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Pediatrics 2006;117;1078-1086
DOI: 10.1542/peds.2005-2575

ARTICLE

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The authors have indicated they have no financial relationships relevant to this article to disclose.

ABSTRACT

OBJECTIVE. The purpose of this study was to determine the prevalence of severe fatigue in adolescent boys and girls, to explore the role of lifestyle factors in fatigue, and to investigate whether severe fatigue in a healthy population is associated with depression, anxiety, and comorbid factors also observed in chronic fatigue syndrome patients.

METHODS. In a sample of 1718 boys and 1749 girls, fatigue severity and duration were measured using a multidimensional questionnaire (Checklist Individual Strength). In addition, self-reports of depressive symptoms, anxiety, chronic fatigue syndrome-related symptoms, and lifestyle characteristics were assessed by means of questionnaires. Prevalence rates of severe fatigue and severe fatigue for ≥1 month, based on a clinical cutoff score of the Checklist Individual Strength, were determined for boys and girls separately, and gender-specific predictors of fatigue were identified by multiple regression analysis.

RESULTS. The data showed high prevalence rates of severe fatigue in adolescents. Remarkable differences between boys and girls were observed: 20.5% of girls and 6.5% of the boys scored above the clinical cutoff score on the Checklist Individual Strength. Of these subjects 80.0% of the girls and 61.5% of the boys reported severe fatigue for ≥1 month. Of the examined lifestyle characteristics, only sleep characteristics and the participation in sports played a role in predicting fatigue in both genders. Moreover, in girls, fatigue was associated with higher age, an early menarche, medication use, and the absence of an additional job. Overall, girls scored higher on depression, anxiety, and chronic fatigue syndrome-related symptoms. However, the relation between fatigue and these comorbid symptoms did not differ between genders. In both girls and boys, the duration of fatigue was positively related to fatigue severity, severity of depression and anxiety, and the number of chronic fatigue syndrome-related symptoms.

CONCLUSIONS. Fatigue prevalence among adolescents is high, especially in girls. Adolescent girls seem to be more vulnerable to symptoms of fatigue and comorbidity than boys. Interestingly, despite a female predominance in complaints, the relation

www.pediatrics.org/cgi/doi/10.1542/peds.2005-2575

doi:10.1542/peds.2005-2575

Key Words
fatigue, prevalence, adolescents, gender differences, predictors

Abbreviations
CFS—chronic fatigue syndrome
CIS—Checklist Individual Strength
CDC—Centers for Disease Control and Prevention
BDI—Beck Depression Inventory
STAIC—State-Trait Anxiety Inventory for Children

Accepted for publication Dec 27, 2005

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

between fatigue and depression, anxiety, and chronic fatigue syndrome-related symptoms was not gender specific and emerged as a cluster. In both genders, fatigue duration was associated with the severity of fatigue and the level of psychological comorbidity and chronic fatigue syndrome-related symptoms, and we, therefore, hypothesize that enduring severe fatigue may form a risk factor for the development of chronic fatigue syndrome.

FATIGUE IS A common complaint among adolescents and is often attributed to hormonal changes during puberty, psychological struggles, and new educational and social demands. High rates of school absenteeism as a consequence of severe fatigue indicate that the impact of fatigue in youngsters should not be underestimated.[1,2] Findings in adults suggest that severe unexplained fatigue might precede the development of fatigue-related illnesses, such as chronic fatigue syndrome (CFS),[3,4] a disabling condition characterized by persistent severe fatigue accompanied by additional symptoms, like headaches, myalgia, unrefreshing sleep, and cognitive disturbances, that cannot be explained by medical or psychiatric illness.[5]

Although prevalence studies on CFS in children and adolescents have been performed,[6,7] only recently have population- and school-based studies on severe or prolonged fatigue in adolescents been published.[8–10] From these studies, it can be concluded that fatigue complaints are frequently reported and that prevalence rates of disabling fatigue and fatigue illnesses are lower among adolescents than adults.

