Scientific Abuse in Seizure Research Related to Aspartame

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Summary of Aspartame-Induced Seizures Issue

As of 1995 more than 7% of the aspartame toxicity reactions reports sent to the U.S. Food and Drug Administration (FDA) involve seizures and convulsions (DHHS 1995). The FDA stopped accepting aspartame toxicity reaction reports in 1995 (Food 1995). In a study looking at 551 aspartame reactors, Roberts (1988) found that grand mal, petit mal, and absence seizures occurred in 18% of the cases.

In 1986, Food and Chemical News reported that 80 cases of aspartame-induced seizures had been reported to Dr. Richard Wurtman at M.I.T. (Food 1986). Dr. Wurtman reported three cases in The Lancet (Wurtman 1985). Walton (1986, 1988) published reports of nine cases of seizures linked to aspartame use.

Both the U.S. Air Force's magazine "Flying Safety" and the U.S. Navy's magazine, "Navy Physiology" published articles warning about the many dangers of aspartame including that the ingestion of aspartame may make pilots more susceptible to seizures and vertigo (US Air Force 1992)

In an independent double-blind study of aspartame in children with generalized absence epilepsy, Camfield showed that a single dose of 40 mg/kg of aspartame mixed in liquid exacerbated EEG spike-wave discharge. The authors stated:

> "Aspartame appears to significantly increase the duration of time that children with absence epilepsy have spike wave on their EEG. In this study, the children spent 40% more time in spike wave after aspartame than after sucrose."

The subjects were not on anti-seizure medication during the study. The authors called for a longer study to be conducted.

I believe that the aspartame-induced seizures are at least partially caused by the synergistic effects of formaldehyde and excitotoxins derived from aspartame metabolism. However, many researchers believe that the adverse neurological effects of aspartame may be at least partially due to the phenylalanine derived from aspartame ingestion. Because the phenylalanine from aspartame is in free-form (unbound to protein), it is absorbed suddenly and can spike the blood plasma levels of phenylalanine (Caballero 1986, Matalon 1988, Stegink 1987). This sudden "rush" of phenylalanine does not happen when ingesting food because protein is broken down slowly and the phenylalanine is gradually absorbed. Nor does this phenylalanine "rush" occur when ingesting aspartame in capsules (Stegink 1987).

Maher (1987) points out that increased levels of phenylalanine along with an increase ratio of phenylalanine to other Large Neutral Amino Acids (LNAAs) can inhibit enzymes needed to synthesize the neurotransmitters and diminish the production of brain catecholamines and serotonin. The hypothesis is that this change in brain chemistry will lead to a lowering of the seizure threshold and persons ingesting aspartame will become more susceptible to having seizures.

Wurtman (1988) reviews the research to show that a dose of 60 times more aspartame is needed for rodent studies to simulate the change in phenylalanine/LNAA ratio change that occurs in humans. Based on these findings, several research teams have found that aspartame lowers the seizure threshold in animals (Diomede 1991, Garrattini 1988, Guiso 1988, Kim 1988, Maher 1987, Pinto 1986, Pinto 1988)

Hopelessly Flawed Double-Blind Studies Funded by Monsanto/NutraSweet

Shaywitz (1994) concludes that "our findings indicate that, in this group of vulnerable children, APM [aspartame] does not provoke seizures." Rowen (1995) concludes that "aspartame, in acute dosage of ~50 mg/kg, is no more likely than placebo to cause seizures in individuals who reported that their seizures were provoked by aspartame consumption." Trefz (1994) reports that doses of 15 mg/kg and 45 mg/kg of aspartame in PKU heterozygotes does not change EEG spectral parameters. (The Trefz (1994) study appears to have been published in summary form as Benninger (1991), Benninger (1993a) and Benninger (1993b)). Others have cited these studies as evidence that aspartame does not cause seizures (Lajtha 1994, Butchko 1994).

These results appear very convincing, but these industry-sponsored studies are so flawed so as to be nearly worthless. Below are a selection of major problems

with these studies.

Rowen (1995) Flaws

- 16 of the 18 subjects were taking anti-seizure medication during the study.
- The aspartame was given in capsules so that instead of spiking the plasma phenylalanine level and significantly changing the phenylalanine/LNAA ratio the phenylalanine was absorbed very slowly -- more like what happens when ingesting food (Stegink 1987). These researchers discussed in detail the issue of plasma phenylalanine and LNAA levels. It was particularly absurd is that they gave the aspartame in capsules even though they cited industry research (Burns 1990) which proves capsule administration of aspartame eliminates the spike in plasma phenylalanine levels! Simply stated, the researchers were pretending to test the hypothesis that phenyalalnine/LNAA ratio changes would cause seizures, but they knowingly administered aspartame in a way that eliminated the possibility of a large change in plasma phenylalanine levels and phenylalanine/LNAA ratios.

