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Migraine: Intelligence, Social Class, and Familial Prevalence

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British Medical Journal, 1971, **2**, 77–81

Summary

Groups of individuals with headache, unilateral headache, and migraine, and a fourth group who had not had a headache in the previous year, were identified by questionnaire from a random sample of adults in the general population. Intelligence and social class were assessed in about 400 individuals. There was no evidence that individuals with migraine were more intelligent or of higher social class. There was, however, a suggestion that the more intelligent individuals with migraine, and those in social classese I and II, were more likely to consult a doctor for their headaches. This trend might explain the origin of the hypotheses associating migraine with intelligence and with social class.

Random samples of individuals with migraine with headache and without headache in the previous year were the probands for a family study. There were 524 first-degree relatives over 21 years of age who lived in South Wales. Headache histories, obtained "blindly" from over 99% of these relatives with a standard questionnaire, were classified as migraine, possible migraine, headache, or without headache in the previous year. The prevalence of migraine in the families of the migrainous probands was nearly twice as high as the prevalence in the other families, but this difference was not statistically significant. It is suggested that family history should not be included in the definition of migraine and that heredity is much less important in migraine than is usually supposed.

Introduction

The extensive literature on migraine mentions many characteristics of the sufferers. Often there is little evidence to support these hypotheses, and in part this is due to the difficulty of obtaining suitable controls for comparison with the migraine groups. It has long been thought that migraine is commoner among the more intelligent, and also in the higher social classes. These views are based on clinical impressions, but such associations can be satisfactorily tested only in representative community samples. The methods used should reduce the possibilities of bias to a minimum. This paper describes an epidemiological study designed to test these hypotheses.

Migraine has long been accepted as a familial condition, and this was stressed by Liveing (1873). Subsequent studies have strengthened this impression—for example, Balyeat and Rinkel (1931), Grimes (1931), Lennox (1941), Leyton (1954), Walker (1959), Selby and Lance (1960), and Childs and Sweetnam (1961). References to a familial tendency are often brief and the method used is uncertain. Some give the percentage of migrainous patients with a "positive family history." Others give detailed family trees, but these may be highly selected. Most published work confirms the tendency of migraine to run in families. Two methodological difficulties, however, may seriously affect this conclusion. One is the problem of defining migraine. Different authors give differing definitions—none completely satisfactory—and many give no definition at all. A definition is especially important as the other weakness of most studies is the possibility of bias. This may occur in the selection of patients with migraine or in the collection of data from their families.

Most published data come from selected series of patients. It is difficult to know how selected they are and hence whether they are typical of all migraine sufferers in the general population. Selection may be of considerable importance, as shown in a community study where only about half the women with clinically diagnosed migrane had consulted a doctor because of it (Waters and O'Connor, 1970). Details of the families of migraine patients are often obtained in a manner in which bias is almost inevitable. Thus patients may be asked "Does anyone else in your family have migraine headaches similar to yourself?" (Wolff, 1963). Frequently the patient's description of attacks of their relatives is regarded as sufficient and relatives are not questioned about their headaches. Probands with migraine are perhaps more likely to know of affected relatives than are controls. No doubt many are correctly described, but probands may sometimes imagine that relatives are affected when in fact they are not.

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After a community study the first-degree relatives of random samples of individuals with migraine, headache, and no headache in the preceding year were investigated. This approach is similar to the statistical genealogical proband method of Weinberg (1931). Efforts were made to reduce to a minimum the possible biases in the collection of information from their familites.

Methods

Selection of Individuals for Study.—Questionnaires on headache were completed by 94% of a random sample of adults drawn from the electoral roll of the Pontypridd area of Glamorgan. From the 1,718 completed self-administered questionnaires, random samples of individuals aged 21 to 74 years were identified with no headache in the previous year, with headache (and no migraine features), with unilateral headache, and with migraine. The migraine group consisted of those reporting a headache with (1) a unilateral distribution, (2) a preceding warning, and (3) accompanying nausea. In a separate study nearly 90% of this group with three features were diagnosed clinically by a neurologist as migraine (Waters and O'Connor, 1970). Individuals from all four groups were brought to a clinic and examined; details of ophthalmological tests and blood pressure have been reported (Waters, 1970a, 1971).