In the present study we determined the prevalence of severe fatigue in a healthy Dutch school-based population according to a clinical cutoff score of the CIS, as applied in research regarding CFS in adolescents.[11] Moreover, comorbidity of depression, anxiety, and CFS-related symptoms and the potential role of lifestyle correlates of fatigue were investigated to examine whether fatigue in a normal population is associated with comorbid factors also seen in CFS cases. We not only focused on gender differences in prevalence of severe fatigue but also examined whether the correlates of fatigue were different for girls and boys. Moreover, we investigated whether duration of severe fatigue was related to fatigue severity, depression, and anxiety and to the presence of CFS-related symptoms to explore whether a continuum exists between severe fatigue in a healthy sample and CFS.

METHODS

Participants

A total of 3467 adolescents (1718 boys and 1749 girls) participated in the study. Of this sample, 11 boys and 2 girls were excluded because of observed unreliable answering tendencies. Data were collected at 6 Dutch secondary schools in the proximity of Utrecht University Medical Center (radius: 30 km). All students in first grade to students in the pregraduation grade were asked to participate. Students and their parents were informed in writing. Data were collected in 3 waves (March and April 2002: n girls = 519, n boys = 538; March and April 2003: n girls = 392, n boys = 320; February, March, and April 2004: n girls = 838, n boys = 860). For both girls and boys, mean fatigue scores did not differ between waves (respectively, $F = .53$, $P = .59$; $F = .21$, $P = .81$). Participation rates in these waves were, respectively, 89%, 84%, and 95%. Nonresponse because of enduring absenteeism occurred in <1% of the cases. This study has been approved by the Medical Ethical Committee of the University Medical Center Utrecht.

Measures

Paper-and-pencil questionnaires were distributed to the students by instructed tutors who monitored completion of the questionnaires.

Fatigue

Self-reported fatigue was measured with the Checklist Individual Strength (CIS)[12] questionnaire, which consists of the following 4 subscales together composing a multidimensional total fatigue score: (1) severity of fatigue; (2) concentration; (3) motivation; and (4) physical activity. The response to each of the 20 statements is scored on a 7-point Likert scale (1 = "yes, that is true" to 7 = "no, that is not true"). Participants are instructed to indicate how they felt during the last 2 weeks. In addition, when the level of fatigue as indicated on the questionnaire was present for a period >2 weeks, they were asked to specify this period choosing from the following answering categories: "2 weeks to 1 month," "1 to 2 months," "2 to 3 months," "3 to 4 months," or "longer than 4 months."

The CIS was originally developed to measure fatigue in the adult population. Reliability analysis on the subscales of the questionnaire in the present adolescent sample showed Cronbach's α of .93 (severity of fatigue), .86 (concentration), .65 (motivation), and .70 (activity). Exclusion of 1 item of the activity subscale resulted in an α of .80. This item was a metaphorical question and, therefore, hard to understand for some adolescents.

Analysis of the distribution of fatigue and the selection of severely fatigued cases was based on scores on the severity of fatigue subscale of the CIS. According to an adolescent CFS study by Stulemeijer et al,[11] the cutoff point for severe fatigue was set at a score of 40 on the severity of fatigue subscale. Prevalence rates of severe fatigue, severe fatigue for ≥1 month, and severe fatigue for ≥3 months were determined. The latter is in accordance with the United Kingdom Royal College Report

(1996) on the symptoms duration criterion of CFS in children.

CFS-Related Symptoms

The presence of Centers for Disease Control and Prevention (CDC) CFS-related symptoms was explored.[13] The CFS-related symptom list was adapted from the CDC side symptoms criteria and consisted of the symptoms unrefreshing sleep, muscle pain, joint pain, headaches, tender lymph nodes, concentration problems, and memory problems but did not include items about "postexertion malaise" and "sore throat." Memory and concentration problems were included as 2 separate items because they derive from distinct cognitive function disturbances. The presence of symptoms in the past 2 weeks was examined using a dichotomous (yes/no) scale.

Depression

The 21-item Beck Depression Inventory (BDI) was used to measure depressive symptoms in the past week.[14] The BDI has been reported to be a valid and reliable depression measure in adolescents and is widely used in this population. Scores on the questionnaire range from 0 to 63. In the present study, the item concerning lack of sexual desire was excluded for analysis because of a large number of missing values on this question. Although fatigue is a symptom of depression, to avoid overlap between our fatigue and depression measures, the BDI item concerning fatigability was excluded for analysis.