  Capsule administration of aspartame slows the absorption of methanol and may reduce its toxicity somewhat similar to the way ingestion of food with methanol may slightly reduce its toxicity (Posner 1975). Capsule administration of aspartame also eliminates the quick absorption of the excitotoxin, aspartic acid (Stegink 1987). When aspartic acid is absorbed quickly, it can be excitotoxic (Blaylock 1994, Olney 1980) especially in conjunction with formaldehyde derived from methanol as discussed in the Methanol article.
- The study consisted of only single dose of aspartame ingestion!

This results of this study only apply to people who ingest a single dose of encapsulated aspartame while taking anti-seizure medication. Not only is this study worthless, but key information was not put in the abstract, namely, the fact that the subject were on anti-seizure medication and that the aspartame was given in capsules.

Shaywitz (1994) Flaws

- Nine out of 10 children were taking anti-seizure medication during the study.
- Again the aspartame was given in capsules at a dose of 34 mg/kg per day. This makes the experiment worthless since they were testing the hypothesis of changes in plasma phenylalanine to LNAA ratios as described above. It also reduces the toxicity of other aspartame breakdown products as described above.
- The experiment lasted only two weeks. The Rowen (1995) study used individuals who had experienced aspartame-induced seizures and it was only one day long (with other flaws described above). This short study used

epileptic children who had not reported aspartame-induced seizures. A cynic might wonder if the researchers were able to make this study slightly longer than the Rowen (1995) study because the subjects had not reported aspartame-induced seizures.

Trefz (1994) Flaws

- Like the other studies, aspartame was given in slow-dissolving capsules despite the fact that the researchers were claiming to test the effects of the spike in phenylalanine levels and the change in phenylalanine to LNAA ratios.
- The aspartame was given with meals which would further slow the absorption of aspartame breakdown products.
- This study was longer than the others, ~ 3 months. However, an analysis of seizure cases by the U.S. Centers for Disease Control (CDC 1984) shows that most seizures linked to aspartame do not begin to appear until after 3 or more months of real-world (i.e., non-encapsulated) aspartame.

What did industry scientists know or should have known?

1. These researchers must have known that administering the aspartame in capsules would mean that they were not testing the phenylalanine and LNAA changes as they claimed.
2. The researchers should have known that given encapsulated aspartame would reduced the toxicity of the methanol and the excitotoxic amino acid.
3. These researchers must have known that allowing the subjects to take anti-seizure medication during the study would drastically reduce the liklihood of seizures.

FDA Gift to Monsanto

In 1992, the FDA published an analysis of reports of seizures associated with consumption of aspartame (Tollefson 1992). The report concludes:

> "In most cases, information obtained from the complaintants' medical records as well as data on consumption patterns, temporal relationships, and challenge tests did not support the claim that the occurrences of the seizures were linked to consumption of aspartame."

Monsanto scientists repeated the FDA conclusion in their postmarketing surveillance report published in 1994 (Butchko 1994). Shaywitz (1994) also used this FDA report to bolster their conclusion.

What they do not mention is that this FDA analysis has major flaws and is provably biased, rendering it useless.

A short summary is in order for those who have not yet read the History of Aspartame Frequently Asked Questions (FAQs) report. During the FDA approval process, a number of government officials were rewarded with jobs connected to the aspartame industry (GAO 1986). This included two US Attorneys investigating the manufacturer for pre-approval research fraud who were hired by the manufacturer's law firm (one during the investigation itself). The Director of the FDA's Bureau of Foods was given a job as the Vice President of the National Soft Drink Associaton (GAO 1986). The FDA Commissioner was rewarded with a high-paying consulting position with the public relations company of the manufacturer (Burston Marsteller) not long after approving aspartame (GAO 1986). After these and other employees were given jobs related to the aspartame industry, the FDA supported the manufacturer unconditionally. The FDA redirected aspartame reaction reports to the AIDS Hotline (Turner 1987). In addition, the FDA told its regional offices to not report aspartame toxicity reactions to the Washington, D.C. headquarters (CNI 1984). The extreme FDA bias continues to this day leading some people to refer to the FDA as a Monsanto subsidiary.

