

## Seizures And Aspartame

Donald J. Fishman, M.D.

Over half the food eaten today contains aspartame as sweetener. This substance, made from aspartic acid and phenylalanine, has been proposed to increase brain phenylalanine levels and adversely affect catecholamine or serotonin synthesis. Since diminished brain monoamine levels have been related to depressed seizure threshold in animal preparations, there have been highly publicized assertions that high aspartame doses might also increase the likelihood of seizures in symptomless but susceptible people.

Wurtman presented three brief histories of patients who experienced seizures after aspartame ingestion. A 42-year-old woman drinking 4 quarts of diet cola and the same amount of Nutrasweet lemonade *daily* became "moody," experienced episodes of headache and nausea, visual hallucinations, déjà vu, and finally a grand mal seizure. A 27-year-old man had multiple symptoms with headache and grand mal seizure, and a history of consuming 4 to 5 glasses of aspartame-sweetened cola daily. A 36-year-old professor drinking 900 ml or more of aspartame-sweetened iced tea daily had a solitary seizure in bed one night. Angiography demonstrated a left posterior frontal venous angioma judged an "incidental finding." A personal case has been seen of a 7-year-old boy who experienced a solitary seizure several hours following the ingestion of 2 liters of diet cola.

The FDA, in January 1986, requested that possible adverse effects be reported. Approximately 3,400 reports have been received, including 190 reports of seizures attributed to aspartame. Investigation of these 190 reports failed to confirm a reasonable discrete cause-and-effect relationship in any. Several cases involved unusually high amounts of total liquid ingested, suggesting that water intoxication may have played a part.

Three centers are presently involved in challenge studies of known seizure patients, as well as patients reported anecdotally as having had a seizure in relationship to Nutrasweet ingestion. Since aspartame is about 200 times sweeter than sugar, it takes only 2 grams to replace the sweetness of 1 pound (454 grams) of sugar. A 60-kg person who consumed 2 grams of aspartame in one dose would receive a phenylalanine load of about 18.6 mg/kg, which is substantially less than the daily phenylalanine intake from dietary sources (50-200 mg/kg). At least 2 cases in the Yale study were reported after ingestion of 6 to 8 liters of diet cola (about 33 mg/kg). These patients were subjected to a placebo controlled challenge of 50 mg/kg of aspartame and this failed to precipitate problems.

At the present time there would seem to be little evidence to support the idea that aspartame per se precipitates seizures. However, case reports suggest that water intoxication may well play a role in some cases. This would seem to be one of many clinical settings in which our patients would be well advised to live by basic principles, particularly one of the most ancient: "Nothing In Excess." ■

#### References:

1. Wurtman RJ: Aspartame: Possible Effect on Seizure Susceptibility (letter). *Lancet* 1985; 2:8463:1060.
2. Aspartame: Review of Safety Issues, Council on Scientific Affairs: *JAMA* 1985 254:400-402.
3. Tolefson L: Federal Drug Administration: Clinical Nutrition Branch: Personal Communication.
4. Shaywitz B: Dept. of Neurology, Yale University: Personal Communication.
5. Plato: *Dialogues: Protagoras*.

PSY



In  
This  
Issue

Intracranial Neoplasms  
Parkinson's Disease and Sinemet CR-4  
Evaluating Memory Dysfunction

p. 2  
p. 3  
p. 3

# Intracranial Neoplasms

## Meningioma Detection: CT vs. MRI

Birgit A. Ehlers, M.D.

77-year-old female with left anterior clinoid/optic nerve meningioma with involvement of the canal and apical portions of the left optic nerve.