Assessment of Intelligence, Social Class, and Headaches in Relatives.— Intelligence was assessed with AH4 Group Test of General Intelligence (National Foundation for Educational Research). This test has been designed for use with a cross-section of the adult population and uses verbal, numerical, and diagrammatic "biases" (Heim, 1967). The scores given here are the sums of parts I and II. Social class was determined with the classification of occupations (General Register Office, 1966). The names and addresses of the first-degree relatives (parents, siblings, children) over 21 years of age were obtained from random samples of those in the migraine, headache, and no-headache groups. Relatives living anywhere in South Wales were visited and a short administered questionnaire on headaches occurring during the year immediately preceding the survey was completed. With each visit the family tree was checked but individuals were not told which member of their family was the proband. Each assessment was made by one observer throughout the study. All observers were unaware of individual headache histories at the time of the assessment.

Results

INTELLIGENCE AND SOCIAL CLASS

Overall, 168 (89%) of the men and 246 (84%) of the women randomly selected for these tests came to the clinic. Details of response rates by age and headache group have been given (Waters, 1970a). Five men and 10 women refused either to start or to complete the intelligence tests; there were six, one, four, and four individuals in the no-headache, headache, unilateral headache, and migraine groups respectively. The mean intelligence score declined with age, and this decline was similar to that expected in tests of this type (A. W. Heim, personal communication, 1970). The age distribution of the four headache groups differed significantly ($P<0.001$) in women, but not in men ($P>0.7$). The mean intelligence scores, and standard deviations, are therefore given for women in three age groups in Table I. There was no evidence that individuals with migraine had a higher mean intelligence, and analyses of variance showed no significant differences between the groups. The distribution of intelligence scores in the 163 men is shown in Fig. 1. A higher proportion of the more intelligent migraine sufferers had consulted a doctor about

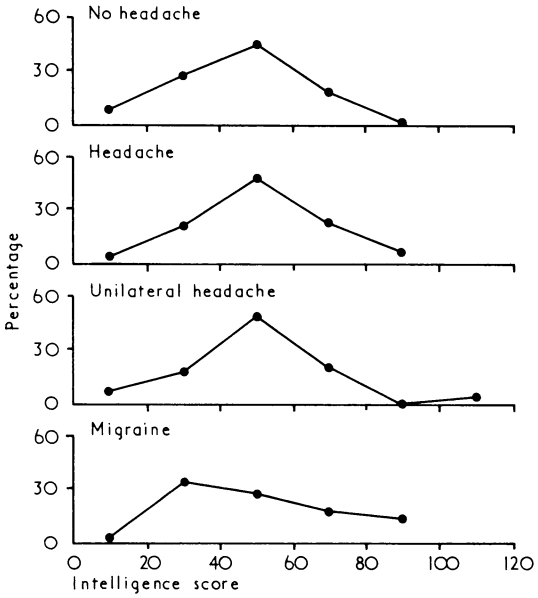

FIG. 1—Intelligence scores (AH4—National Foundation for Educational Research) in 163 men by headache group.

TABLE I—*Mean Intelligence Score (AH4), and Standard Deviation, By Headache Group*

	Men	Women		
	21–74 Years	21–34 Years	35–54 Years	55–74 Years
No headache (in previous year)	(48) 44·8±18·1	(5) 48·0±16·7	(22) 33·5±18·3	(24) 26·0±13·8
Headache	(53) 51·7±17·6	(22) 50·9±16·8	(29) 41·0±21·2	(12) 29·4±22·2
Unilateral headache	(28) 49·4±18·1	(14) 65·6±15·3	(23) 46·4±19·7	(13) 30·8±16·1
Migraine	(34) 50·4±23·5	(25) 54·1±19·5	(36) 41·3±20·6	(11) 20·7±12·9
Differences between groups	$P>0.2$	$P>0.5$	$P>0.2$	$P>0.2$

Numbers in subgroups are given in parentheses.

