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Papers

Childhood predictors of self reported chronic fatigue syndrome/myalgic encephalomyelitis in adults: national birth cohort study

Russell Viner, Matthew Hotopf

Abstract

Objective To study childhood risk factors for chronic fatigue syndrome in adult life.
Design Examination of data from the 1970 British birth cohort.
Participants 16 567 babies born 5-11 April 1970, followed up at 5, 10, 16, and 29-30 years.
Main outcome measures Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) identified by self report at age 30 years. Data from childhood from questionnaires given to parents and teachers. Maternal mental health assessed with the malaise inventory.
Results 93 (0.8%, 95% confidence interval 0.7 to 1.0) of 11 261 participants reported ever having CFS/ME, and 48 (0.4%, 0.3 to 0.6) had the condition currently. Higher risk of CFS/ME was associated with having a limiting longstanding condition in childhood (odds ratio 2.3, 1.4 to 3.9), female sex (2.3, 1.4 to 2.6), and high social class in childhood (2.2, 1.4 to 3.5). Higher levels of exercise in childhood were associated with lower risk (0.5, 0.2 to 0.9). Maternal psychological disorder, psychological problems in childhood, birth weight, birth order, atopy, obesity, school absence, academic ability, and parental illness were not associated with risk of CFS/ME.
Conclusions We identified no association between maternal or child psychological distress, academic ability, parental illness, atopy, or birth order and increasing risk of lifetime CFS/ME. Sedentary behaviour increased the risk.

Introduction

Chronic fatigue syndrome (CFS) is a common disabling condition characterised by persistent unexplained fatigue[1] that imposes a considerable burden on families and the health services. In the United Kingdom, the term myalgic encephalomyelitis (ME) is often used by patients to describe the symptoms of CFS. We have used the term CFS/ME to refer to self reported CFS or ME. The aetiology of CFS remains unclear. Longitudinal studies in adults have suggested that past psychiatric disorder may have a role.[2] Other studies have implicated a range of biological and psychosocial risk factors, including female sex,[3] stressful events,[4] high academic achievement,[5] infections such as mononucleosis[6] and viral meningitis,[2] higher levels of routine exercise,[7] birth order,[8] atopy,[9] and physical symptoms and diagnoses.[10]

While factors at the family level are known to be important, it is unclear whether these operate primarily at the environmental or genetic level.[11] Small case-control studies have suggested that maternal overprotectiveness and depression[12] may be associated with increased risk of disease in adult life, and a recent cross sectional epidemiological study showed an association between maternal psychological distress and parental report of ME/CFS in children.[13] Cohort studies of childhood risk factors for adult illness, however, have not been published.

We used longitudinal data from the 1970 British birth cohort study to explore whether childhood risk factors were associated with lifetime risk of developing CFS/ME by the age of 30 years. Prematurity, birth order, obesity, atopy, chronic limiting conditions, high exercise levels, school factors (high academic achievement and absence from school), and psychological factors including poor maternal mental health and childhood behaviour problems have all been proposed as possibly associated with the lifetime risk of CFS/ME.

Methods

The 1970 British cohort study (BCS70) is a cohort study that enrolled 16 567 babies born in England, Scotland, and Wales on 5-11 April 1970. Participants were followed up at 5 (n = 13 135), 10 (n = 14 875), 16 (n = 11 622), and 29-30 (n = 11 261) years of age. As the survey at 16 years coincided with a national teachers' strike and national school leaving examinations, sample sizes for some questions were considerably smaller. Between 10 and 30 years, loss to follow up was highest in those from lower socioeconomic groups and those with a disability (loss of about 5% in both groups).[14]

CFS/ME was identified by self report questionnaire completed at 30 years. Participants were asked whether they had ever had CFS/ME, whether they currently had CFS/ME, and at which age their condition developed. Measures of socioeconomic status (father's social class and maternal educational achievement) in childhood were obtained from interviews with parents at 10 years. Socioeconomic status at 30 years was derived from participants reported current occupation. Data on ethnicity were recorded at 30 years.