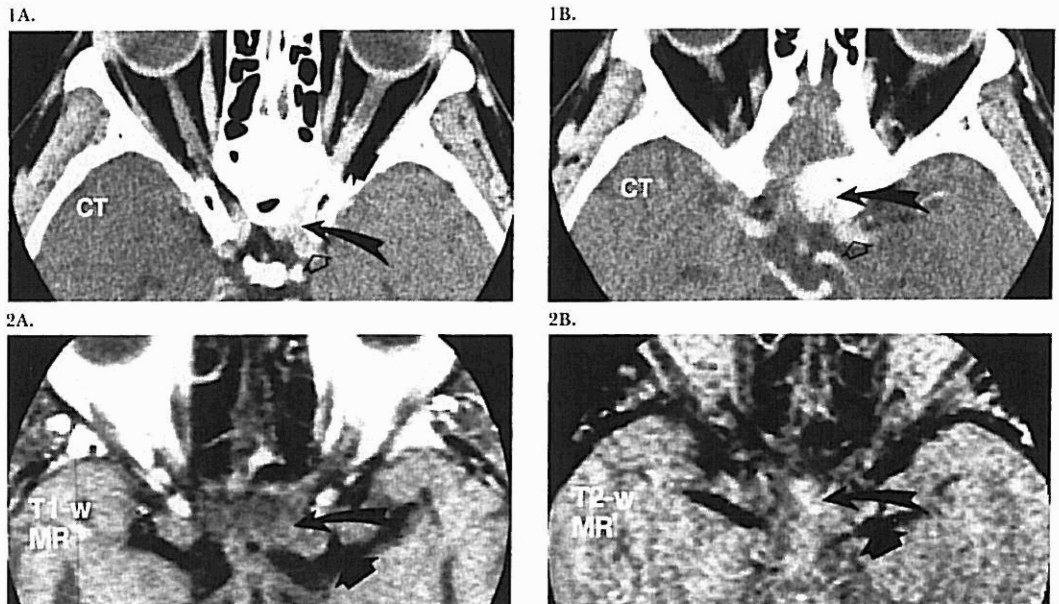
Figures 1A & B: Contrast CT scan of orbit. Axial images. Enhancing meningioma of anterior clinoid process (curved arrows). En plaque extension along left optic nerve (arrow). Enhancing middle cerebral artery (open arrows) is poorly differentiated from meningioma.

Figures 2A & B: T1-weighted axial (A) and T2-weighted axial (B) MR images. Meningioma (curved arrows) is poorly differentiated from brain tissue on T1-weighted image. Slightly increased intensity is noted in meningioma on T2-weighted image. Middle cerebral artery (arrows) is clearly differentiated from meningioma.

The clinical presentation of patients with intracranial neoplasms varies from such nonspecific symptoms as headache, nausea, and subjective mental status changes (seen in up to 50% in the early stages of tumor growth) to signs such as seizures, altered visual or sensory function, focal weakness, or loss of verbal fluency.

Magnetic resonance imaging (MRI) has unquestionable superiority and greater sensitivity over computed tomography (CT) in detecting tissue changes that result from most intracranial neoplasms. With meningiomas, however, CT more often readily identifies and characterizes the tumor. Meningiomas represent 15% of all intracranial tumors in adults (3-4% in the pediatric population), and are the most common extra-axial neoplasm. The typical age presentation is between 40 and 60 years, with women affected twice as frequently as men.

With MRI, meningiomas tend to be isointense to brain on both T1- and T2-weighted sequences. On more heavily T2-weighted images (long repetition time and long echo time), slight hyperintensity occurs in 40%. Therefore, the only clues to the presence of a meningioma may be indirect signs of a mass. These slowly expanding tumors indent the surface of the brain and, with the slow expansion, the underlying brain atrophies; therefore, little mass effect may be seen. Other clues which may be present on MR are white-matter buckling, distortion, edema, and base of tumor abutting dura.



Calcification (present in 20%), easily identified on CT, is difficult to identify on MR. Hyperostosis, if identified on MR, is less obvious than on CT scans. Paramagnetic contrast agents help depict these lesions on MRI but have not yet been approved for general use.

Meningiomas have a typical appearance on CT. They may be minimally hyperdense on non-contrast-enhanced CT. On contrast-enhanced CT there is classically a dense, uniform enhancement of these well-circumscribed lesions, with a broad base along a dural surface. Calcification within the tumor is easily identified. Adjacent bony change (usually hyperostosis) is readily seen with CT.