Anxiety

The Dutch version of the State-Trait Anxiety Inventory for Children (STAIC) was used to measure trait anxiety (trait scale).[15] The scale contains 20 items. Responses are scored on a 3-point scale (1 = "almost never," 2 = "sometimes," and 3 = "often").

Lifestyle Characteristics

To determine time spent on extracurricular activities, subjects were asked to report how many hours weekly they spent on homework, sports (at school and extracurricular), leisure time activities and hobbies, friends and nightlife (bars, cinemas, and nightclubs), and whether they had an additional job. Questions about substance use (cigarettes, alcohol, and drugs) on a regular basis were included. Sleep characteristics were measured by self-reports of bedtimes, time it takes to fall asleep (sleep-onset latency), and rise times during school days and weekends. Sleep latency was assessed as an indicator of enduring arousal at nighttime, and total nocturnal sleep was calculated as an indicator of night time sleep.

Other Measures

BMI was calculated as self-reported body weight divided by the square of self-reported body height (kg/m^2). Fatigue- and illness-related absenteeism in the past month ("0 classes," "1–5 classes," "6–10 classes," "11–20 classes," and ">20 classes") was investigated. Subjects were asked to report medication use and, for girls, questions about the use of oral contraceptives, experience of menarche, and age at menarche were included.

Data Analysis

All of the analyses were performed with SPSS 12.0 (SPSS, Chicago, IL). Before analysis, all of the variables were tested for normality, and extreme values (>3 SD) were excluded. Group differences in normally distributed data sets were assessed by Student's t test and χ^2 analysis of variance. The χ^2 or Fisher's exact test was used for categorical and dichotomous parameters. Log-transformed data were used on the CIS-20, BDI, and STAIC questionnaires, whereas untransformed means and SDs are presented in the tables. Multiple regression analysis was conducted to determine the contribution of predictor variables to fatigue severity. All of the independent variables were entered at once, which is the most conservative method (less type 1 errors). The following dichotomous variables were included: medication use, use of oral contraceptives, complaints of unrefreshing sleep, muscle pain, joint pain, headaches, tender lymph nodes, concentration problems and memory problems, and having an additional job. Continuous variables in the model were: age; age at menarche; anxiety; depression; sleep latency and total nocturnal sleep; and hours spent on homework, sports, leisure time activities, nightlife, and with friends. R^2 was specified for variable clusters (comorbid complaints and lifestyle characteristics) entered in the model to determine the relative contribution of the clustered variables. In the analyses, the number of cases varied because of incidental missing values. Percentages were calculated based on the observed number. The significance level for all of the analyses was set at $P < .05$.

RESULTS

Subject Characteristics

We included 3454 adolescents in this study. Subject characteristics of the 1707 boys and 1747 girls in our study sample are presented in Table 1. Age, BMI, and medication use did not differ between genders.

Fatigue

The total score of the CIS questionnaire shows that girls were much more fatigued than boys (Table 2). This gender difference was because of higher scores on the subscales severity of fatigue, motivation, and concentra-

TABLE 1 **Subject Characteristics**

Characteristic	Girls	Boys
No.	1747	1707
Age, mean (SD), y[a]	14.7 (1.4)	14.6 (1.4)
Weight, mean (SD), kg	53.21 (8.60)	56.8 (11.64)
Height, mean (SD), cm	167.0 (6.9)	172.0 (11.0)
BMI, mean (SD)[a]	19.04 (2.41)	19.05 (2.47)
Medication use, %[a]	9.6	10.1
Oral contraceptives, %	13.0	—
Menarche, yes, %	79.7	—
Age at menarche, mean (SD)	12.40 (1.07)	—

[a] Student's *t* test was not significant.