At 5, 10, and 16 years, mothers were asked to complete 19 items from the Rutter parental A scale of behaviour disorder. At 10 years, teachers completed a 53 item social development scale, with items drawn from the Conner teacher rating scale and the Rutter teaching scale. A 14 item subscale for problems/impulsivity/hyperactivity in conduct and an eight item subscale for attention deficit has been previously identified by factor analysis.[15] As thresholds indicative of likely disorder were not available for these modified instruments, we defined high scorers for all child behaviour scales as scores greater than 1 SD from the sample mean in the direction of greater problems. At 16 years,

teenagers completed the 12 item self report general health questionnaire (GHQ 12) to screen for recent psychological distress. Scores of ≥4 indicated psychological disturbance.[16] Self esteem at 10 and 16 years was measured in school with the Lawrence self esteem questionnaire (Lawseq) for children, validated for these age groups.[17] Scores >1 SD below the population mean defined low self esteem.

At 5, 10, and 16 years mothers completed the Rutter malaise inventory, a 24 item self completion scale designed to assess psychiatric morbidity. In the standard scoring system used at 5 years, positive or negative responses are obtained for each item and a total score between 0 and 24 is then obtained by summation of all positive responses.[18] Alternative scoring systems were used in the 10 and 16 year surveys. At 10 years, mothers were asked to rate themselves on each item on a Likert scale between 0 ("seldom or never") to 100 ("most of the time"). We derived a total malaise score by summation of all responses divided by 100, providing a score from 0 to 24 somewhat comparable with that produced by the standard scoring system. At 16 years, mothers were asked to rate their response to each question as "most of the time," "some of the time," and "rarely or never." We added the positive ("most of the time") answers to produce a total score between 0-24. Participants also completed the malaise inventory at the age of 30 years using the standard binary scoring system. A score ≥7 on the binary scoring system has been suggested to indicate a high risk of psychiatric disorder, and we used this to define high scorers for maternal malaise scores at 5 and 16 years and for the participant's own score at 30 years.[18] As this threshold is not appropriate for the Likert scoring system, we defined a high score for maternal malaise at 10 years as a score >1 SD above the mean.

At 10 years participants completed two verbal and two non-verbal subscales of the British ability scales for the assessment of cognitive attainment. Age appropriate T scores were calculated with reference norms appropriate for 1980.[19] High intellectual ability was defined as a mean T score in the highest 10%, which approximates to a mean T score ≥60 (equivalent to IQ ≥120).

Also at 10 years parents were interviewed to obtain a history of severe or prolonged illness in either parent in the previous 5 years. Mothers provided information on the child's history of atopy (ever had asthma, eczema, or allergic rhinitis), how often the child played sport in his or her spare time, and the number of days off school that term because of health or emotional problems. Teachers' reports provided data on the usual number of hours of sport played by the child at school each week. The presence of a longstanding condition in the child was recorded from both medical examination and maternal report at 10 years, with maternal report of whether the condition considerably limited the child's daily life. School doctors measured the child's height and weight at 10 years. Obesity was defined as body mass index ≥95th centile.[20]

Analysis

We explored differences between those with any CFS/ME and the remainder of the cohort with *t* tests for continuous variables and χ^2 test for categorical variables. We then used logistic regression to assess factors associated with the risk of ever having CFS/ME. Factors were initially assessed at univariate level and then examined after adjustment for sex, father's social class in childhood, and mother's educational status. We used a final multivariable model to determine which factors were independently associated with CFS/ME, entering all variables shown to be significantly ($P<0.05$) associated simultaneously, including sex, father's social class, and mother's education. Adult psychological morbidity (high scorer on malaise inventory at 30 years) was also included a priori in the multivariable model to control for potential confounding of self report CFS/ME status. We used Stata 8 (StataCorp, College Station, TX) for analyses.

Results

Of the 11 261 participants, 93 (0.8%, 95% confidence interval 0.7 to 1.0) reported ever having CFS/ME and 48 (0.4%, 0.3 to 0.6) had the condition currently. Two participants who reported age of onset of illness at 2 years were removed from the analysis as lifetime fatigue is likely to represent a condition other than CFS/ME. Of the 91 remaining participants, reported age at onset of CFS/ME ranged from 14 to 29 years, with a median of 24 years (mean 22.9, SD 4.6 years).

Table 1 shows the associations of demographic, biological, and social factors with lifetime risk of CFS/ME. Odds ratios are shown unadjusted and adjusted for sex, father's social class in childhood, and mother's education. Risk of lifetime CFS/ME was significantly increased by female sex, high socioeconomic status in childhood, and having a longstanding medical condition in childhood that considerably affected home or school life, or both. A parent's report of a child playing sport in his or her spare time significantly decreased the risk of later CFS/ME.