TABLE II—*Relationship between Intelligence Score (AH4) and Consulting a Doctor for Migraine*

	Intelligence Score (AH4)	No. Tested	Doctor Consulted	
			No.	%
Men	0—39	13	7	54
	40—59	10	7	70
	60—	11	8	73
Women	0—39	35	20	57
	40—59	23	15	65
	60—	14	10	71

TABLE III—*Headache and Social Class*

Sex	Headache Group	Social Class			
		I and II	III	IV and V	Total
Men	No headache (in previous year)	5 (10)	25 (51)	19 (39)	49 (100)
	Headache	9 (17)	29 (55)	15 (28)	53 (100)
	Unilateral headache	3 (10)	16 (52)	12 (39)	31 (100)
	Migraine	4 (11)	21 (60)	10 (29)	35 (100)
Women	No headache (in previous year)	9 (16)	27 (49)	19 (35)	55 (100)
	Headache	11 (18)	28 (45)	23 (37)	62 (100)
	Unilateral headache	5 (10)	28 (55)	18 (35)	51 (100)
	Migraine	12 (16)	42 (57)	20 (27)	74 (100)

Figures in parentheses are percentages.

TABLE IV—*Relationship between Social Class and Consulting a Doctor for Migraine*

	Social Class	No. Examined	Doctor Consulted	
			No.	%
Men	I and II	4	4	100
	III	21	12	57
	IV and V	10	7	70
Women	I and II	12	9	75
	III	42	27	64
	IV and V	20	12	60

TABLE V—*Number of First-degree Relatives over 21 Years of Age Living in South Wales and outside South Wales*

Probands		Siblings		Parents		Children		Total		
Group	No.	In Area	Out of Area	In Area	Out of Area	In Area	Out of Area	In Area	Out of Area	% Out of Area
No headache ..	40	93	30	21	0	30	6	144	36	25·0
Headache	40	68	30	31	2	15	3	114	35	30·7
Migraine	75	147	59	72	5	47	10	266	74	27·8
Total ..	155	308	119	124	7	92	19	524	145	27·7

their headaches (Table II), though these differences were not significant statistically.

The distribution of individuals by headache group and social class (Table III and Fig. 2) shows no evidence of a higher proportion of individuals with migraine in social classes I and II. Though the number of these social classes was small there was a tendency, not statistically significant, for a higher proportion of migraine sufferers in social classes I and II to consult a doctor for their headaches (Table IV).

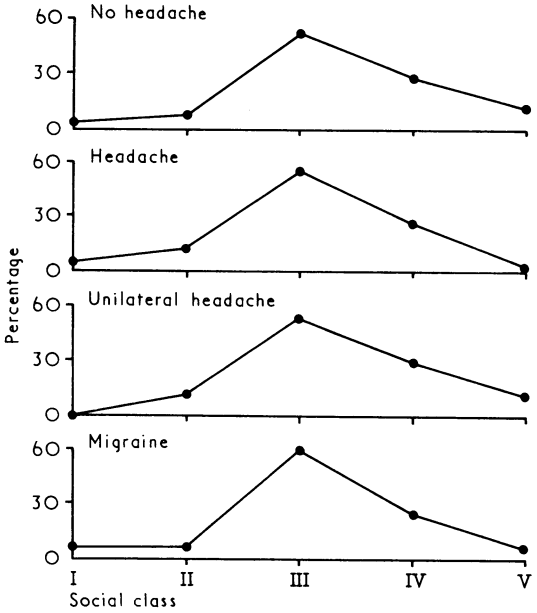

FIG. 2—Social class and headache group in 168 men.