TABLE 2 **Fatigue, Comorbid Complaints, and Absenteeism**

Variable	Girls	Boys	*P*
CIS score[a]			
Severity of fatigue	27.54 (12.68)	21.26 (10.44)	<.001
Concentration	15.72 (7.36)	14.64 (6.71)	<.001
Motivation	10.48 (4.70)	9.69 (4.07)	<.001
Activity	5.32 (3.05)	5.38 (3.02)	NS
Total score	59.06 (22.43)	50.98 (18.55)	<.001
CFS-related symptoms (past 2 wk), %[b]			
Unrefreshing sleep	64.3	43.2	<.001
Muscle pain	16.4	10.2	<.001
Joint pain	10.3	8.5	NS
Headaches	66.4	39.3	<.001
Tender lymph nodes	10.8	4.5	<.001
Concentration problems	32.1	20.6	<.001
Memory problems	17.5	10.7	<.001
Sum of complaints	2.18 (1.47)	1.37 (1.29)	<.001
Depression, BDI score[a]	6.02 (5.85)	3.96 (4.79)	<.001
Anxiety, STAIC score[a]	30.98 (7.01)	26.94 (5.79)	<.001
Fatigue- and illness-related absenteeism (past month), %[b]			
0 classes	52.3	64.0	<.001
1-5 classes	23.3	18.0	
6-10 classes	10.1	7.9	
11-20 classes	7.4	4.7	
>20 classes	6.9	5.4	

NS indicates not significant.
[a] Student's *t* test; values shown are mean (SD).
[b] χ^2 test/Fisher's exact test; values shown are percentages.

tion. There was no difference between boys and girls on the subscale measuring activity.

Depression, Anxiety, and CFS-Related Symptoms

On both the depression (BDI) and the anxiety (STAIC) questionnaires, girls scored higher than boys did (Table 2). Moreover, more girls than boys reported the following CFS-related symptoms: tender lymph nodes, muscle pain, headaches, unrefreshing sleep, and memory and concentration problems. The total number of CFS-related symptoms was also significantly higher in girls (2.18 on average) than in boys (1.37).

Lifestyle Characteristics

Table 3 presents lifestyle characteristics of girls and boys. Girls spent more time on homework than boys, whereas boys participated more hours in sports and spent more time on other leisure time activities and with friends. Sleep latency during the week and total nocturnal sleep in weekends was longer for girls than for boys. An equal proportion of boys and girls had an additional job. The prevalence of adolescents who smoked cigarettes was not different between boys and girls. A higher proportion of boys used alcohol and drugs.

Prevalence of Severe Fatigue in Adolescents

Distribution of Fatigue

Figure 1 shows the distribution of the CIS severity of fatigue subscale for girls and boys. The data in this figure show that there was a substantially higher prevalence of high fatigue scores in girls than in boys. For boys, the distribution was skewed to the right, meaning that the majority of boys reported no or little fatigue.

Severe Fatigue Prevalence Rates

Severe fatigue was defined as a score of ≥40 on the CIS severity of fatigue subscale. This cutoff score was based on an adolescent CFS study by Stulemeijer et al.[11] As can be expected from the distributions, there was a major gender difference in the prevalence of severe fatigue. Of the girls, 20.5% (n = 359) and of the boys, 6.5% (n = 112) scored >40. Severe fatigue lasting for ≥1 month was reported by 80.0% of the severely fatigued girls and by 61.5% of the severely fatigued boys (χ^2 = 17.80; P < .001; prevalence rates in the total sample: 16.4% of all girls and 4.0% of all boys). Even 46.9% of the severely fatigue girls and 35.2% of the severely fatigued boys were fatigued for ≥3 months (χ^2 = 4.56; P < .05; prevalence rates in the total sample: 9.6% and 2.3%, respectively).

Compared with boys, a higher proportion of girls reported fatigue- and illness-related absenteeism. In both genders, higher proportions of severely fatigued subjects reported school absenteeism compared with their nonfatigued counterparts (girls: χ^2 = 74.17, P < .001; boys: χ^2 = 26.71, P < .001). No differences were observed between the severely fatigued boys and girls (χ^2 = 2.90; P = .575).

