
GENETIC PREDISPOSITION TO FEBRILE CONVULSIONS

A PRELIMINARY STUDY

*CESAR NORONHA RAFFIN **

*ROBERTO GIUGLIANI ***

*JORGE ARMBRUST-FIGUEIREDO ****

The participation of genetic factors in convulsive disorders is a controversial subject. Some investigators consider it to be high and others low. Autosomal dominant, autosomal recessive, sex-linked recessive, and polygenic mechanisms of inheritance have been proposed ^{4,5,6}.

One of the factors that brings special difficulty to define the influence of heredity is the heterogeneous nature of the problem. In an attempt to isolate a supposedly more homogeneous group of patients, and to try to define whether or not a genetic predisposition is present, we developed a study of subjects who had had febrile convulsions. Febrile convulsions was defined as an epileptic event occurring in a previously normal child during a febrile illness unrelated to a nervous system disease ^{1,3,7}.

MATERIAL, METHODS AND RESULTS

Patients attending the Hospital das Clínicas, Faculdade de Medicina de Ribeirão Preto, USP, who had shown at least one well-characterized episode of febrile convulsion were referred to the Febrile Convulsions Ambulatory, and studied during the period of January to December, 1979. A complete family history was obtained in addition to clinical and laboratory data. Relatives with febrile convulsions were considered only when the report given left no margin for doubt. Of the 128 patients studied, 18 (14,3 % of the sample) had at least one relative affected by febrile convulsions. The pedigrees of these patients can be seen in figure 1. The age of the probands varied between 8 months and 16 years, with a mean age of 4 years and 5 months.

Family recurrence was always unilateral (only on the paternal or only on the maternal side), which is not in agreement with a polygenic mechanism of inheritance ⁸.

* Médico pós-graduando de Neurologia; ** Médico pós-graduando de Genética Médica; *** Prof. Titular de Neurologia — FMRP, USP.