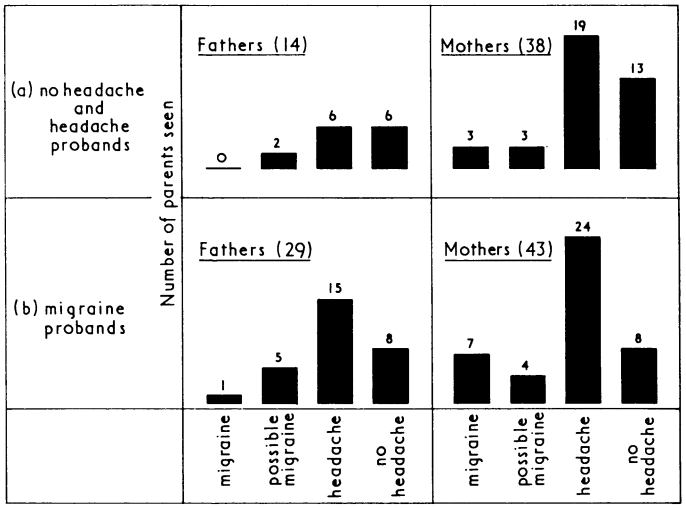

FIG. 3—Headache status of parents of (a) 80 probands (40 men and 40 women) without headache or with headache only and (b) 75 probands (35 men and 40 women) with migraine. (For definitions see text.)

FAMILY STUDY

The 155 probands had 669 first-degree relatives who were over the age of 21 years. Of these, 524 were living in South Wales (Table V). There is no significant difference ($0{\cdot}7 < P < 0{\cdot}8$) in the number of the first-degree relatives of the three groups of probands who left South Wales. The mean ages, with standard deviations, are given in the several subgroups in Table VI. Community studies have shown that the prevalence of headache is significantly related to age and sex (Waters, 1970b). The age and sex distributions of the first-degree relatives of the three groups of probands, however, were not thought to be sufficiently different to introduce any important biases in headache prevalence.

Administered questionnaires were completed for 519 first-degree relatives (over 99% of those living in South Wales). From these questionnaires each individual was classified as migraine (three features), possible migraine (one or two features), headache (none of the three features), or placed in the no-headache group (for a validation of this classification see Waters and O'Connor, 1970). Data for the probands' siblings are given in Table VII and for their parents in Fig. 3. Data for the children show similar differences between groups. Taken together, the families of probands without headache also had a higher proportion of first-degree relatives without headache, but this difference was not significant ($0{\cdot}2 < P < 0{\cdot}3$).

TABLE VI—*Number and Mean Age (with Standard Deviation) of Probands and First-degree Relatives (Over 21 Years of Age Living in South Wales)*

		Probands		Brothers		Sisters		Fathers		Mothers		Sons		Daughters	
Group		No.	Mean Age (±S.D.)	No.	Mean Age (± S.D.)	No.	Mean Age (± S.D.)	No.	Mean Age (± S.D.)	No.	Mean Age (± S.D.)	No.	Mean Age (± S.D.)	No.	Mean Age (± S.D.)
Men	No headache	20	49 (16)	22	54 (13)	18	49 (18)	2	56 (4)	8	68 (11)	7	33 (6)	9	33 (13)
	Headache	20	43 (15)	15	41 (8)	21	41 (13)	4	60 (7)	9	62 (8)	3	23 (2)	3	24 (2)
	Migraine	35	43 (7)	38	41 (17)	25	43 (13)	15	68 (9)	21	64 (8)	20	29 (7)	9	29 (8)
Women	No headache	20	49 (15)	24	48 (13)	29	54 (15)	3	60 (3)	8	68 (10)	7	30 (9)	7	30 (10)
	Headache	20	46 (13)	19	44 (9)	13	54 (18)	5	62 (10)	13	66 (11)	3	33 (8)	6	28 (5)
	Migraine	40	43 (12)	40	45 (13)	44	44 (14)	14	65 (7)	22	64 (7)	8	34 (7)	10	27 (5)

The families of the probands with migraine did have a higher proportion of individuals with migraine. The prevalence of migraine, defined here as headaches with all three features, was 5% and 6% in the families of the headache and no-headache probands but 10% in the families of the probands with migraine. These differences are not statistically significant ($0{\cdot}1<P<0{\cdot}2$).

TABLE VII—*"Headache" Status of Siblings (Over 21 Years of Age)*

Probands		Siblings (over 21 Years)				
Group	No.	No Headache	Headache	Possible Migraine	Migraine	Total
No headache	40	28 (30)	39 (42)	20 (22)	6 (7)	93 (100)
Headache ..	40	15 (22)	42 (62)	8 (12)	3 (4)	68 (100)
Migraine ..	75	41 (28)	62 (42)	29 (20)	15 (10)	147 (100)

Percentages are given in parentheses.

