Childhood Risk Factors for Adults With Medically Unexplained Symptoms: Results From a National Birth Cohort Study

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Objective: The purpose of this study was to test the hypothesis that the prior experience of physical illness in childhood is associated with later experience of medically unexplained symptoms. **Method:** A nested case-control study was performed within a prospective birth cohort study: the Medical Research Council National Survey of Health and Development. The 5% most symptomatic individuals at age 36 years were identified and screened for physical illness. Subjects without defined physical diagnoses (N=191) were compared with the remainder of the sample (N=3,107) for childhood exposures. **Results:** There was a powerful relationship between poor reported health of the parents when subjects were aged 15 years and symptoms at age 36; the relationship was independent of current psychiatric disorder. Medically unexplained symptoms were associated with abdominal pain in childhood but not with defined childhood diseases. **Conclusions:** Medically unexplained symptoms appear to be related to prior experience of illness in the family and previous unexplained symptoms in the individual. This may reflect a learned process whereby illness experience leads to symptom monitoring.

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Medically unexplained physical symptoms account for up to 50% of new medical outpatient visits (1) and are associated with considerable disability (2–4) and psychiatric disorder (5–8). It has been suggested that prior experience of illness in childhood may predispose an individual to later medically unexplained symptoms. Craig et al. (9) categorized patients who attended primary care facilities into one group that presented with physical disease and the following two groups with psychiatric disorder: patients who presented with psychological symptoms and patients who presented with physical symptoms. Patients were asked about previous experiences of illness and parenting. Psychiatric disorder was associated with reports of adverse parenting regardless of how it presented. However, patients who presented with physical symptoms reported higher than average rates of physical illness in themselves or their parents before the patients reached age 17; prior experience of illness appeared to be a specific risk factor for presentations with physical symptoms.

Previous studies have been retrospective, leading to potential recall bias. We present a prospective cohort study that followed subjects from birth to 36 years. The main hypotheses we tested were that 1) individuals with medically unexplained symptoms would tend to come from families with high rates of physical illness during the individual's childhood, and 2) subjects who suffered from unexplained symptoms would be more likely to have suffered from defined physical illnesses in childhood.

METHOD

The Medical Research Council National Survey of Health and Development is a national birth cohort established in 1946. The sur-

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vey was based on a sample, stratified by socioeconomic class, of all single, legitimate births that occurred in England, Wales, and Scotland in 1 week of March 1946. The sampling procedure and follow-up have been described elsewhere (10). The final sample consisted of 5,362 individuals. Nineteen waves of data collection have been performed, with interviews of parents and teachers during the study subjects' childhood and of the subjects themselves in adulthood. If any hospitalizations were reported, the hospital was contacted and asked to provide details of the admission. The mothers of survey members were asked if they would allow their child to take part in the study. The initial data collection was carried out in the 1940s and 1950s, before the development of modern notions of informed consent and ethical committee approval for epidemiological studies. Written informed consent was obtained for later waves of data gathering when subjects were ages 36 and 43.

Outcome

When subjects were age 36, research nurses administered a structured interview. For the purposes of this study, six health complaints--rheumatism and arthritis, backache and sciatica, dizziness, headache, abdominal pain and acid indigestion, and chest pain--were used. All symptoms but chest pain were assessed according to the survey members' reports from a structured checklist of symptoms administered by the research nurse. Chest pain was assessed on an angina questionnaire (11). The prevalence of individual symptoms has been reported elsewhere (8). Approximately 5% of the sample endorsed three or more symptoms, and this was chosen as the cutoff. This cutoff broadly approximates to the notion of "abridged somatization" (1). This subsyndromal diagnosis is associated with significant disability and probably represents a clinically relevant level of symptoms.

The survey's records for subjects who scored more than 3 on the symptom checklist were scrutinized. The aim was to reclassify those who were symptomatic but whose symptoms could be explained by defined organic pathology. Records of interviews when subjects were ages 36 and 43 were summarized. Any hospital admissions in the decade before 1982, or any details of physical disorders that could be associated with the symptoms reported in 1982, were recorded. A consensus meeting was held at which the summaries of illness experience were discussed by three investigators experienced in liaison psychiatry (M.H., R.M., and S.W.). The aim was to exclude those survey members with organic pathology that the investigators felt was pertinent to symptoms at 36 years.