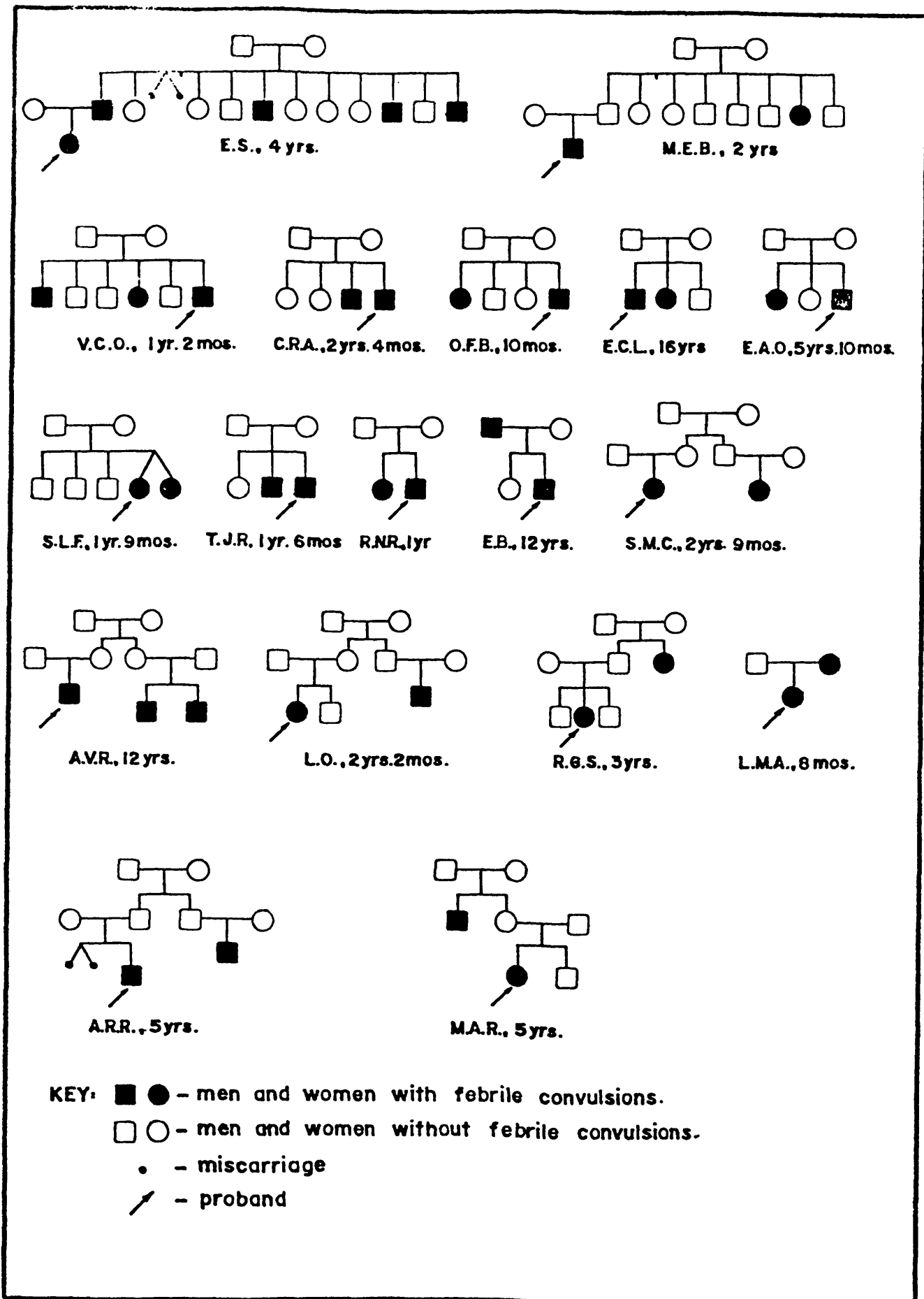


Figure 1 — Pedigrees of the 18 familial cases of febrile convulsions. Above each pedigree the initials and the age of the proband are indicated.

When, in the familial cases, the probands and affected relatives were considered, the slight male predominance among the affected (24 males and 17 females) did not differ significantly from the proportion observed among the nonaffected (46 males and 42 females) (chi-square 0,467 and $P < 0,5$), which discards simple sex-linked recessive inheritance. Sex-linked dominant inheritance is excluded by the occurrence of male-to-male transmission in one of the families.

The absence of consanguinity between the parents of the affected patients, and the fact that in many families the affected subjects were distributed through several generations, suggests no autosomal recessive inheritance.

CONCLUSION

Thus, the segregation observed in the pedigrees (unilateral recurrence, affected patients distributed through several generations, males and females almost equally affected) seems to be more compatible with an autosomal dominant mechanism of inheritance, with incomplete and probably low penetrance, which is in agreement with the findings of Frantzen et al.².

Enlarging the sample and setting up a control group are necessary measures, now underway, for mathematical testing of the data obtained and for the elaboration of a more definite hypothesis.

SUMMARY

The participation of genetic factors in the origin of convulsive disorders is a controversial matter. In an attempt to study the influence of heredity in a selected group of patients, we evaluated 128 subjects that presented febrile convulsions. Of these, 18 (14,3 % of the sample) had at least one relative affected by the same problem. Even though a more definite conclusion depends on sample enlargement and on setting up a control group, pedigree observation suggests the participation of an autosomal dominant gene, with incomplete and probably low penetrance, in the etiology of febrile convulsions.

RESUMO

Predisposição genética à convulsão febril: um estudo preliminar.

A participação de fatores genéticos na origem dos distúrbios convulsivos é controversa. Procurando estudar a influência da hereditariedade num grupo selecionado de pacientes, avaliamos 128 indivíduos que apresentaram convulsão febril. Desses, 18 (14,3 % da amostra) tinham pelo menos um familiar afetado pelo mesmo problema. Embora uma conclusão mais definitiva dependa da ampliação da amostra e da constituição de um grupo controle, a observação dos heredogramas sugere a participação de um gene autossômico dominante, de penetrância incompleta e provavelmente baixa, na etiologia da convulsão febril.

REFERENCES

1. AICARDI, J. — Les convulsions hyperpyrétiques de l'enfant. Arch. Franç. Pédiat. 29:5, 1972.
2. FRANTZEN, E.; LENNOX-BUCHTHAL, M. A.; NYGAARD, A. & STENE, J. — A genetic study of febrile convulsions. Neurology (Minneapolis) 20:909, 1970.
3. LENNOX-BUCHTHAL, M. A. — Febrile convulsions: a reappraisal. Electroencephalogr. Clin. Neurophysiol., suppl. 32, 138 pp., 1973.
4. LENNOX, W. G. — Significance of febrile seizures. Pediatrics 11:341, 1953.
5. METRAKOS, J. D. & METRAKOS, K. — Genetics of convulsive disorders: I. Introduction, problems, methods and base lines. Neurology (Minneapolis) 10:228, 1960.
6. OUELLETTE, E. M. — The child who convulses with fever. Pediat. Clin. N. Am. 21:467, 1974.
7. TAYLOR, D. C. & OUNSTED, C. — Biological mechanisms influencing the outcome of seizures in response to fever. Epilepsia 12:33, 1971.
8. TSUBOI, T. — Polygenic inheritance of epilepsy and febrile convulsions: analysis based on a computational model. Brit. J. Psychiat. 129:239, 1976.

Departamento de Neuropsiquiatria e Psicologia Médica — Faculdade de Medicina de Ribeirão Preto — 14100 Ribeirão Preto SP — Brasil.