Epilepsy Precipitated by Food Sensitivity: Report of a Case with Double-Blind Placebo-Controlled Assessment

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Although there are over two-hundred reported cases of epilepsy related to food sensitivity, many physicians discount these reports and consider food sensitivity or "allergy" to be an exceedingly rare factor in epilepsy. (For reviews see Davison, 1952, Stevens, 1965, Campbell, 1970). Part of this skepticism stems from the fact that well-controlled studies of food and its relation to epilepsy have rarely been reported. Consequently, such factors as patient expectations, psychological associations to food, and hysterical epilepsy could be alternative explanations for the induction of seizures by a particular food.

We here report a case of epilepsy precipitated by ingestion of specific foods in which carefully controlled, double-blind confirmation of the food-epilepsy relationship was demonstrated.

Case Report

The patient is a 19 year old white, single woman who is the youngest of 4 children. She first developed seizures at the age of 17. Her seizures were characterized by an aura consisting of a sense of being in a different place followed by a loss of consciousness and tonic-clonic movements of the extremities. She had an average of 1 to 2 seizures per week, each lasting 1 hour to 13 hours, usually 2 to 4 hours. She frequently injured herself during the course of these seizures and was occasionally incontinent of urine. She was seen by a neurosurgeon whose evaluation included a neurological examination, EEG and CT scan, all of which were normal. His diagnosis was hysterical epilepsy. The seizures increased in frequency and severity and during her 18th year she was hospitalized 18 times for control of seizures. She was treated with tegretol, 600 mg per day, mysoline, 1000 mg per day and dilantin, 400 mg per day. Blood levels of these medications were consistently in the therapeutic range. Numerous additional EEGs during the 2 year course of the illness were usually recorded as abnormal, with paroxysmal 3-5 per second slow-wave activity and occasional temporal spikes being the most common findings. She received extensive evaluations at several prominent midwestern medical centers without relief. Because of her failure to respond to adequate chemotherapy, her seizures were considered by some to be hysterical in nature and she was treated by 3 different psychiatrists. She was seen in individual psychotherapy with them but apart from typical adolescent concerns around individuation and sibling rivalry, no prominent psychiatric disorder could be elicited.

Her past medical history included allergies to dust, pollen and mold, and there was a family history of allergies in both her father and 2 siblings. Several of the seizures followed food ingestion within 1-2 hours.

Laboratory Studies

Hematological workup was normal except for an eosinophil count of 9. Serum proteins were normal and an immune globulin screening was also within normal limits. IGE was 59 units/ml, blood histamine 4.8 mg/100 ml, and serotonin 114 nanog/ml. Blood levels of trace minerals were: zinc 97.9, copper 115.7,

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iron 102.6, chromium 0.88, nickel 2.0, manganese 0.42 and aluminum 1.91; T-3 146, T-4 7.1. Following an oral tryptophan load (80 mg/Kg) urinary kynurenic acid was 5.9, xanthurenic acid 7.1, (normal, less than 3 mg/24h), VDRL non-reactive. Fasting blood glucose was 89. FIGLU was 3.2 mg/24 h (following a histidine load; upper limit of normal, 3.0 mg/24 h), corproporphobilinogen 49. Blood levels of vitamins were within normal limits. She had positive skin tests to several foods and airborne allergies.

The patient began systematic testing of individual foods following a 4-day elimination diet (Randolph, 1962). She showed strong reactions including tachycardia, cutaneous hypothermia and seizures when given beef or substances derived from beef and several other foods. She showed none of these reactions to other foods including chicken.

Double-blind Testing

In order to verify these reactions, double-blind controlled presentations of beef and chicken were arranged as described by May (1976). Approximately 6 grams of beef or chicken obtained at a local supermarket were chopped up and placed in gelatin capsules. Following a baseline recording period of 1 hour, the capsules of beef or chicken were given to the patient in random, double-blind sequence. The actual sequence of presentations was chicken-beef-chicken-beef. In order to monitor sympathetic nervous system function, pulse and peripheral skin temperature were recorded. The EEG was continuously monitored during the 6-hour study. The EEG showed short bursts of 5 per second slow wave activity and diffuse 6 per second spike and wave discharges.