Discussion

INTELLIGENCE AND SOCIAL CLASS

Lennox (1941) thought migraine affected "brain-using more than muscle-using persons." This view is often stated, sometimes in the more specific form that patients with migraine are more intelligent (Selinsky, 1939; Callaghan, 1968; Simpson, 1968). Aring (1962) even said that the patient with migraine "is almost invariably intelligent." Blau (1969), however, pointed out that migrainous subjects are not necessarily intelligent. The time taken off work may depend on the person's job, with the intellectual more often compelled to stop work during migraine than the manual worker (Childs and Sweetnam, 1961). If this is so, migraine would appear to be commoner in those of higher intelligence. In the study reported here a representative group of individuals with migraine have had their intelligence assessed and then compared with that of unselected individuals without migraine living in the same area. This investigation gives no evidence to support the hypothesis that individuals with migraine are on average more intelligent. In fact the distributions of intelligence scores were similar in all groups. The difficulty in defining migraine has been mentioned, but the method of this study was such that biases are unlikely to have affected the conclusions.

Fothergill (1784) found "sick headache" mostly in the "middle and upper ranks of life." Migraine is said to be commoner in the professional classes (Lennox, 1941), but, again, there seems to be no hard evidence for this statement and the data from the present study do not support the hypothesis. Another epidemiological study found that Swedish schoolchildren with migraine show no demonstrable differences in social class when compared with other children of ages between 7 and 13 years (Bille, 1962).

Though the present study does not suggest that migraine sufferers show any important differences in intelligence or social class, it does show a tendency for more of the intelligent individuals with migraine and those in social classes I and II to consult a doctor because of their headaches. Thus it seems possible that the clinical impression that migraine patients attending doctors are more intelligent, and more likely to belong to the higher social classes, may be correct. It is the inference from this, that migraine has a predilection for such groups, that lacks evidence. Migraine patients consulting their doctors are a selected group and may well not be typical of all migraine sufferers in the community. These results show how important it is when studying conditions such as migraine, in which not all cases are known to the medical profession, to base such research on representative samples and hence avoid possible biases in selection.

If patients with migraine attending their general practitioners are selected it is reasonable to assume that sufferers attending neurological or migraine clinics may show greater differences from unselected individuals with migraine. The realization that migraine patients who consult a doctor might differ from other individuals with migraine may not be new. Liveing (1873) wrote: "Another class of cases for which we are often consulted, and which are met with for the most part in a somewhat higher social grade than the last, are those where a similar development . . . [is] brought about by excessive brain work." Liveing did not actually say migraine was commoner in the higher social classes or brain workers but simply that such groups often attended a doctor for migraine. This statement is supported by the present study.

FAMILIAL PREVALENCE OF HEADACHES

The data from the first-degree relatives of probands with migraine, headache, and without headache in the previous year suggest that the prevalence of migraine was highest in the relatives of migraine sufferers. The differences between the prevalence of migraine in the families of these three groups, however, were not as large as might be expected from other reports in the literature. In fact, in this study they do not reach the usually accepted levels of statistical significance. Migraine is invariably stated to be a familial disorder, but there are differences of opinion about the mechanism of inheritance. Wolff (1963) suggested a recessive gene, while Barolin (1970) preferred a dominant inheritance; Dalsgaard-Nielsen (1965) believed in a polygenic type of inheritance, but Pratt (1967) thought there was no satisfactory simple model. Most studies, however, have contained possible biases, and these may overestimate the familial nature of migraine. In this study every effort was made to keep biases to a minimum.

In view of the similarity of the prevalences in the families of the three groups of probands, the sensitivity of the questionnaire should be considered. In the migraine group (those with the three features—unilateral distribution of headache, warning, accompanying nausea) a separate clinical validation has shown that nearly 90% would be diagnosed by a neurologist as migraine (Waters and O'Connor, 1970). The possible migraine group (with only one or two features) presents more difficulties because only 12 to 60%, depending on the combinations of features, would be diagnosed clinically as migraine, and it is impossible, so far, to identify from the questionnaire which individuals would be so diagnosed. In this study the proportion with possible migraine is not highest in the families of migraine sufferers, and this possible migraine group seems unlikely to have led to important biases between the families of the three groups of probands.