In order to examine the potential effect of bias caused by this process, subsidiary analyses used three alternative outcomes. First, an inclusive outcome was generated, which simply consisted of all subjects who had three or more symptoms. Second, an exclusive outcome was generated, for which any subject with evidence of new physical disease at age 43 was excluded. Finally, total symptoms were analyzed as an ordered categorical variable. Results of these analyses are not reported unless they differed from the findings for the main study.

Parental Health During Childhood

When the subjects were age 15, their mothers were asked about their general health and about any serious illness in the fathers that led to more than 3 months of sick leave. They were also asked whether they suffered from any of the following health complaints: asthma, eczema, or hay fever; chronic cough; rheumatism; anemia; heart trouble; kidney trouble; or "other." For the purposes of the analyses reported here, these were dealt with as the total number of complaints (range=0–7). Mothers also reported whether they or the fathers suffered from "nerves." At each wave of data gathering, parental death was recorded.

Childhood Illness

All hospitalizations during childhood were recorded, and the relevant hospital was contacted for details of the admission. It was therefore possible to generate a variable for physical diseases that occurred between birth and age 15 years and led to at least 3 weeks of hospitalization. Subjects with conditions such as mental handicap, psychiatric disorder, and ill-defined conditions were excluded from this group. During the subjects' childhood, their mothers were asked about the presence of abdominal pain on three occasions (when the subjects were ages 7, 11, and 15). Persistent abdominal pain was defined as pain present at all three times. This variable was used in a previous article on the cohort (12).

Potential confounding variables included gender, father's socioeconomic class, highest educational level attained, and marital status at age 36 years. At age 36 the survey members were administered the Present State Examination (PSE) (13), a semistructured psychiatric interview. From the PSE a validated, ordered categorical variable, the "index of definition," can be calculated that corresponds to different levels of psychiatric disorder. For the main analyses reported here, the total PSE score was used.

Statistical Analyses

All analyses were performed by using STATA (14). The study used a nested case-control design: subjects with symptoms were compared with the remainder of the sample interviewed at age 36. After univariate analyses assessing the strength of relationships between risk factors and outcome, logistic regression analysis, weighted for sampling fractions, was performed. Two models were used. Model 1 controlled for the potential confounding variables described earlier, except for PSE score. Model 2 added the subjects' total PSE score at age 36. Hence, any relationships reported in the second model were independent of current psychopathology. For ordered categorical data, we used likelihood ratio tests for trend. When analyses were performed with total symptom count (range=0–6) as the main outcome, ordinal regression analysis (15) was used to control for the same confounding variables.

RESULTS

In 1982, 3,322 (62%) of the 5,362 original survey members were interviewed. When those survey members who had died or emigrated were excluded from the denominator, the proportion of responders rose to 83%. The representativeness of the original sample has been described elsewhere (10). Survey members who had suffered a physical illness in childhood were less likely to be interviewed at age 36 years (χ^2=53.6, df=1, p<0.001); this was accounted for by their higher death rates. No other associations were detected between independent variables and follow-up status.

Table 1 demonstrates the relationship among multiple physical symptoms, sociodemographic variables, and psychiatric disorder. Physical symptoms were slightly more common in women, but this difference was not significant. Physical symptoms were more common in individuals with lower educational level and those who were widowed, divorced, or separated. There was a strong relationship between the outcome and psychiatric disorder.