Following the 25 minute baseline period, the

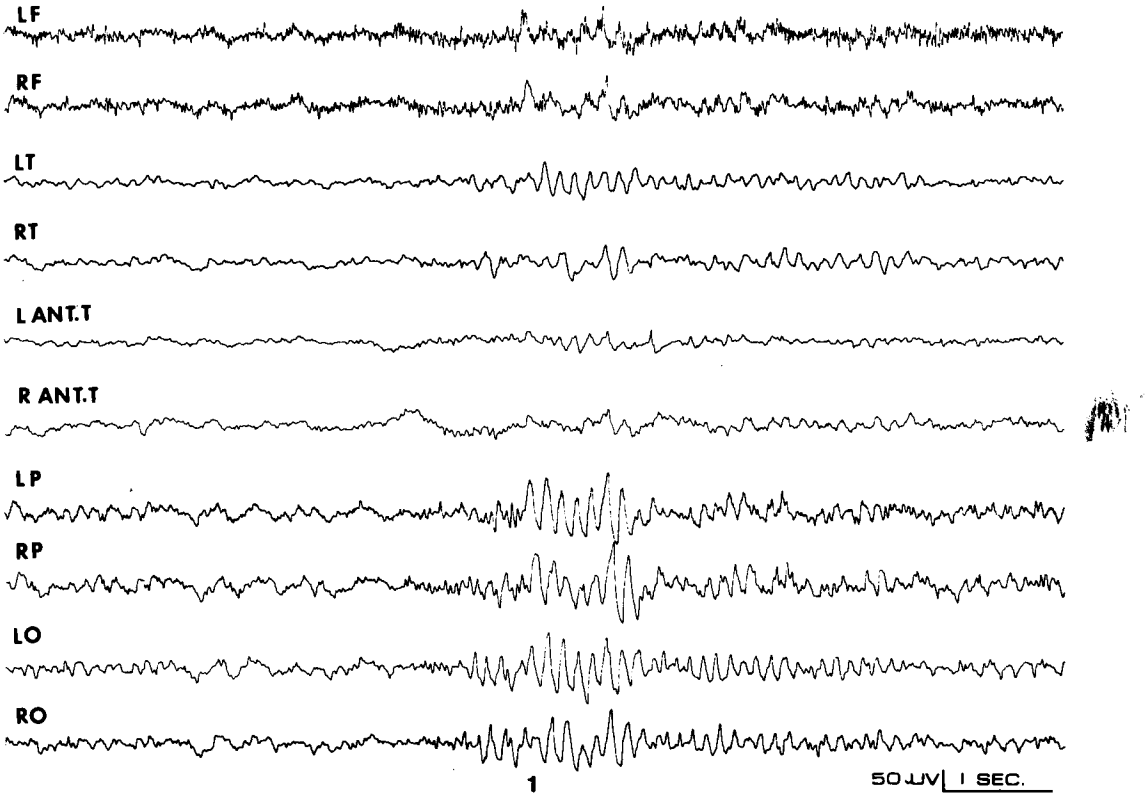

Figure 1 Short burst of 5 per second slow activity followed by 8 per second alpha waves. Reference on joined ear leads.

