Letters

Excitotoxic Disorders

Marcia Barinaga's article about the potential of exogenous excitatory amino acids to induce neurodegenerative diseases (Research News, 5 Jan., p. 20) needs clarification. The best studied excitotoxic disorder is lathyrism, a form of irreversible spastic paraparesis caused by excessive continuous intake of the seed of *Lathyrus sativus* (LS, known as chickling or grass pea) or other neurotoxic *Lathyrus* species (*1*). Lathyrism has affected certain European, Asian, and African populations throughout human history and is endemic today in parts of Bangladesh, Ethiopia, and India. Risk factors other than the amount of grass pea intake appear to include malnutrition, physical exhaustion, and being male. Primate studies have confirmed the likely etiological role of beta-*N*-oxalylamino-L-alanine (BOAA), a quisqualate receptor agonist present in LS seed in concentrations approximating 1% (*2*), but well-nourished macaques continuously fed either LS seed or BOAA develop only reversible clinical signs consistent with the earliest phase of the human disorder. The motor performance of subjects with long-standing lathyrism may deteriorate slowly with advancing age, but there is little evidence to suggest a progressive neuronal disorder akin to the more familiar neurodegenerative diseases such as amyotrophic lateral sclerosis (ALS). Thus, lathyrism is a largely self-limiting disease comparable to many other human neurotoxic disorders that stabilize after the culpable agent is withdrawn. Similarly, Canadians with memory and motor dysfunction following oral exposure to the kainate receptor agonist domoic acid are not likely to develop an ongoing fatal neurodegenerative disorder in forthcoming years.

By contrast, the Western Pacific ALS Parkinsonism-dementia (PD) complex is a progressive, terminal neurodegenerative disease that shows, in its various clinical and neuropathological forms, remarkable similarities to ALS, PD, and Alzheimer's disease found elsewhere. There is widespread agreement that ALS-PD is triggered by disappearing environmental factors peculiar to the life-style of the affected populations of the Marianas Islands of Guam, the Kii Peninsula of Honshu Island, Japan, and southeastern Irian Jaya, Indonesia; the weight of evidence indicates that ALS-P-D is related to use of the seed of the neurotoxic cycad plant (*Cycas* spp.) for medicine or food. Cycad seed contains about 2% cycasin, the glycone of the potent nucleic acid alkylating agent methylazoxymethanol (MAM), which has carcinogenic, teratogenic, and neurotoxic properties. MAM also methylates free amino acids to produce unknown excitotoxic agents. Beta-*N*-methylamino-L-alanine (BMAA) is a low-potency excitotoxin present (0.02%) in cycad seed. Huge subconvulsive doses of BMAA produce in macaques a constellation of clinical, electrophysiological, and neuropathological changes that shows some similarities to ALS-PD, but the changes fall short of a model of the human disease (*3*). Because BMAA is only one of several potential neurotoxins present in or generated by cycad seed, it is premature to assign a causal role to any single agent. Current research is focused on the identification of cycad chemicals that behave as "slow toxins," hypothetical substances that initiate an irreversible sequence of cellular events leading to progressive neuronal degeneration and the clinical appearance of ALS-PD years or decades later. Given that lathyrism is a largely nonprogressive disorder, exogenous slow toxins are most unlikely to act as typical excitotoxic amino acids; rather the search in cycad seed is focused on compounds that employ cell surface receptors to gain access to selected neurons, enter the cell's nucleus, and therein alter genomic expression. Because oral doses of cycasin induce muscle weakness and wasting in grazing animals, it is conceivable that human long-latency neurotoxins are masquerading as carcinogens that alkylate DNA, RNA, and proteins. The action on nondividing nerve cells of agents that induce uncontrolled division of nonneural cells is largely unexplored.