We next investigated whether, in the severely fatigued subjects, fatigue duration was related to fatigue severity. We classified subjects as "severely fatigued <1 month" and "severely fatigued >1 month." Fatigue severity was significantly higher in the "severely fatigued >1 month" groups of both genders (F = 10.33; P < .001). Interestingly, higher depression scores (F = 16.61; P < .001), as well as higher anxiety scores (F = 5.70; P < .05) were found in these groups. In addition, more CFS-related symptoms were reported (F = 7.15; P < .05) compared with subjects with severe fatigue for less than 1 month. Interactions between gender and fatigue duration were not found, indicating that the differences

TABLE 3 **Lifestyle Characteristics**

Variable	Girls	Boys	*P*
Time spent on, h/wk[a]			
Homework	6.82 (4.17)	5.6 (3.73)	<.001
Sports	6.80 (3.91)	7.76 (4.48)	<.001
Leisure time activities	4.08 (3.36)	6.54 (6.38)	<.001
Friends	6.15 (5.31)	7.17 (6.22)	<.001
Nightlife	2.25 (2.60)	2.27 (2.93)	NS
Additional job (yes)[b]	40.5	40.8	NS
Substance use[b]			
Cigarettes	6.5	7.3	NS
Alcohol on schooldays	9.1	17.4	<.001
Alcohol in weekend	41.1	46.7	<.05
Drugs	2.1	5.8	<.001
Sleep school days[a]			
Sleep-onset latency	40 min (32 min)	34 min (28 min)	<.001
Total nocturnal sleep	8 h 25 min (54 min)	8 h 28 min (55 min)	NS
Sleep weekends[a]			
Sleep-onset latency, min	29 min (26 min)	28 min (27 min)	NS
Total nocturnal sleep, min	9 h 50 min (84 min)	9 h 41 min (84 min)	<.001

[a] Student's *t* test; values shown are mean (SD).
[b] χ^2 test/Fisher's exact test; values shown are percentages.

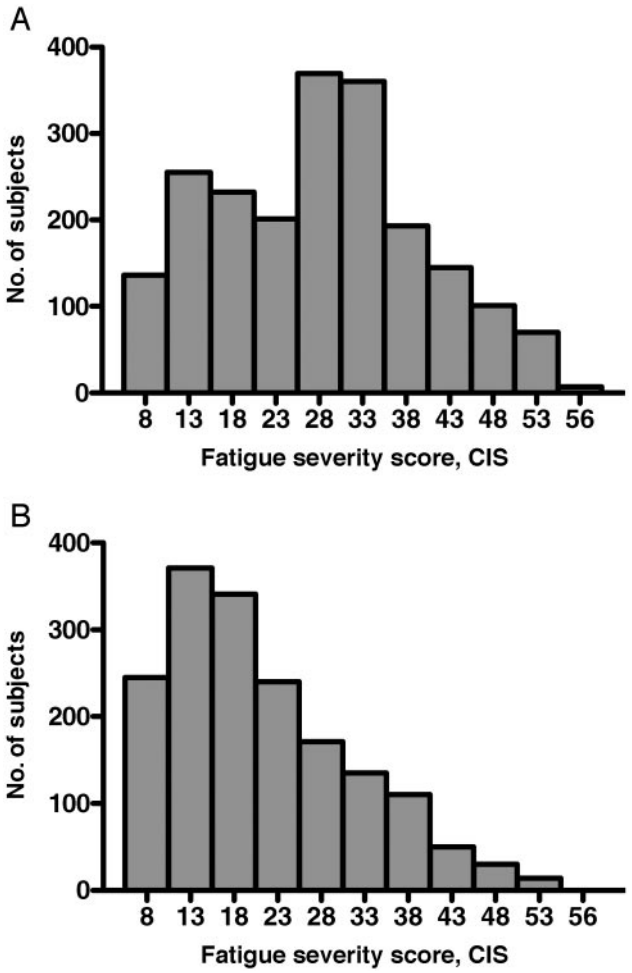

FIGURE 1
Distribution of self-reported fatigue in girls (A) and boys (B).

between severely fatigue subjects suffering from fatigue for >1 month and subjects with severe fatigue <1 month were not gender specific.

Predictors of Fatigue in Boys and Girls

To identify putative gender-specific predictors of the level of fatigue in the whole sample, multiple regression analysis was conducted (Table 4). Interestingly, in girls, medication use, higher age, and lower age at menarche were associated with higher levels of fatigue. Both in girls and in boys, higher depression and anxiety scores were related to higher fatigue scores. In boys, fatigue was associated with the CFS-related symptoms of unrefreshing sleep, muscle pain, and memory and concentration problems. In girls, fatigue severity was also related to unrefreshing sleep, muscle pain, and concentration problems. In addition, headaches and tender lymph nodes were significantly related to fatigue scores in girls only.