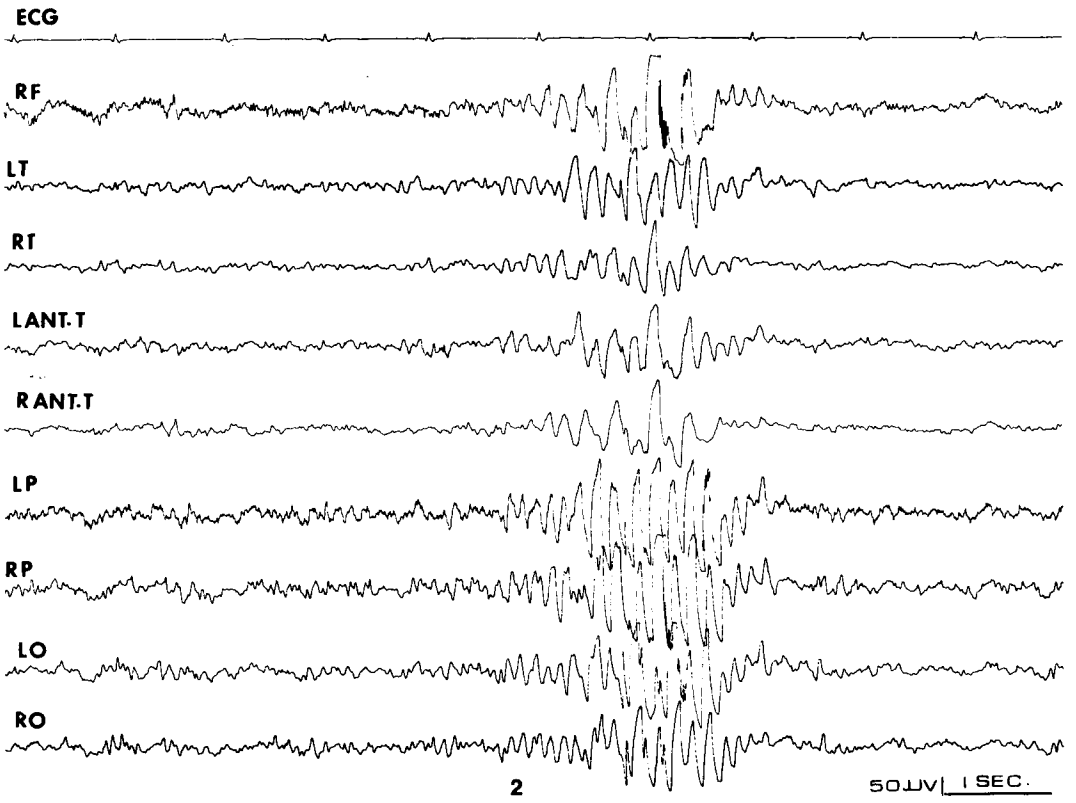

Figure 2. Diffuse 6 per second spike and wave discharges. Reference on joined ear leads.

first capsules (chicken) were given. There was no significant response in any of the measures during the subsequent hours. The EEG continued to show short bursts of 5 per second slow activity and diffuse 6 per second spike and wave discharges (Figs. 1 and 2).

At 60 minutes the second set of capsules (beef) was given. Ten minutes after ingesting the beef, the patient's pulse had increased from about 70 to 85. At this time she became unresponsive to verbal or physical stimuli.

At 110 minutes, she had the first of 6 grand mal convulsions characterized by tonic-clonic movements of all extremities. It lasted about 10 minutes. There was no incontinence. The EEG showed only motor activity which completely obscured the recording (Fig. 3A and 3B). No EEG buildup was seen prior to the seizure nor were there post-ictal EEG phenomena. All six seizures were similar to the first one but shorter, ranging from 1-3 minutes in length. The patient was given pyridoxine (300 mg I.M.) at 120 and 142 minutes. Following the last seizure the patient was somnolent for about 15 minutes. She then awoke and gradually became alert. The pulse returned to 74-76 and her skin temperature rose to 32°C. At 180 minutes the next set of capsules (chicken) was given. The pulse remained in the 74-80 range, skin temperature rose slightly to 34°C and there was no evidence of seizure activity during the next hour. At 250 minutes, the next set of capsules (beef) was given. Fifteen minutes later the pulse again increased to 120-124, skin temperature dropped to 26°C, and the patient had the first of a series of eight more grand mal seizures, most lasting 1-3 minutes each (Fig. 4).

Again, the EEG showed only muscle artifact. Following the last seizure the skin temperature rose to approximately 32°, and the pulse dropped to the 80-90 range. After about 10 minutes of somnolence, the patient gradually became alert.