Table 2 shows the association of behavioural and psychological factors in childhood and adulthood with lifetime risk of CFS/ME. There were no significant associations between maternal or child psychological factors and risk of disease. A high score on the malaise inventory at 30 years was strongly associated with increased risk of CFS/ME.

We then included factors significantly associated with lifetime risk of CFS/ME at the previous stage in a multivariable model (table 3). A limiting longstanding medical condition in childhood, female sex, and high social class in childhood were independently associated with a higher risk of CFS/ME, while higher levels of exercise in childhood were independently associated with lower risk. High malaise scores in adulthood were also significantly associated with higher risk. When we added to this model the childhood factors that were not individually associated with risk of CFS/ME, effect sizes or significance were not substantially altered (except for high score on general health questionnaire at 16 years, which attenuated the significance but did not alter the effect size of limiting medical condition in childhood, probably because of the low number for adolescent general health questionnaire score). When we repeated these analyses using CFS/ME within the previous 12 months as the outcome variable the result was not materially different to that for lifetime CFS/ME (data not shown).

Discussion

In this large longitudinal population based study, we found no association between childhood or adolescent behavioural or psychological problems or maternal psychological morbidity and the risk of self reported CFS/ME by the age of 30 years. Children at higher risk for CFS/ME had higher socioeconomic backgrounds, played sport rarely, and had limiting physical or mental longstanding conditions other than CFS/ME.

Strengths and limitations

We used data from a large national birth cohort assessed in early and mid-childhood, adolescence, and adulthood. The participants became adults at a time when CFS/ME was increasingly recognised. The lifetime prevalence of CFS/ME in this cohort was 0.8%. In all participants with CFS/ME onset of illness was

Table 1 Biological, demographic, and social factors and unadjusted and adjusted odds ratios (95% confidence intervals) for lifetime risk of CFS/ME. Figures are percentages of participants, unless stated otherwise

Factors	No of participants	Ever had CFS/ME	Never had CFS/ME	Unadjusted OR	Adjusted OR†
Father in professional/managerial occupation	9 508	49***	31	2.2 (1.4 to 3.5)***	—
Mother achieved A levels or equivalent/degree/diploma	10 002	20	17	1.3 (0.7 to 2.1)	—
Female sex	10 405	71***	51	2.3 (1.4 to 2.6)****	—
"Non-white" ethnicity	11 266	4	4	1.2 (0.4 to 3.3)	1.5 (0.5 to 4.9)
Mean birth weight (g)	10 394	3330	3310	1.1 (0.7 to 1.6)	1.3 (0.8 to 2.1)
Birth order (2nd or higher child)	10 358	62	59	1.0 (0.8 to 1.3)	1.0 (0.7 to 1.3)
Presence of longstanding medical condition significantly affecting home or school life at 10 years	9 624	27**	14	2.1 (1.3 to 3.4)**	2.3 (1.4 to 3.9)**
History of atopy by 10 years	9 170	24	22	1.2 (0.8 to 1.6)	1.2 (0.8 to 1.6)
Obesity at 10 years (BMI >95th centile)	8 771	3	5	0.5 (0.1 to 2.2)	0.6 (0.2 to 2.4)
Sport played in spare time at 10 years:	9 692				
Never or hardly ever (reference category)		16	8	1‡	1‡
Sometimes		42	39	0.5 (0.3 to 1.0)	0.5 (0.3 to 1.0)
Often		42**	54	0.4 (0.2 to 0.7)	0.5 (0.2 to 0.9)
Played >2 hours/week of sport at school at 10 years	8 925	52	44	1.4 (0.9 to 2.2)	1.3 (0.8 to 2.1)
Days of school missed due to health or emotional reasons in past year at 10 years:	9 730				
<7 (reference category)		54	62	1	1
7-30		39	34	1.3 (0.8 to 2.1)	1.3 (0.8 to 2.1)
>30		8	5	1.8 (0.8 to 4.2)	2.0 (0.9 to 4.7)
High score on British ability scales (mean T score ≥60) at 10 years	8 315	6	7	0.8 (0.3 to 2.2)	0.8 (0.3 to 2.2)
Significant illness (physical or mental) in either parent before 10 years	7 982	24	24	1.2 (0.7 to 2.0)	1.3 (0.8 to 2.2)

Significance shown for difference between groups and for odds ratios: *P<0.05, **P<0.01, ***P<0.001, ****P<0.0001.
†Adjusted for sex, father's social class in childhood, and mother's education.
‡P for trend 0.04.