One feature that is sometimes included in the definition of the migraine is that other members of the family have similar headaches. Wolff (1963) considered migraine and the headache of hypertension as the only headaches with a familial tendency. The data given here do not suggest that a history of similar headaches in other members of the family is likely to be of much help clinically in diagnosing migraine. But the inclusion of a family history of similar headaches in the definition should be criticized on other grounds. Migraine is a condition in which the diagnosis of borderline cases is often difficult. Such a definition may accept some cases, because of their family history, and reject similar cases because of its absence. This can be carried to extremes and migraine can be "shown" to be an inherited family trait and that "there is no acquired migraine" (Grimes, 1931). Authors have even fallen into the trap of including a "positive family history" as part of their definition of migraine and then gone on to show that a high proportion of their series of patients had relatives with similar headaches.

Even if migraine is more prevalent in certain families, and further evidence from unbiased populations is needed on this

point, it does not necessarily follow that this is genetically determined. Members of a family tend to share the same environment, and any characteristic occurring in certain families may therefore be the result of acquired rather than congenital disease. Whatever the cause of migraine this community-based family survey suggests that heredity is less important than is usually supposed.

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Further Observations on the Relation between Iron and Folate Status in Pregnancy

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Summary

This study was planned to determine whether iron deficiency in pregnancy predisposed to the development of folate deficiency and also the smallest daily iron supplement that maintained haemoglobin levels in pregnancy.

Three groups of women were given oral ferrous fumarate supplying 30, 60, and 120 mg of iron; a fourth group was given 1 g of parenteral iron in early pregnancy followed by oral iron (60 mg); a fifth group received a placebo. Tablets were taken once daily.

Oral iron 30 mg once daily maintained haemoglobin levels throughout pregnancy. Women whose marrows lacked demonstrable iron at the 37th week had a significantly higher incidence of megaloblastic haemopoiesis (28·7%) than those with demonstrable iron stores (15·3%); women taking oral iron did not have a lower frequency of megaloblastosis than those given a placebo. We concluded that iron does not have a direct effect on folate status in pregnancy, that the association of iron deficiency and megaloblastic anaemia in pregnancy is the result of poor nutrition, and that there is no cause-and-effect relation between them.

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Introduction

Women who are iron deficient throughout pregnancy are sometimes said to be more likely to become folate deficient as well. Thus it was reported that in pregnancy iron-deficient women were more likely to have an excess of hypersegmented neutrophils in blood films, lower serum folate levels, and megaloblastic haemopoiesis in marrow films than pregnant women who had received ample iron (Chanarin, Rothman, and Berry, 1965). A higher frequency of megaloblastic anaemia in pregnancy in the iron-deficient group was reported by Lowenstein, Brunton, and Hsieh (1966) and by Willoughby (1967). Similar findings were reported in iron-deficient infants by Vossough, Leikin, and Purugganan (1968).

Some further supportive evidence has come from the responses of patients to iron therapy. Gross, Keefer, and Newman (1965) reported the disappearance of an abnormal excretion of formiminoglutamic acid in infants with both iron deficiency and megaloblastic haemopoiesis given iron alone, and Velez, Restreppo, Bustamente, and Vitale (1965) reported the disappearance of megaloblastic marrow change on iron therapy in patients with iron deficiency due to hookworm infestation, coupled with malnutrition.

Abnormalities in folate metabolism such as reduced levels of formiminotransferase enzyme in iron-depleted rats were noted by Vitale, Streiff, and Hellerstein (1965) and Vitale, Restreppo, Velez, Riker, and Hellerstein (1966) but not by Burns and Spray (1969).

There are varying explanations for some of these observations relating iron and folate status. It could well be that some workers are reading too much into minor variations in marrow morphology. Even where iron and folate deficiency coexist both could be due to underlying nutritional causes and not have any cause-and-effect relation. The topic is of particular importance in pregnancy, when iron and folate deficiency