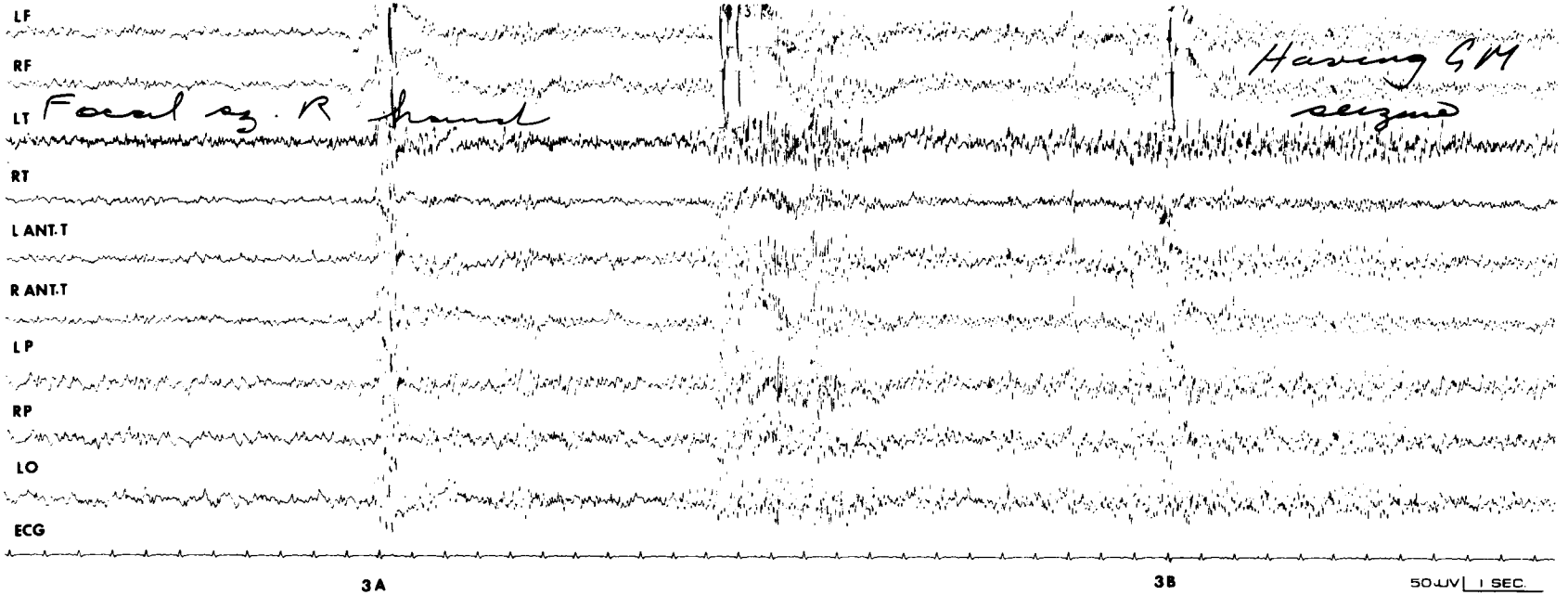

Figure 3a Focal convulsion of right hand with no seizure discharges, only muscle activity.

Figure 3b Generalized convulsion. No seizure discharges. Only muscle activity potentials. Reference on joined ear leads.