In summary, CT still has use in evaluating patients for possible intracranial neoplasm such as meningioma if no abnormality is identified on MRI. ■

### References:

1. Zimmerman RD, Flenting CC, Saint-Louis A, et al: MRI in Intracranial Meningiomas. *AJNR* 1985; 6:149-157.
2. Brant-Zawadzki M, Badami JP, Mills CM, et al: Primary Intracranial Tumor Imaging: A Comparison of Magnetic Resonance and CT. *Radiology* 1984; 150:436-470.
3. Whelan MA, et al: CT of the Base of the Skull. *Radiologic Clinics of North America*, Vol 22, No. 1, March 1984.
4. Naheedy MH, et al: MRI and CT of Sellar and Parasellar Disorders. *Radiologic Clinics of North America*, Vol 25, No. 4, July 1987.
5. Brant-Zawadzki M, Norman D: *Magnetic Resonance Imaging of the Central Nervous System*. Raven Press, New York.

## Parkinson's Disease: Sinemet CR-4 May Reduce End-Of-Dose Failure

Brian H. Avin, M.D.

Some patients with Parkinson's disease have a decreased therapeutic response to standard Sinemet that presents as a wearing-off phenomenon or end-of-dose failure. This results as blood levels of levodopa diminish. When blood levodopa levels rise, improved therapeutic response occurs. Frequent dosage administration with standard Sinemet initially helps alleviate these problems, but this approach is inconvenient and only partially effective. Sinemet CR-4, a new Sinemet formulation, may be effective in reducing fluctuations in therapeutic response. Clinical trials of the drug are now underway.

Sinemet CR-4 is composed of carbidopa 50 mg. and L-dopa 200 mg., housed in an erodible polymeric matrix that allows slow release of the product into the intestine. Carbidopa is an inhibitor of aromatic amino acid decarboxylation; levodopa is an aromatic amino acid. Carbidopa helps prevent the metabolism of levodopa to dopamine in the peripheral circulation, thus allowing more levodopa to reach the brain.

With Sinemet CR-4, dosing frequency can be reduced 25-50% relative to standard Sinemet. Clinical fluctuations are reduced throughout the day and occasionally are eliminated. The percentage of time with good motor function is increased. Patients with mild to moderate fluctuations, especially end-of-dose wearing-off, benefit most. Nearly all patients who have completed the initial phase of the CR-4 trials have requested long-term treatment because of clinical improvement.

The following inclusion criteria apply to the current clinical trials. Patients must be 35 years or older. All patients in this study should exhibit predictable deterioration in motor behavior which occurs at various intervals after dosing with anti-Parkinson medication. They may also demonstrate other evidence of advanced or complicated Parkinson's disease, including dyskinesias, bradykinesia, freezing episodes, or rapid oscillations (also known as the "on-off phenomenon"). Patients must require Sinemet four or more times per day for treatment of their motor fluctuations.


Exclusion criteria restrict patients with specified clinical or laboratory indications of renal, hepatic, hematologic, cardiovascular, pulmonary, or neoplastic disease; patients who are pregnant or who are likely to become pregnant during the trial; patients who are presently on concurrent therapy such as dopamine agonists (bromocriptine), monoamine oxidase inhibitors, methyl dopa, and neuroleptic drugs such as phenothiazines, thiozanthenes, butyrophenones, or phenylpiperazines. All such drugs must be discontinued at least 14 days prior to the study. Patients with narrow-angle glaucoma and patients with suspicious undiagnosed skin lesions or a history of melanoma are also excluded.

The Neurology Center is participating in the clinical investigation of Sinemet CR-4. The medication is supplied to patients free of charge. For further information, contact Anita R. Wenning, Nurse Practitioner. ■

Complaints of memory loss and forgetfulness appear frequently in a variety of medical settings. Unfortunately, laboratory findings and mental status examination may not provide an adequate basis for differential diagnosis. Moreover, the geriatric patient typically presents with additional symptoms or complicating history such as subdued affect, elevated blood pressure, distractibility, past alcohol abuse, or recent traumatic loss. These simultaneously raise the diagnostic possibilities of depression (or some other psychiatric disorder), vascular illness, or alcoholic encephalopathy, in addition to the possibility of a deteriorating cognitive condition such as Alzheimer's disease (AD). Neuropsychological evaluation is a powerful diagnostic tool that is helpful in detecting potentially reversible "dementia."