Table 2 shows the relationship between parental ill health when the study subjects were age 15 years and multiple physical symptoms at age 36. There were strong relationships between the outcome and parental ill health. These were present after control for the main sociodemographic variables (model 1) and when psychiatric disorder was controlled (model 2). Death of a parent before the age of 15 was not associated with physical symptoms at age 36 (death of father: odds ratio=0.8; 95% CI=0.3–2.0; death of mother: odds ra-

TABLE 1. Relation of Multiple Physical Symptoms to Sociodemographic Characteristics and Psychiatric Disorders in a National Birth Cohort Study (N=3,298)

Variable	N[a]	Percent With Multiple Physical Symptoms	Crude Odds Ratio		Model 1 (controls for sociodemographic factors)	
			Odds Ratio	95% CI[b]	Odds Ratio	95% CI
Gender						
Male	1,643	5.1				
Female	1,655	6.5	1.2	0.9–1.7	0.8	0.6–1.2
Father's socioeconomic class[c]						
Professional	178	6.2				
Managerial	600	5.5	1.2	0.5–2.4	1.0	0.5–2.3
Skilled nonmanual	399	4.0	0.6	0.3–1.4	0.4	0.2–1.0
Skilled manual	832	5.5	0.9	0.4–1.8	0.6	0.3–1.3
Semiskilled manual	493	4.7	0.9	0.4–2.0	0.6	0.3–1.5
Unskilled manual	149	9.4	1.7	0.7–4.1	1.2	0.4–3.1
Other	647	7.4	1.7	0.8–3.4	1.2	0.5–2.6
Educational status[d]						
No qualifications	1,191	7.0				
Below O level	246	7.3	1.2	0.6–2.2	1.1	0.6–2.0
O level	627	5.7	0.8	0.5–1.3	0.9	0.6–1.6
A level	778	4.5	0.6	0.4–1.0	0.7	0.4–1.1
Degree or higher	296	3.7	0.6	0.3–1.4	0.5	0.2–1.3
Unknown	118	5.1	0.7	0.2–1.9	0.7	0.2–2.1
Marital status						
Married/cohabiting	2,886	5.7				
Never married	242	3.7	0.6	0.3–1.5	0.7	0.3–1.6
Previously married	17	10.0	2.0	1.1–3.6	1.4	0.7–2.7
Index of definition on PSE						
1	1,540	2.7				
2	1,012	5.4	1.9	1.1–3.0	1.9	1.7–3.1
3	298	9.4	4.0	2.2–7.1	4.1	2.3–7.4
4	219	9.6	4.2	2.2–7.8	4.5	2.3–8.6
5+	201	21.4	8.4	4.9–14.5	7.8	4.5–14.2

[a] There were missing data for some variables.
[b] Confidence interval. Adjusted for sampling fraction only.
[c] When subject was age 15 years.
[d] O level=examinations usually taken at age 16 and required before A level. A level=examinations usually taken at age 18 and required for entry to a university.

tio=1.1; 95% CI=0.4–3.1). In order to understand better the nature of physical illness associated with the outcome, we determined whether there was any effect modification between poor health of the parents when the study subjects were age 15 and the parents' death in the next 10 years. For fathers (but not mothers), there was a significant interaction term (χ^2=5.7, df=1, p=0.02). Below average perceived health in the fathers was associated with the outcome if they lived for the next 10 years (odds ratio=2.2; 95% CI=1.0–4.7) but not if they died during that period (odds ratio=0.6, 95% CI=0.1–3.0).

Reports of the fathers having suffered from "nerves" were associated with the outcome (odds ratio=2.3; 95% CI=1.1–5.2), but no relationship was detected for the mothers' self-reports of nerves (odds ratio=1.4; 95% CI=0.8–2.5). Childhood physical diseases were not associated with later symptoms (table 2). Persistent abdominal pain was associated with symptoms.

Using the alternative procedures to define outcomes (inclusive, exclusive, and total symptoms) led to only two differences in the main finding: fathers' self-reports of nerves were not associated with any of the other outcomes. Abdominal pain in the child was not associated with the outcome when expressed as total symptoms. Parental ill health was strongly associated with all outcomes.