With regard to lifestyle characteristics, decreased participation in sports was related to fatigue in both girls and boys. None of the other extracurricular activities emerged as significant correlates of fatigue apart from having an additional job in the female group, which was associated with lower fatigue scores. Substance use was not associated with fatigue in our sample. Finally, shorter nocturnal sleep during school days predicted fatigue in girls, whereas shorter nocturnal sleep in weekends was related to fatigue in boys.

The total explained variance of fatigue in the regression model for girls was high, being 50.5%, and in the model for boys, 37.2%. In both models, the major part of the variance was explained by depression and anxiety

TABLE 4 **Predictors of Fatigue in Girls and Boys**

Variable	Girls				Boys			
	β	t	P	ΔR^2	β	t	P	ΔR^2
Age	0.10	3.22	<.05	0.078	0.03	0.90	NS	0.028
Age at menarche	−0.05	−2.06	<.05		—	—	—	
Body mass index	0.02	0.88	NS		0.01	0.27	NS	
Medication use	0.05	2.51	<.05		0.03	1.58	NS	
Oral contraceptives	0.02	0.95	NS		—	—	—	
Depression (BDI)	0.23	7.47	<.001	0.335	0.17	5.94	<.001	0.242
Anxiety (STAIC)	0.17	5.65	<.001		0.19	6.72	<.001	
CFS-related symptoms (past 2 weeks)				0.083				0.084
Unrefreshing sleep	0.27	11.66	<.001		0.25	10.65	<.001	
Muscle pain	0.05	2.12	<.05		0.06	2.58	<.05	
Joint pain	0.00	0.21	NS		0.04	1.76	NS	
Headaches	0.05	2.25	<.05		0.02	1.01	NS	
Tender lymph nodes	0.05	2.26	<.05		0.04	1.87	NS	
Concentration problems	0.10	4.29	<.001		0.07	2.91	<.05	
Memory problems	0.03	1.23	NS		0.07	2.94	<.05	
Lifestyle				0.009				0.018
Hours spent on (weekly)								
Homework	0.02	0.93	NS		−0.00	−0.16	NS	
Sports	−0.07	−3.33	<.05		−0.13	−5.86	<.001	
Leisure time activities	−0.03	−1.61	NS		0.02	0.95	NS	
Friends	−0.02	−0.83	NS		−0.00	−0.10	NS	
Nightlife	−0.00	−0.08	NS		−0.02	−0.84	NS	
Additional job (yes/no)	−0.05	−2.11	<.05		0.00	0.15	NS	
Substance use								
Cigarettes	0.03	1.22	NS		0.03	1.38	NS	
Alcohol on schooldays	0.01	0.33	NS		0.01	0.53	NS	
Alcohol in weekend	−0.02	−0.88	NS		−0.04	−1.49	NS	
Drugs	−0.00	−0.02	NS		0.04	−0.18	NS	
Sleep school days								
Sleep-onset latency	−0.03	−1.02	NS		0.04	1.41	NS	
Total nocturnal sleep	−0.04	−1.45	NS		−0.06	−2.20	<.05	
Sleep weekends								
Sleep-onset latency	0.03	1.09	NS		−0.00	−0.23	NS	
Total nocturnal sleep	0.06	2.84	<.05		0.00	−0.48	NS	

NS indicates not significant.

(33.5% for girls and 24.2% for boys) and the CFS-related symptoms (8.3% for girls and 8.4% for boys).

DISCUSSION

In the present study we determined the prevalence of severe fatigue in an adolescent school-based population and identified comorbid complaints. We specifically focused on gender differences in prevalence and the gender specificity of the correlates of fatigue. In addition, we investigated whether the duration of fatigue was related to fatigue severity and to the severity of comorbid complaints. Finally, we examined the potential role of lifestyle factors as predictors for fatigue severity.