The complete neuropsychological examination assesses intelligence, abstract thinking, concentrated attention, mental flexibility, language skills, visuospatial processing, memory, sensory-motor function, and personality factors. Ideally, testing is prescriptive and designed with the referral question(s) and patient's mental stamina in mind. Recent research by Moss and Tierney and their colleagues suggests that even very brief test batteries have a classification accuracy as high as 96% in discriminating between AD and normal aging, and between

*(continued on next page)*



## Evaluating Memory Dysfunction

Linda R. Sapin, Ph.D.

## Evaluating Memory Dysfunction

*continued*

different types of dementia. Another recent report reviewed the efficacy of neuropsychological assessment in differentiating between AD and solvent encephalopathy in elderly workers, in the absence of a positive neurologic diagnosis with CT scan, EEG, and laboratory studies.

Even when memory dysfunction is associated with a known diagnostic entity such as diencephalic or bitemporal lesions, head injury, anoxia, encephalitis, or cerebrovascular accident, neuropsychological consultation is often requested to illuminate the psychological and behavioral correlates of brain dysfunction. It can also establish a set of baseline measures to which future performance can be compared. The utility of neuropsychological testing was recently discussed at an NIH conference on dementia, where it was recommended that this type of evaluation be added to the list of standard laboratory tests in cases of suspected dementia.

A number of neuropsychological variables typically differentiate benign from pathological memory loss. For example, depressed patients may demonstrate quantifiable impairment in short-term memory. The use of cueing and recognition paradigms generally improves their performance upon delayed retesting, but does not usually assist the patient with dementia. Moreover, the dementia patient is likely to demonstrate disruptions in visuospatial processing and abstract thinking, which generally remain intact in individuals with depression and benign senescent forgetfulness. It should be pointed out that clinical depression may co-exist with dementia, and that the two are not always readily identifiable as mutually exclusive diagnostic entities.

As neuropsychological examination refines the distinctions between benign and pathological memory loss, and offers an opportunity to track cognitive function with serial testing, clinicians may find neuropsychological consultation valuable in the evaluation of memory dysfunction. ■

#### References:

1. Moss MB et al.: Differential Patterns of Memory Loss Among Patients with Alzheimer's Disease, Huntington's Disease and Alcoholic Korsakoff's Syndrome. *Arch Neurol* 1986; 43:239-246.
2. Tierney MC et al.: Psychometric Differentiation of Dementia. *Arch Neurol* 44:720-722.
3. White RF: Differential Diagnosis of Probable Alzheimer's Disease and Solvent Encephalopathy in Older Workers. *Clin Neuropsychol* 1987; 1:153-160.
4. NIH Consensus Development Conference on Differential Diagnosis of Dementing Diseases. July 6-8, 1987; Bethesda, Maryland.

The Neurology Center Report is published three times a year as a public service. © 1987, The Neurology Center, P.A. All rights reserved.

Editor: Philip D. Pulaski, M.D.  
Managing Editor: Terri Goren  
Copy Editor: Janet Rapmund

Barlow Building  
5454 Wisconsin Avenue  
Chevy Chase, Md. 20815  
Phone: (301) 652-3040

University Medical Bldg.  
2141 K Street, N.W.  
Washington, D.C. 20037  
Phone: (202) 223-1450

Physicians Building  
9715 Medical Center Dr.  
Rockville, Md. 20850  
Phone: (301) 424-5630

Wheaton Plaza  
South Annex  
11160 Veirs Mill Road  
Wheaton, Md. 20902  
Phone: (301) 949-6655

Dominion Federal Bank Bldg.  
7799 Leesburg Pike  
Falls Church, Va. 22043  
Phone: (703) 827-4090  
(Opening Winter 1987)

The  
Neurology  
Center **REPORT**

5454 Wisconsin Avenue Chevy Chase, MD 20815

BULK RATE  
U.S. POSTAGE PAID  
LANHAM, MD  
PERMIT NO. 4410

P  
Peter R. Breggin, M.D.  
4628 Chestnut St.  
Bethesda, MD 20814