Table 2 Behavioural problems and malaise inventory scores and unadjusted and adjusted odds ratios (95% confidence intervals) for lifetime risk of CFS/ME. Figures are percentages of participants

	No of participants	Ever had CFS/ME	Never had CFS/ME	Unadjusted OR	Adjusted OR†
Factors at 5 years					
Child behaviour problems: Rutter score (>1 SD above mean, maternal report)	9 149	9	13	0.7 (0.3 to 1.5)	0.8 (0.3 to 1.8)
High score on maternal malaise inventory (≥7)	9 203	25	23	1.1 (0.7 to 1.9)	1.3 (0.8 to 2.4)
Factors at 10 years					
Low child self esteem (>1SD below mean)	8 425	13	15	0.8 (0.4 to 1.7)	0.8 (0.4 to 1.8)
Child behaviour problems:					
High score on Rutter scale (>1 SD above mean, maternal report)	9 222	15	16	1.0 (0.5 to 1.8)	0.8 (0.4 to 1.6)
High score on conduct/impulsive/hyperactive scale (>1 SD above mean, teacher report)	8 626	11	14	0.8 (0.4 to 1.7)	0.9 (0.4 to 2.2)
High score on maternal malaise inventory (≥1 SD above mean)	9 081	15	15	1.0 (0.5 to 2.0)	1.0 (0.5 to 1.9)
Factors at 16 years					
High score on adolescent GHQ (≥4)	3 967	26	21	1.3 (0.6 to 3.0)	1.0 (0.4 to 2.4)
High score on maternal malaise inventory (≥7)	6 132	13	10	1.3 (0.6 to 3.1)	1.5 (0.6 to 3.8)
Factors at 30 years					
High score on malaise inventory (≥7)	11 261	41	16****	3.6 (2.3 to 5.4)****	2.9 (1.8 to 4.6)****
Professional/managerial occupation	10 980	39	37	1.1 (0.7 to 1.7)	0.8 (0.5 to 1.3)

Significance shown for difference between groups and for odds ratios: *P<0.05, **P<0.01, ***P<0.001, ****P<0.0001.
†Adjusted for sex, father's social class in childhood, and mother's education.

Table 3 Multivariate model of factors predicting lifetime risk of CFS/ME (n=8512)

Factor	OR (95% CI)	P value
Presence of longstanding medical condition significantly affecting home or school life at 10 years	2.2 (1.3 to 3.8)	0.003
Sport played in spare time at 10 years:		
Never or hardly ever (reference category):	1	P=0.04 for trend
Sometimes	0.5 (0.3 to 1.0)	
Often	0.5 (0.2 to 0.9)	
Female sex	2.4 (1.4 to 4.3)	0.003
Father in professional/managerial occupation in childhood	2.5 (1.4 to 4.3)	0.001
Mother achieved A levels or equivalent/degree/diploma*	1.1 (0.6 to 2.1)	0.6
High scorer on malaise inventory at 30 years	2.6 (1.6 to 4.3)	<0.0001
Professional/managerial occupation at 30 years*	0.8 (0.5 to 1.5)	0.6

*Mother's education status and socioeconomic status at 30 years were included a priori in model.

after the survey at 10 years, and only two participants reported age of onset before the 16 year survey. When examining potential risk factors for self reported lifetime CFS/ME, we were able to control for current socioeconomic status and psychological morbidity, the best documented associations of CFS/ME in adult life.[2 21] Maternal psychological morbidity was assessed with a validated instrument at three periods during participants' childhood and adolescence. The final multivariable model was robust to the inclusion of other childhood variables.

Our estimated prevalence for current and lifetime CFS is comparable with that in other epidemiological studies. The main weakness of this study, however, is the reliance on self reported CFS/ME. The diagnosis of CFS requires certain physical and mental disorders to be absent,[1] and a proportion of the CFS/ME group might not have met diagnostic criteria. Our case group probably included those with illness diagnosed by a physician as well as those with self diagnosed illness. Similarly, participants who did not report the diagnosis may have been misclassified. The epidemiology of self reported fatigue states may differ from that of states defined with operational diagnostic criteria.[1 13] Our finding that individuals with CFS/ME are more likely to come from high socioeconomic backgrounds is at odds with results of epidemiological studies that have found operationally defined CFS in adults to be more common in lower socioeconomic groups.[22] This may truly reflect increased risk with high social class in childhood, but may also reflect the self reported nature of our sample, as CFS clinical samples show bias towards higher social groups.