DISCUSSION

The large, population-based sample and the prospective design of this study have allowed us to go further than previous retrospective research in establishing associations between childhood risk factors and unexplained symptoms in adulthood. The outcome we used was somewhat arbitrary, being based on a cutoff of a number of physical symptoms. Unfortunately, the total number of physical symptoms used in the survey was small. If a longer checklist had been included, the top 5% of subjects who were most symptomatic would have been more precisely defined. This limitation is likely to lead to random misclassification and effectively to reduce observed associations (16). Our definition depended on post hoc judgments about whether subjects' symptoms were explained or unexplained. We may have missed individuals with defined physical causes of their symptoms. However, the sample was young and community based; and very few symptomatic individuals progressed to more severe illnesses at

TABLE 2. Relation of Multiple Physical Symptoms at Age 36 to Parents' and Own Health in Childhood in a National Birth Cohort Study (N=3,298)

Variable	N[a]	Percent With Multiple Physical Symptoms	Model 1 (controls for sociodemographic variables)		Model 2 (controls for sociodemographic variables and total PSE score)		Analysis	
			Odds Ratio	95% CI	Odds Ratio	95% CI	χ^2 (df=1)	p
Father's health[b]							19.9	<0.0001
Excellent	790	3.5						
Good	1,215	4.4	1.2	0.7–2.1	1.3	0.7–2.3		
Average	566	8.0	2.6	1.5–4.7	2.7	1.5–4.8		
Not very good	136	8.8	2.9	1.3–6.8	2.6	1.1–6.5		
Poor	28	14.3	9.4	2.3–38.7	6.2	1.4–28.4		
Mother's health[b]							11.0	0.0009
Excellent	742	3.2						
Good	1,224	5.1	1.4	0.8–2.6	1.4	0.8–2.6		
Average	735	7.6	2.2	1.2–4.0	2.1	1.2–3.9		
Not very good	134	10.5	3.1	1.3–7.1	2.5	1.0–5.8		
Poor	3	—						
Number of ailments in father[b]							5.8	0.01
0	2,033	4.8						
1	582	6.9	1.6	1.0–2.5	1.4	0.9–2.2		
2	107	8.4	2.3	1.0–5.3	2.3	0.9–5.5		
3+	17	5.9	1.9	0.3–14.3	2.7	0.3–25.1		
Number of ailments in mother[b]							3.5	0.06
0	1,846	5.0						
1	739	5.4	1.2	0.8–1.9	1.2	0.7–1.9		
2	206	9.7	2.1	1.2–3.9	1.6	0.9–3.1		
3+	49	10.2	1.8	0.6–5.9	1.7	0.6–5.0		
Father took more than 3 months' sick leave[b]								
No	2,394	5.0						
Yes	387	7.2	1.9	1.1–3.1	1.7	1.0–2.9		
Physical disease in child[c]								
No	2,807	5.7						
Yes	491	6.5	1.2	0.7–1.8	1.0	0.6–1.6		
Persistent abdominal pain in child								
No	2,356	5.4						
Yes	52	13.5	3.2	1.2–8.3	2.6	1.0–6.9		

[a] There were missing data for some variables. [b] When subject was age 15 years. [c] From birth to age 15 years.

follow-up, suggesting that misclassification is unlikely to be a major problem.

Physical disease in childhood was not associated with medically unexplained symptoms in adulthood. This finding concurs with the generally good psychosocial outcome for physically ill children surviving to adulthood (17). In contrast, abdominal pain was associated with common psychiatric disorders in later life (12), as well as with medically unexplained symptoms. Previous research suggesting that adults with medically unexplained symptoms recall more sickness in childhood probably reflects the presence of medically unexplained symptoms (rather than defined physical illness) at this time.

The finding that parental ill health was associated with unexplained symptoms confirms previous research (9, 18), but the reasons for this finding are not clear. The exact nature of the ill health reported in parents was obscure, but there are some clues. Parental death was not associated with the outcome, nor was poor health of the father, when he subsequently died; this suggests that severe or fatal family illness is not associated with later unexplained symptoms. The association is therefore with parents who have suffered either non-life-threatening physical diseases or medically unexplained symptoms.

There is some evidence that physical symptoms have a heritable component (19). There is also evidence from retrospective studies that children in families in which one or both parents are ill respond to common symptoms differently than do children with healthy parents. This is true for illness behavior related to both physical illnesses such as diabetes mellitus (20) and minor physical symptoms (21). As a result, children whose parents have poor perceived health may respond differently to common physical symptoms. Further developmental and genetic work is required to disentangle the possible mechanisms by which unexplained symptoms are transmitted through families.

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