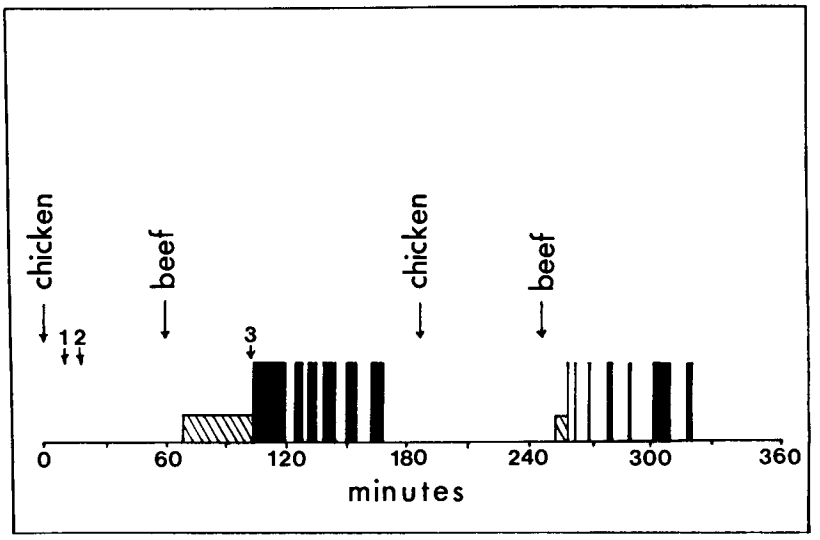

Figure 4 Sequence of double-blind challenges. Capsules containing 6 grams of chicken or beef were given at the indicated times. There was no response to the chicken. Within 15 minutes of beef ingestion, patient became unresponsive (hatched area). Patient then had a series of grand mal seizures (solid bars). Numbers 1, 2 and 3 locate points where EEG illustrations were recorded.

Discussion

Several extensive reviews of the relationship of allergy to epilepsy are available (Davison, 1952; Campbell, 1974; Speer, 1970), but standard textbooks of neurology tend to consider allergy an extremely rare precipitant of seizures (e.g., Brain, 1978). However, there is reason to believe that such patients are not so rare. Several authors have reported a high incidence of allergic phenomena in epileptic patients. (Beauchemin, 1935; Cinca and Dimitria, 1976; Chobof et al., 1950; Dees and Lowenbach, 1951). Cunningham (1975) found a significantly higher mean eosinophil count in epileptics compared with controls. Furthermore, most allergists have found that food allergies are more likely to be associated with epilepsy than other types of allergy (Campbell, 1970) and food allergies—especially "masked" food allergies—are difficult to diagnose unless specific studies including elimination diets or provocative food testing are carried out (Randolph 1962). Therefore, unless systematic food testing is carried out, most cases of food-related epilepsy will be missed. In addition, the availability of generally effective anti-convulsant medication may have contributed to a waning interest in undertaking the detailed food-testing necessary to make a definitive diagnosis (Editorial, Lancet, 1979). Diagnosis would be greatly facilitated if criteria for the identification of probable food-sensitive epileptics were known.

Foreman (1952) suggested four criteria to help identify individuals who might have seizures on an allergic basis. His criteria were: 1) personal history of allergy, 2) family history of allergy, 3) eosinophilia, and 4) positive skin tests for specific food allergens.

This patient presented with a personal and family history of allergy, eosinophilia (9%) and positive skin tests for allergens. Double-blind testing with a suspected food (beef) and a "safe" food (chicken) showed a reaction to the beef only. The patient had a non-specific epilepti-form EEG abnormality prior to food testing but showed no clear EEG evidence of seizure activity during her seizures. A significant nonconcordance between clinical and EEG seizures has been described (Goldenson, 1963) and experimental epilepsies without EEG findings have also been reported (Pollock, 1949).

However, the absence of EEG seizure activity and the unusually long duration of the

seizures, raises the possibility of a functional basis for her seizures. In such cases, if the seizure has a prominent functional component, it is usually possible to make a positive diagnosis of hysterical epilepsy on clinical grounds such as the criteria developed by Roy (1977 a,b). Patients with hysterical epilepsy are characterized by a significantly higher incidence of a family history of psychiatric disorder, a past history of psychiatric disorder, suicide attempts and sexual maladjustment. This patient met none of these criteria.

The mechanisms which mediate the association of allergy and epilepsy are still unknown. As a working model we would suggest that patients who develop epilepsy following food ingestion have two defects: one, a lower threshold for seizure activity indicated in this patient by non-specific EEG changes in her baseline EEG; and second, an allergic disorder which produces a seizure-inducing change in brain activity. Several mechanisms could be proposed to link allergy with epilepsy. The process may involve a direct toxic effect of partially metabolized food (Klee, 1979); an effect of histamine, bradykinin, or other chemical mediator of allergic phenomena on the brain or brain vasculature (Bell, 1975), a pyridoxine-dependent state induced by interference with pryidoxine metabolism by an allergy-mediator substance (Chutorian and Nicholson, 1976), or a prostaglandin-mediated reaction (Rosenkranz, 1978).