Tollefson (1992) Flaws

- Tollefson inappropriately classified seizures as "Group D -- highly unlikely" related to aspartame if the subjects refused to release their medical records. This shows extreme bias as such cases would obviously be more appropriately categorized in a "possible aspartame reaction" category since the cases may or may not be caused by aspartame -- more information was needed.
- Tollefson inapropriately classified seizures as "Group D -- highly unlikely" related to aspartame if there was any possible factor in the patient's life that could have caused or contributed to those seizures. This is akin as categorizing smoking or stress as "highly unlikely" for contributing to heart disease if the patient eats a diet which could contribute to heart disease! Clearly, these patients should have been classified in a "possible aspartame reaction" category.
- The authors inappropriately declared ineligable, 35% of the non-Group D seizure victims because the seizures occured more than 13 hours after ingestion of aspartame. This is absurd because 1) it is thought that aspartame may lower the seizure threshold and therefore, aspartame-caused seizures could occur long after phenylalanine levels return to normal; 2) an animal study has shown that excitotoxins can accumulate in areas of the brain not protected by the blood brain barrier and remain there for as much as 24 hours (Inouye 1976); 3) formaldehyde adducts appear to accumulate from aspartame ingestion (Trocho 1998); and 4) a journal article immediately following this biased analysis,

Carroll (1992), points out that food reactions can be delayed up to 48 hours after ingestion!

- The authors claim that only 251 cases of seizures due to aspartame ingestion have been reported to the FDA. In reality, the FDA splits the categories into: "Seizures and Convulsions," "Grand Mal," "Petit Mal," "Complex Partial Seizures," and "Simple Partial Seizures." The 251 cases quoted by the authors referred only to the "Seizures and Convulsions" category as of 1995. There have been over 500 seizures reported to the FDA (DHHS 1995) at probably a reporting rate of far less 1% (Gold 1996) leading to well over 50,000 cases of seizures which have already been linked to aspartame consumption.
- Even with the major flaws in classifying adverse reaction reports, 76 of 251 cases were still categorized as Group A and Group B meaning that a rechallenge with aspartame lead to furthur seizures. Clearly, one cannot possibly conclude that this analysis shows no link between aspartame and seizures as implied in the abstract.

What is particularly disturbing about this analysis -- aside from its major flaws -- is that independent research was totally ignored in favor of aspartame industry-sponsored research. For example, the one-day industry study of aspartame and headache (Schiffman 1987) was listed, but not the much longer independent study (Koehler 1988). An aspartame industry-sponsored International Workshop was cited (Dews 1987), but the authors completely ignored an International Conference which invited both independent and industry researchers and which focused largely on the aspartame and seizure issue (Wurtman 1988). Most of the rest of the citations are from publications of aspartame industry-funded scientists.

Aspartame Industry Pumps Out Its Own Animal Research

Not surprisingly, the aspartame industry has its own selection animals studies which claim that aspartame does not lower the seizure threshhold (Cain 1989, Dailey 1987, Dailey 1988, Dailey 1989, Dailey 1991, Jobe 1988, Lasley 1988, Meldrum 1988, Nevins 1986, Thai 1988, Tilson 1989). The discussion sections of some of these studies and the review by Sze (1989) points to the huge doses of aspartame in rodents needed to lower the seizure threshold in many of the independent studies. The implication is that normal doses of aspartame ingested by humans could not possibly cause lower the seizure threshold.

What these researchers fail to mention is that Wurtman (1988) showed that it takes approximately 60 times more phenylalanine given to rodents to cause the changes in phenylalanine/LNAA ratio seen in humans. Therefore, the aspartame doses given to the rodents in these experiments are really not very high after

adjusting for differences between rodent and human metabolism. If the seizures from aspartame are caused by the combination of methanol/formaldehyde and the excitotoxic amino acid from aspartame as I believe may be the case, it is important to note that methanol is 10 times more acutely toxic in humans than in rodents (Roe 1982) and it takes five times more excitotoxins given to rodents to simulate human ingestion (Olney 1988, Stegink 1979, page 90).

It is also not surprising that Monsanto/NutraSweet attempted to challenge the Wurtman (1988) conclusion that it takes 60 times the dose of phenyalanine given to rodents to change the phenylalanine to LNAA ratio similar to what happens in humans (Hjelle 1992). The results in this study are ridiculous and do not even come close to matching the results of other, independent research (Perego 1988, Pinto 1988, Wurtman 1983, Yokogoshi 1984). The numerous studies that Hjelle (1992) claims their results are similar to actually have results far different. This will be discussed in more detail when the research abuses related to aspartame and phenylalanine are looked at.

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