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Aspartame  
Seizure



## Seizure and mania after high intake of aspartame

The fairly widespread use of the artificial sweetener aspartame (*N*-L- $\alpha$ -aspartyl-L-phenylalanine 1-methyl ester), marketed under brand names such as Canderel, Equal, NutraSweet, and Tri-Sweet, has engendered considerable controversy, including suggestions of significant neurochemical changes.<sup>1</sup> Data presented by Wurtman<sup>2</sup> indicate that aspartame alone can almost double rat brain phenylalanine levels, while aspartame-carbohydrate combinations can raise brain tyrosine levels and suppress the physiologic increase in tryptophan that follows a carbohydrate-rich meal.<sup>3</sup> \*Such neurochemical changes could certainly be postulated to have potential behavioral impact, particularly in predisposed individuals. The following case is presented as a possible instance of such impact.

### Case report

A 54-year-old married woman with no known medical difficulties other than a 20-year history of a unipolar affective disorder, initially treated for several years with psychoanalytic psychotherapy, continued to experience recurrent major depressive episodes until she was started 11 years ago on imipramine, 150 mg at bedtime. A dramatic response to this tricyclic had occurred. However, whenever the medication had been discontinued or tapered below 150 mg/d, she experienced a breakthrough of depressive symptomatology within several weeks. A decision was thus ultimately made for maintenance on imipramine at the 150 mg/d dosage at bedtime.

The patient had been taking this agent at this level for five

years, with semiannual psychiatric visits for renewal of her prescription and brief assessment of mental status, when she suddenly experienced a grand mal seizure, followed by a profound behavioral change. Immediately after the seizure she was hospitalized for a neurologic evaluation, including CT scan. The evaluation did not elucidate the etiology of her seizure. During the hospitalization a psychiatric consultation was obtained because of euphoria, thought by the patient's internist to be quite out of character. At the time of the consultation she displayed psychomotor acceleration, flight of ideas, and grandiosity. The imipramine was discontinued and the possibility of using lithium carbonate raised, but the patient insisted on going home and was discharged on no medication.

At home she continued to display manic symptomatology, including insomnia, flight of ideas, irritability, and psychomotor acceleration. After three weeks the family insisted on psychiatric hospitalization. On admission, a diagnosis of mania was made and the patient was started on lithium carbonate, 300 mg qid. Two days after admission it was learned that it had been her custom to consume large amounts of iced tea (both she and her family reported that during the summer months her daily intake of it approached one gallon). In years past she had sweetened the tea with sugar. However, during the several weeks prior to the seizure and onset of mania, because of concern about her weight, she had used an iced tea preparation sweetened with aspartame.

As it was thought that the behavioral disturbance could be secondary to massive ingestion of aspartame, the lithium carbonate was discontinued, and within four days all evidence of manic activity had subsided. The patient was discharged six days after admission and appeared to be at her baseline level of functioning. Two months after discharge

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(on no medications) she reported recurrence of insomnia, depressive affect, and irritability, and requested that her imipramine be reinstated. This was done, again at a dose of 150 mg at bedtime. Over the ensuing 13 months she has functioned well, with no evidence of either depression or manic episodes. She continues to ingest large amounts of iced tea, sweetened with sugar rather than aspartame.

### Discussion

This patient's clinical course suggests that high intake of aspartame may have triggered a seizure and subsequent manic episode. Although sustained treatment with imipramine could of course provoke mania in a bipolar patient, this does not appear likely in this case. There was no history of manic episodes, no known family history of bipolar illness, and no difficulty provoked by the same dose of imipramine five years prior to and one year subsequent to the use of aspartame. The high level of caffeine absorbed could also conceivably have played a role, but again there was at least a six-year history of consumption at essentially the same level without difficulty. Clinicians should bear in mind the possible impact of aspartame on catecholamine and indolamine metabolism, and inquire about use of this artificial sweetener when assessing patients with affective disorder. □

### REFERENCES

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