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Ads in Scientific Journals

As an editor, I took a special interest in the recent letters (2 Feb., p. 515) about *Discover's* advertisements. Both Paul Hoffman, editor of *Discover*, and Martin Gardner seem to suggest that if a journal accepts ads for questionable products, the reasons must be financial. Although financial considerations are important to any journal, I believe

the issue is more complicated. Consider, for example, advertisements for books. There are books that are above reproach, that would be enthusiastically praised by any reviewer—serious, well-written scholarly works, or carefully thought out, inspiring textbooks. Other books are clearly "bad books" that any informed scientist would label as "pseudoscientific."

Not every book, however, falls conveniently into one of these two groups. It would clearly take a multidimensional graph to plot the quality of books, but there is surely a continuum between good books and bad books. What does one say about an ad for a book that contains a few wildly speculative and irresponsible claims combined with a large number of new and apparently valid insights? What about the badly written, confusing textbook that encourages rote memorization and number-plugging, but contains no demonstrable errors of fact? Is the electromagnetic theory text that makes this beautiful subject into an undifferentiated boring collection of formulas any less dangerous to the minds of our students than one that is unambiguously pseudoscientific?

There is also, of course, a continuum in the quality of submitted manuscripts, but at the *American Journal of Physics* we make an attempt to provide a careful description of what our policy is, and we have an elaborate and time-consuming refereeing system to provide advice to the editor. Unless we are to set up a refereeing system for ads, so that every advertised book is in some sense vouched for by the editor, I do not see how I could refuse an ad for a book that is at least tangentially related to physics. Similar considerations apply to ads for other products; does the editor of *Science* guarantee the specifications of every measuring instrument advertised in its pages? This is not quite a "free speech" issue, but I would feel extremely uncomfortable if I were to reject an ad simply on the basis of my own reaction to the advertising copy.

There appears on our masthead page every month the following notice.

> It is the policy of the American Association of Physics Teachers that the Editor of the *American Journal of Physics* has responsibility for its content. The Editor has the right to refuse an announcement, advertisement, or other material he or she deems inappropriate. Acceptance of an advertisement, announcement, or other material does not imply endorsement by either the American Association of Physics Teachers or the *American Journal of Physics*.

Although I helped write those words, I intend rarely if ever to exercise that right. [Perhaps it is fortunate for my readers that I had in hand the manuscript for Martin Gardner's stimulating essay on realism—*Am. J. Phys.* **57**, 203 (1989)—before he learned of my stance on this issue.] I can imagine ads I *would* refuse, for instance ads containing language or photographs that I considered blatantly sexist or racist; but it is my present intention not to refuse advertisements, even for books that I know should never have been written and ought never to be read. (I must confess that in the current issue of *Discover* I found ads that would severely test that intention!) Nor do I have any intention of setting up a refereeing system so that we could fairly discriminate between one proffered ad and another; my reviewers and I have quite enough to do trying to make sure that fair and correct decisions are made with regard to submitted manuscripts.

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Grand Canyon Haze

Mark Crawford (News & Comment, 23 Feb., p. 911) does a creditable job of succinctly describing the complex issues surrounding the Environmental Protection Agency's (EPA's) attempts to force scrubbers on the Navajo Generating Station (NGS). It may be of further interest to explain why these issues are so complex. The basic reason is that EPA is in effect looking for a "needle in a haystack" by virtue of trying to implicate a source that at worst, may have an impact on visibility in the Grand Canyon that is so small as to be imperceptible by humans.

Simple but impressive tests have not been able to show any significant link between visibility in the Grand Canyon and power plant operations. In one such case (*1*), shutdown of a large, coal-fired power plant (the Mohave Generating Station) for over 6 months (in 1985) did not produce a detectable effect. The Mohave plant is located approximately 70 miles southwest of the Grand Canyon. At the NGS, observation of the fluctuating emissions over a continuous 4-year period (1984–1988) has also shown no correlation with visibility variations, as measured in a cooperative research program with the government (*2*).

While the massive experiments required to detect and quantify the small impact of the NGS may be grist for statisticians' mills for many years to come, we are in danger of losing sight of the real issue—haze in the Grand Canyon. Haze has always been present at times in the Canyon, but in the post–World War II years it increased, particularly in the summer months. Research clearly demonstrates the dominant impact of urban