We found that girls scored higher than boys on the CIS questionnaire. Severe fatigue, defined according to the clinical cutoff score of the CIS, was reported by a large proportion of adolescents, and especially by girls. In the sample, 20.5% of girls and 6.5% of boys were severely fatigued. Severe fatigue lasting for ≥1 month was observed in 16.4% of the total sample of girls and in 4.0% of the boys. Even 9.6% of the girls and 2.3% of the boys were severely fatigued for ≥3 months. It is very intriguing that we found such a high percentage of adolescents who scored above the clinical cutoff score in a so-called "healthy" population. Our data warrant a follow-up study to investigate whether severe fatigue during adolescence, which is considered to be a crucial period of life, is a predictor for the development of fatigued-related illnesses or other diseases in later life.

A previously performed school-based study also reported a high occurrence of fatigue. Ghandour et al[8] showed that 30.6% of girls reported morning fatigue at least once a week (see also ref 16). We used a more strict definition of fatigue and investigated overall severity of fatigue experienced over at least the past 2 weeks. Moreover, we used a clinically defined cutoff score to identify subjects with severe fatigue, but we still observed a high prevalence of complaints. Only a small number of studies concentrated on severe and enduring fatigue in adolescents. Overall, prevalence rates in these

studies were lower compared with the rates found in our sample.[9,10,17,18] Other prevalence studies in adolescents focused specifically on the determination of rates of fatigue-related illnesses, such as CFS and CFS-like conditions.[6,7] Unfortunately, because of variability in definitions of fatigue, research techniques, time frames used to determine prevalence rates (ie, point prevalence and lifetime prevalence), and sample characteristics, it is hardly possible to make comparisons between studies. Although the questionnaire was not only consisting of fatigue topics, the prevalence rates of severe fatigue might be influenced by the fact that subjects knew that the study was focused on fatigue. Therefore absolute prevalence rates of severe fatigue must be interpreted with some caution.

According to the layperson's view, lifestyle factors, such as extracurricular activities, substance use, and sleep, would be the obvious explanation for higher levels of fatigue in adolescents. However, the data obtained in our sample show that substance use, time spent on homework, leisure activities, nightlife, and time spent with friends were not related to the level of fatigue. Some gender-specific contributors to fatigue were observed. In girls, medication use was positively related to fatigue. Moreover, higher fatigue scores were observed in girls without an additional job. This is in contrast to what reasonably might be expected, although the direction of cause and effect is unclear. In boys, shorter nocturnal sleep during school weeks was related to higher fatigue scores. Longer nocturnal sleep in weekends was associated with fatigue in girls. Overall, however, the contribution of sleep characteristics to fatigue was smaller than we expected.

In both genders, less participation in sports was associated with higher levels of fatigue. A recently published report by the Netherlands Institute for Health Care Research also revealed physical activity to be negatively related to fatigue in adults.[19] Whether decreased physical activity is either a cause or a consequence of fatigue remains to be investigated. It is conceivable, however, that lower levels of physical activity may cause higher perceived fatigue, because in a prospective study focusing on predictors of CFS, Viner and Hotopf[20] found that higher levels of exercise in childhood lowered the risk for the development of CFS later in life. Moreover, physical exercise has been associated with a dampening of depression and anxiety[21] and, thus, may be of influence on fatigue as a correlate.

In line with earlier studies in adolescents[9,10,17,22] and adults[23], girls reported higher levels of fatigue than boys. Moreover, we observed a female/male ratio of 3:1 for severely fatigued cases, which is higher than in most other studies.

Previous research on the development of psychopathology in youngsters might clarify the gender difference in the prevalence of fatigue observed in the present study. There is ample evidence that, apart from higher levels of fatigue, females report more psychological and somatic complaints[9,17,24,25] and mental disorders, like depression and anxiety, in which fatigue is a key symptom.[26–30] Longitudinal studies concerning gender differences in the development of psychological disturbances show that, during adolescence, an increase in psychological symptomatology occurs, especially in girls. This female predominance seems to emerge around the age of 13 years.[31–33] In our sample, age was positively related to fatigue in girls but not in boys. A role of age in fatigue in youngsters was also found by Mears et al[18] and has been earlier reported by Marshall.[6] The age dependency of fatigue in girls in the current study might be because of a differential developmental course in bodily processes in the girls, in analogy to the speculations of the role of hormonal factors in the development of mental disorders around this age. In favor of this explanation are the previous observations that earlier pubertal timing is associated with depression in adolescents and is also an important predictor of other internalizing symptoms, such as panic attacks and eating disorders, during adolescence.[34,35] In line with this finding is our observation that lower age at menarche was associated with higher levels of fatigue. It is tempting to speculate that the gender differences in fatigue are caused by developmental changes in neuroendocrine functioning emerging during puberty.

