less than 0.1% of sufferers. I believe the evidence shows that the true figure is nearer 10%. I therefore consider that the absence of a known affected relative should not deter a neurologist from diagnosing Huntington’s chorea in a patient who shows the characteristic clinical features of the disease.

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References

Charcot-Marie-Tooth disease

Sir,
We read the paper by Brooks and Emery with great interest. We agree with the authors that in Charcot-Marie-Tooth disease slightly affected females are easily missed on clinical examination. If the mode of inheritance in a family is in question it is necessary to detect these female carriers.

The importance of examining nerve conduction in unaffected persons was stressed by de Weerdt and Fryns and van den Berghe, who studied families with the hypertrophic (or demyelinating) type of the disease. In these two families X linked inheritance seemed probable.

However, if the neuronal type of the disease is in question, motor nerve conduction studies are of no help, because motor conduction velocity is usually normal, especially in persons who are only slightly affected. Sensory conduction studies probably discriminate better between affected and unaffected persons.

We would like to draw attention to the use of late response studies (Hoffmann (H) reflex and F response) in hereditary polyneuropathies. In patients with chronic renal failure these studies were abnormal at a time when no clinical evidence of peripheral neuropathy existed and conventional motor and sensory nerve conduction studies were normal. Recently we examined a family with the neuronal type of Charcot-Marie-Tooth disease in which X linked heredity seemed likely. H reflex investigation appeared to discriminate well between affected and unaffected subjects.

In future studies, investigation of the H reflex in families with Charcot-Marie-Tooth disease may contribute to detection of carriers with only minor symptoms and possibly to more insight into the pathophysiological backgrounds of the different genetic forms of Charcot-Marie-Tooth disease.

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References

This letter was shown to Dr Brooks and Professor Emery, who reply as follows:

Sir,
We agree with Drs Heimans and Lindhout that full electrophysiological investigation is necessary in the assessment of patients with Charcot-Marie-Tooth neuropathy and their families.
In 1977 when we were collecting the clinical information which resulted in our publication in 1982, motor nerve conduction velocity measurement was considered useful in distinguishing between demyelinating and neuronal neuropathies, that is, hereditary motor and sensory neuropathies types I and II. However, theoretical objections, as pointed out by Heimans and Lindhout, and practical application in our study showed motor velocities to be of no use in separating affected from normal in families with neuronal disease. Indeed Buchthal and Behse, in the publication referred to, found that sensory conduction abnormalities related better than motor velocities to the clinical state of the patients and biopsy appearance of the sural nerve in both neuronal and demyelinating neuropathies.

Furthermore, when the full range of possible genetic heterogeneity in the Charcot-Marie-Tooth neuropathies is taken into account to include autosomal and X linked, dominant and recessive modes of inheritance, it is clear that comprehensive electrophysiological testing is necessary both to resolve the mode of inheritance and to ascertain which family members are actually affected. This is particularly important when the proband appears to be an isolated male case because of clinically asymptomatic but mildly affected females in autosomal dominant families and the possible existence of X linked forms. It may well be that studies using the H reflex in addition to motor conduction velocity measurement and sensory conduction studies may help to resolve these problems.

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Evidence against a female specific class of neural tube defect

SIR,

The fact that the sex ratio (male/female) of anencephalic babies varies inversely with the population frequency has led to the suggestion that “some environmental factor causes predominantly female anencephalics and that another factor affects the sexes almost equally”. Since the sex ratio in spina bifida does not vary with population prevalence, even though spina bifida and anencephaly show similar epidemiological variations, it was inferred that the factor that caused predominantly female anencephalics caused spina bifida in roughly equal numbers. According to this hypothesis, one would expect proportionately more females (and thus a lower sex ratio) among the anencephalic sibs of female anencephalic probands than among the anencephalic sibs of male probands, since the former group would contain many more cases ‘caused’ by the female specific environmental factor. Because of the clinical implications of the hypothesis with respect to the possible effect of maternal vitamin supplementation on the frequency of neural tube defects within a family,3 we attempted to test it, using data available in the literature.

Family studies of neural tube defects were selected in which the data on probands and sibs were reported by sex and by type of defect.4–11 To these we added updated data from our own study.12 The results are summarised in the table. Patients with both anencephaly and spina bifida are classified as anencephalic (AN), and those with encephalocele as having spina bifida (SB). A family was counted once for each proband.

| TABLE Sex ratios of affected sibs in families of probands with anencephaly (AN) or spina bifida cystica (SB). |
|---|---|---|---|
| Sibs | Male AN | Female AN | Male SB | Female SB |
| Male sibs with AN | 3 | 15 | 13 | 8 |
| Female sibs with AN | 14 | 34 | 21 | 28 |
| Sex ratio, AN sibs | 0.21 | 0.44 | 0.62 | 0.28 |
| Male sibs with SB | 5 | 21 | 30 | 29 |
| Female sibs with SB | 7 | 23 | 33 | 22 |
| Sex ratio, SB sibs | 0.71 | 0.91 | 0.91 | 1.32 |
| Unaffected male sibs | 423 | 1027 | 924 | 1066 |
| Unaffected female sibs | 419 | 896 | 769 | 976 |
| Sex ratio, unaffected sibs | 1.01 | 1.15 | 1.20 | 1.09 |
| Frequency of AN in sibs | 2.0 | 2.4 | 1.9 | 1.7 |
| Frequency of SB in sibs | 1.4 | 2.2 | 3.5 | 2.4 |
| Frequency of NTD in sibs | 3.3 | 4.6 | 5.4 | 4.1 |

Contrary to the hypothesis, the sex ratio of the AN sibs of female AN probands (0.44, column 2) is not lower than that of the AN sibs of male AN probands (0.21, column 1). In fact the difference is in the opposite direction, though not significantly so. The sex ratio of the AN sibs of female SB probands is lower than that of male SB probands (0.28 vs 0.62) but again the difference is not significant, and the numbers are too small to carry much weight.

There is an excess of males among the unaffected sibs in all categories. While the excess in the sibs of female AN probands could reflect selective prenatal loss of female AN embryos, a similar argument would have to apply to the unaffected sibs of male SB probands. These data, therefore, provide no support for the James hypothesis.
Correspondence

A P Brooks and A E H Emery

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