFS, but they are also consistent with those of case-control evidence and concerns within patient groups that higher levels of exercise predispose to chronic fatigue states. However, our finding regarding exercise is contrary to a cross-sectional Dutch school-based study reporting that higher participation in sports reduced the risk of severe fatigue and a cross-sectional US study that found no association. These differences may reflect reverse causality in the cross-sectional studies in that fatigued adolescents were less likely to participate in sports. Additionally, our exercise variable included lifestyle activity as well as sports in contrast to the other studies. It is notable that our definition of being physically active (1 hour of exercise on ≥ 2 days per week) is roughly similar to the current recommendations for adolescents of the President's Council on Physical Fitness and Sports and the National Association for Sport and Physical Education: “teens should do at least 20 minutes of vigorous activity 3 days a week and 30 minutes of moderate activity 5 days a week.” This suggests that promotion of healthy levels of physical activity, while associated with a clear health benefit, may also increase fatigue in contemporary adolescents.

Our findings suggest that sedentary behavior and exercise may influence the development of fatigue in different ways. Inactivity may predispose to fatigue through
cardiorespiratory and muscle deconditioning or through a lack of the beneficial effects of regular exercise on health.24 Conversely, high levels of exercise may produce fatigue through muscle fatigue or metabolic changes in the central nervous system.22 Our finding of independent effects for sedentary behavior and exercise is supported by evidence that sedentary behavior and physical activity, while correlated, have different determinants and track differentially from childhood.23 It is also consistent with recent reports that sedentary behavior and physical activity have independent effects on cardiovascular risk.24

These findings suggest that divergence in either direction from healthy, age-appropriate levels of activity increases the risk for persistent fatigue and that health promotion toward achieving healthy levels of activity in adolescence may prevent fatigue states. Our findings cannot necessarily be extrapolated to treatment for fatigue states but suggest that both prolonged rest and overexertion may increase rather than reduce fatigue, supporting graded rehabilitation treatment paradigms.

We found that crowding, an indicator of deprivation, was associated with higher risk of persistent fatigue. Whereas clinical samples of adolescents with CFS frequently show a strong social class bias to higher social groups,25 findings from population-based surveys in adults show that operationally defined CFS is more common in lower socioeconomic status.26 We found no association between ethnicity and persistent fatigue after adjustment for socioeconomic status. This is contrary to findings in reports from clinical samples that CFS is more common in white adolescents,25 although this is likely to be confounded by social class. Birth outside the UK was associated with lower risk of fatigue, independently of socioeconomic status. This suggests that either the experience of fatigue or its reporting may be influenced by cultural changes linked with migration.

Our finding that depressive symptoms increased the risk of persistent fatigue is consistent with a large literature showing that fatigue is associated with depression both in the general adult population27 and in those with persistent fatigue states.28 Young people with CFS have higher levels of psychological distress than healthy peers,29 and studies from psychiatric clinics suggest that around one-third of young people with CFS have significant depression.30 However, we are unaware of population studies of the relationship of persistent fatigue and depression in adolescents. While there may be significant clinical overlap between persistent fatigue and depression, it is notable that these conditions have distinct endocrinological profiles,31 and in epidemiological samples the heritability of fatigue and depression appear independent.27

We did not find smoking to be an independent risk factor for fatigue, contrary to reports from cross-sectional studies among adolescents.22 Our finding that having a long-standing illness increased the risk of persistent fatigue confirms findings in adults.26

Prevalence of self-reported CFS was low (0.07%) and similar to estimates from previous reports,5 although school-based studies are likely to significantly underes-
Persistent severe fatigue is commonly observed in adolescents, although CFS itself is rare. Being highly sedentary or highly active independently increased the risk of persistent fatigue, suggesting that divergence in either direction from healthy, age-appropriate levels of activity increases the risk for persistent fatigue. The strong association of depressive symptoms with persistent fatigue confirms that mental health is important in the etiology of chronic fatigue states. These findings need to be further explored in prospective and clinical samples; however, they suggest the possibility that promotion of healthy levels of activity and emotional well-being in adolescence may prevent persistent fatigue states.

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Author Contributions: Dr Viner had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Viner, Clark, Taylor, Bhai, Head, Booy, and Stansfeld. Acquisition of data: Clark, Taylor, Klineberg, Head, and Stansfeld. Analysis and interpretation: Viner, Clark, Taylor, Bhai, Head, Booy, and Stansfeld.
tion of data: Viner, Clark, Bhui, Klineberg, Head, and Stansfeld. Drafting of the manuscript: Viner and Bhui. Critical revision of the manuscript for important intellectual content: Viner, Clark, Taylor, Bhui, Klineberg, Head, Booy, and Stansfeld. Statistical analysis: Viner, Bhui, Head, and Booy. Obtained funding: Viner, Clark, Taylor, Bhui, Head, Booy, and Stansfeld. Administrative, technical, and material support: Clark, Klineberg, Booy, and Stansfeld. Study supervision: Viner and Bhui.

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