A second possibility would be that gender differences in fatigue prevalence and psychological symptoms are because of a lower threshold of girls to report complaints like fatigue and distress. However, from a meta-analysis by Davis et al,[36] it can be concluded that females not only perceive events as more stressful but are also exposed to more stressful situations. This gender difference was especially seen in adolescents. Moreover, whereas in the current study, more depression, anxiety, and CFS-related symptoms were observed in girls, regression analysis showed no gender specificity in the associations between fatigue on the one hand and depression, anxiety, and CFS-related symptoms on the other. Thus, despite the female predominance in fatigue, depression, anxiety and CFS-related symptoms, these symptoms seem to emerge as a cluster in both boys and girls. In line with this observation, Hickie et al[37] showed in a twin study that 24% of the variance of fatigue has a common genetic background with a cluster of depression, anxiety, and distress. Therefore, we hypothesize that factors that determine fatigue, depression, anxiety, and CFS-related symptoms are similar in boys and girls, but that in girls a higher sensitivity in stimulus processing develops during adolescence. Indeed, it has been shown that genders also reliably differ in objective measures of stimulus processing, such as pain threshold and serotonin receptor sensitivity.[38,39]

We observed that subjects with severe fatigue for ≥1

month reported higher fatigue severity than subjects who felt severely fatigued for <1 month. The latter was true for both genders. Moreover, duration of fatigue also was related to the extent of comorbid complaints. Higher depression and anxiety scores and higher numbers of CFS-related symptoms were reported by subjects with severe fatigue >1 month compared with subjects with shorter durations of severe fatigue. In view of the relation between the number of CFS-related symptoms and fatigue severity and duration, we propose that this relation may imply that severe fatigue and the duration of fatigue are risk factors to develop CFS. However, this hypothesis was not tested in this study. We did not examine impairment and the relation between fatigue and exertion or rest, and no diagnosis was made by a physician to exclude medical illness related to fatigue. Moreover, longitudinal research is needed to find out whether healthy adolescents with enduring severe fatigue, accompanied by complaints of depression, anxiety, and CFS-related symptoms are a high-risk group for the development of CFS. Because clinical diagnosis to detect CFS was not an aim of the study, we cannot rule out that some subjects fulfilled the CDC criteria. However, based on the Dutch prevalence rate of CFS in adolescents, 10 to 20 per 100 000,[40,41] we expect that this rate is too low to account for the high prevalence of severe fatigue in our sample.

CONCLUSIONS

The present study showed high prevalence rates of severe fatigue in adolescents. A striking difference was found between girls and boys; that is, 20.5% of girls and 6.5% of boys reported severe fatigue. In addition, highly significant gender differences were found in comorbid depression and anxiety and in reported CFS-related symptoms. With respect to gender-specific predictors of fatigue, lifestyle characteristics played only a minor role in the explanation of the level of fatigue. Despite a female predominance in complaints, the relation between fatigue and comorbidity was not gender specific and emerged as a cluster of which causal factors remain to be established. Adolescent girls, however, seem to be more vulnerable for symptoms of fatigue and comorbidity than boys. In girls, some data favor a role for hormonal changes during puberty: the relation to lower age at menarche and the age gradient. Fatigue duration was associated with the severity of fatigue, the level of psychological comorbidity, and CFS-related symptoms. On the basis of our data, we hypothesize that enduring severe fatigue may form a risk factor for the development of CFS.

ACKNOWLEDGMENTS

We thank C. D. J. Tersteeg-Kamperman, M. Donker, and M. Maas for their contribution to the data collection and processing.

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