Loss to follow up of those from disadvantaged groups is a common limitation of birth cohort studies, and cohort members born to single mothers or teenage mothers or with fathers in manual occupations were under-represented in early follow up surveys. Efforts were made to improve follow up of such groups in the 30 year survey, and 62% of participants in the 30 year survey were born into a manual social class compared with 64% of the birth cohort. We believe that it is unlikely that this small difference significantly influenced our finding that high childhood social class increased the risk of CFS/ME.

Comparison with other studies

Retrospective studies have proposed maternal overprotectiveness and depression[12] as possible aetiological factors for later disease. In contrast, we found no association with maternal psychological morbidity measured in early and mid-childhood and adolescence using a commonly used screening instrument for depression. We also found no association between risk of illness and maternal scores at 5 and 10 years on the eight item somatic subscale of the malaise inventory[18] (data not shown), suggesting that maternal somatisation is not linked with later illness. Our findings, however, confirm previous work showing that current psychological morbidity is associated with higher prevalence of CFS/ME in adult life.[2 3 21]

Case-control studies have suggested that people have an excess of physical symptoms and diagnoses before the onset of CFS/ME.[9 10] We found that longstanding physical or mental illness in childhood was more common in those with later CFS/ME, with illness that significantly affected the child's daily life increasing the risk of CFS/ME more than twofold. These reports of illness preceded the onset of CFS/ME by more than four years, excluding confounding by prodromal fatigue states. This finding contrasts with that from a retrospective case-control study that suggested that there were no differences in childhood experience of illness in adults with CFS and healthy controls.[12] Possible mechanisms for this association may include both biological and psychological vulnerabilities associated with chronic illness. The lack of association of school absence with lifetime CFS/ME suggests that the effect of chronic illness is not mediated through longterm school absence. Contrary to previous suggestions that high academic achievement may predispose to illness,[5] we found no association between intellectual ability in childhood and later CFS/ME.

We found no evidence to support the suggestions that chronic illness, whether physical or mental, in either parent is common among adolescents with CFS/ME.[23]

MacDonald et al suggested that higher levels of routine exercise may precipitate or exacerbate CFS/ME.[7] We found that children who routinely played more sport in their spare time had a significantly lower risk of CFS/ME, a finding that was independent of potential confounding by limiting chronic illness or obesity and was also robust to adjustment for sex and socioeconomic status. Children who were sedentary at 10 years had about twice the risk of lifetime CFS/ME. Hours of sport played at school was not associated with risk of CFS/ME, which suggests that the protective effect of exercise lies within the individual and family rather than in timetabled school activities.

Conclusions

Our findings do not support a role for previously suggested risk factors for CFS, including maternal psychopathology, parental illness, childhood or adolescent psychological distress, academic ability, atopy, birth order, birth weight, and obesity in the aetiology of lifetime self reported and physician diagnosed CFS/ME. Contrary to previous suggestions that high levels of exercise increase risk, we found that the most sedentary children were at greatest risk, adding further weight to current public health efforts to promote healthy exercise and reduce sedentary behaviour among children. Further longitudinal studies are needed to assess whether these findings apply to operationally defined fatigue syndromes.

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What is already known on this topic

Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) in adults is associated with higher rates of psychological disturbance

Atopy, higher levels of physical exercise, parental depression and illness, and child psychopathology have been suggested as risk factors

What this study adds

Maternal psychopathology, parental illness, childhood or adolescent psychological distress, academic ability, atopy, birthorder, birth weight, and obesity are not associated with the risk of lifetime self reported and physician diagnosed CFS/ME

Sedentary children are at greater risk of later CFS/ME

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Department of Paediatrics, Royal Free and University College Medical School, Middlesex Hospital, London W1T 3AA
Russell Viner *honorary senior lecturer in adolescent medicine*

Department of Psychological Medicine, Institute of Psychiatry, London SE5 8AF
Matthew Hotopf *professor of general hospital psychiatry*

Correspondence to: R Viner R.Viner@ich.ucl.ac.uk