Allergy—specifically food allergy—should be considered in epileptic patients with a history of asthma, hay fever, or other allergy in themselves or family, and eosinophilia or other indication of allergy such as basophilia, elevated IGE, radioallergosorbent (RAST) tests to specific allergens or positive skin tests. Such patients may well benefit from food sensitivity studies. Food allergy studies can be the basis for effective treatment. This patient has had only one seizure in the past 6 months on a regimen stressing dietary avoidance of specific food allergens and without anticonvulsant medication. In the 6 months prior to this program, she had 31 seizures despite therapeutic doses of anticonvulsant medication.

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REFERENCES

1. BEAUCHEMIN, J.A., Allergic reactions in mental diseases, Am. J. Psychiat., 92:1190, 1935.
2. BELL, I.R., A kinin model of mediation for food and chemical sensitivities: biobehavioral implications, Ann Allergy, 35:206-15, 1975.
3. CAMPBELL, M., Neurologic manifestations of allergic disease, Ann Allergy, 31:485-98, 1973.
4. CAMPBELL, M.B., Neurological and psychiatric aspects of allergy, Otolaryng. Clin. N.A., 7:805-25, 1974.
5. CHOBOF, R., DUNDY, H.D., and PACELLA, B.L., The incidence of abnormal electroencephalographic patterns in allergic children, J. Allergy, 21:334-38, 1950.
6. CHUTORIAN, A.M., and NICHOLSON, J.F., The prevention of postprandial seizures in children, Develop. Med. Child. Neurol., 18:351-7, 1976.
7. CINCA, I., DIMITRIA, R. A clinical and electroencephalographic study of allergic epilepsy, Neurologie (Buc), 21:215-24, 1976.
8. CUNNINGHAM, A.S., Allergy, immunodeficiency and epilepsy, Lancet, 11:975, 1975.
9. DAVISON, H.M., Allergy of the nervous system, Quart. Rev. Allergy Applied Immunol., 6:157-88, 1952.
10. DEES, S.C. and LOWENBACH, H., Allergic epilepsy, Am. Allergy, 9:446-58, 1951.

11. Editorial, Food allergy, Lancet, 1:249-50, 1979.
12. FORMAN, J., Atopy as a cause of epilepsy, Arch. Neurol. Psychiat., 32:517-22, 1934.
13. GOLDENSON, E., EEG and post-ictal behavior in Glaser, G.H., EEG and Behavior, Basic Books, New York, Chapter 12, 1963.
14. GROSSMAN, H.J., and HELMY, J. Electroencephalographic patterns in children with allergic, convulsive and behavior disorders, Ann. Allergy, 20:1-14, 1962.
15. HALL, K., Allergy of the nervous system, Ann. Allergy, 36:49-64, 1976.
16. KLEE, W.A., ZIOUDROU, C., and STREATY, R.S., Exorphins: peptides with opioid activity isolated from wheat gluten and their possible role in the etiology of schizophrenia in Endorphins In Mental Health Research. E. Usdin, W.E. Bunney and N.S. Kline ed., N.Y. Oxford U. Press, 1979, pp. 209-18.
17. MAY, C.D., Objective clinical and laboratory studies of immediate hypersensitivity reactions to foods in asthmatic children, J. Allerg. Clin. Immunol., 58:500-15, 1976.
18. POLLOCK, G.H., Species specificity of agene toxicity, J. Appl. Physiol., 1:802-6, 1949.
19. RANDOLPH, T.G., Human Ecology and Susceptibility to the Chemical Environment, Springfield, Chas. Thomas, 1962.
20. ROY, A., Identification and hysterical symptoms, Br. J. Med. Psychol., 50:317-8, 1977a.
21. ROY, A., Hysterical fits previously diagnosed as epilepsy, Psychological Medicine, 7:271-3, 1977b.
22. ROSENKRANZ, R.P., Effects of intracerebroventricular administration of PGE, E_2 and $F_{2\alpha}$ and electrically induced convulsions in mice, Prostaglandins, 15:925-42, 1978.
23. SPEER, F., Allergy of the Nervous System, Springfield, Chas. Thomas, 1970.
24. STEVENS, H., Allergy and epilepsy, Epilepsia, 6:205-16, 1965.