LETTERS

Letters to the Editor

Letters (~300 words) discuss material published in *Science* in the previous 6 months or issues of general interest. They can be submitted by e-mail (science_letters@aaas.org), the Web (www.letter2science.org), or regular mail (1200 New York Ave., NW, Washington, DC 20005, USA). Letters are not acknowledged upon receipt, nor are authors generally consulted before publication. Whether published in full or in part, letters are subject to editing for clarity and space.

Retraction

WE WRITE TO RETRACT OUR REPORT "SEVERE dopaminergic neurotoxicity in primates after a common recreational dose regimen of MDMA ("ecstasy")" (*1*), following our recent discovery that the drug used to treat all but one animal in that report came from a bottle that contained (+)-methamphetamine instead of the intended drug, (±)MDMA. Notably, (+)-methamphetamine would be expected to produce the same pattern of combined dopaminergic/serotonergic neurotoxicity (*2*) as that seen in the animals reported in our paper (*1*).

The originally published report (*1*) presented results from multiple studies performed in our laboratory over a span of approximately 2 years demonstrating that a novel systemic dose regimen of what we believed was MDMA produced severe dopamine neurotoxicity in two species of nonhuman primates, in addition to the previously reported serotonin neurotoxicity (*3*–*6*). Subsequent to the publication of those findings, we were unable to extend the dopamine neurotoxicity to orally administered doses. Multiple subsequent attempts to reproduce the original findings with systemically administered doses of MDMA identical to those used in the original study were also unsuccessful, under a variety of laboratory conditions.

We then noted that our studies aimed at extending and replicating the finding of MDMA-induced dopamine neurotoxicity were performed using a new batch of MDMA. This new batch of MDMA was determined to be authentic by several methods, including gas chromatography/mass spectrometry (GC/MS).

Upon investigation of our laboratory records, we determined that the studies detailed in our paper (*1*) utilized a batch of MDMA that had been requested on the same date as a batch of (+)-methamphetamine and that both drug requests were for the same amount (10 g) and were processed by the supplier on the same day. Both drugs were delivered to our laboratory on the same day, in the same package. At delivery, the two bottles had different affixed labels, the same delivery reference number, but different batch numbers, as specified in their respective chemical data sheets. Following receipt, both drugs were stored in our laboratory in their original containers, in a locked safe.

When we began to suspect that the two bottles of drug might have borne incorrect labels [i.e., that the putative (±)MDMA was actually (+)-methamphetamine, and vice versa], we requested that a sample of the drug in the bottle bearing the original and intact label of "(+)-methamphetamine HCl" be analyzed by various analytical techniques, including GC/MS. Three independent laboratories found the sample to consist of MDMA, with no evidence of even trace amounts of methamphetamine.

Although the drug sample used in our original studies (*1*) was depleted and the empty bottle labeled MDMA had been discarded, we did have frozen brains from two animals that died shortly after drug treatment during the course of the original experiments (*1*). When these brains were analyzed by GC/MS by three independent laboratories, they were found to contain methamphetamine and its metabolite amphetamine, neither of which is a metabolite of MDMA (*7*). Not even trace amounts of MDMA or its metabolite MDA were found in these brains. Detailed review of our laboratory records revealed that all but one animal in our study (*1*) had been treated with the drug in the bottle labeled "(±)-methylenedioxymethamphetamine HCl" (MDMA) processed on the same date as the bottle labeled "(+)*d*-methamphetamine HCl."

This apparent labeling error does not call into question the results of multiple previous studies demonstrating the serotonin neurotoxic potential of MDMA in various animal species, including several nonhuman primate species (*3*–*6*, *8*). Regarding the dopamine neurotoxic potential of MDMA in nonhuman primates, it remains possible that dose regimens in the range of those used by some humans, but different from those thus far tested, produce dopamine neurotoxicity in primates, as they do in rodents (*9*, *10*). Moreover, lasting effects of MDMA on dopaminergic function in humans have recently been reported (*11*), and some humans with a history of MDMA abuse have developed Parkinsonism (*12*–*14*). However, until the dopamine neurotoxic potential of MDMA in primates can be examined more fully, this possibility remains uncertain.

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15. We gratefully acknowledge helpful discussions with J. Katz, W. L. Hearn, and N. Ator. We are also grateful for the expert chemical analytical assistance of R. Fernandez, T. L. DalCason, M. Courtney, M. Daggett, I. Carroll and associates, and R. Foltz.

Metaphors, Misuse, and Misconceptions

M. K. CHEW AND M. D. LAUBICHLER'S ESSAY "Natural enemies—metaphor or misconception?" (4 July, p. 52) is a useful representation of T. S. Eliot's famous cautionary disclaimer,

> ". . . Words strain
> Crack and sometimes break, under
> the burden,
> Under the tension, slip, slide,
> perish…" (*1*)

We need to have our word and metaphor sensors up and running. Regularly, thinking is burdened with unshapely locutions that misrepresent observations that would do quite well standing alone.

However, we should not ignore the poets and the novelists when searching for an apt descriptor. Could any of us do better than Robert Lowell when he was portraying the early manic phase of his bipolar affective disorder (formerly known as manic depressive disorder)? He rendered his state as "irritable enthusiasm." Nothing in the Diagnostic Statistical Manual even comes close.

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Reference
1. From section 5 of the poem "Burnt Norton," which appears in Eliot's *Four Quartets*.

IN THEIR EXCELLENT ESSAY ON THE (MIS)USE OF metaphorical language in science ("Natural enemies—metaphor or misconception?", 4 July, p. 52), M. K. Chew and M. D. Laubichler note that the metaphor "natural enemy" in the ecological literature should be more precisely described by terms like "parasitism" or "parasitoidy." But isn't "parasitism" an even more normative metaphor? Originally, "parasite" was the title of a highly renowned religious civil servant in attic Greece. The "parasite" was elected by the people for a specified term and looked after the corn sacrificed to the gods (Greek parasitos, literally meaning "alongside of the corn"). The term "parasite" survived through classical plays of Greek comedy originally labeling someone as a kind of blandisher or loiterer. In 1646, Sir Thomas Browne introduced the term into botany, speculating about "parasitical plants," "which live on the stock of others" (*1*). This—now ecological—metaphor was frequently exploited by political propaganda from the age of Enlightenment to present in order to denounce religious, social, or ethnical groups (*2*). Finally, in 1980, molecular biology introduced the "ultimate parasite" to its metaphorical language to highlight the concept of selfish DNA (*3*). The ongoing popularity of this exceedingly normative metaphor is probably due to the emotive tension generated by images that at first seem irreconcilable (DNA versus vermin). The emotional response generated by metaphors interpreting abstract natural phenomena in normative human terms might be a general key—to their acceptance as well as to their misconception.

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POSTMODERN PHILOSOPHERS ARE FIXATED ON scientific language (*1*). Unfortunately, in their Essay "Natural enemies—metaphor or misconception?" (4 July, p. 52), M. K. Chew and M. D. Laubichler repeatedly confuse news releases with scientific litera-

ture (evolutionary biologists do not "employ the metaphor 'survival of the fittest'"). They use loaded metaphors, such as "scientific language has never succeeded in 'cleansing' itself from metaphorical 'impurities,'" that invoke images of Nazi Germany and racism. This is demagoguery.

Chew and Laubichler primarily discuss invasive species. Geological history alternates mass extinctions with speciation. "Maximum diversity" is therefore neither "evolution's telos" nor its "tendency." Contemporary extinctions concern scientists because (i) high diversity may also enhance the ecological stability upon which human life relies, (ii) the current rate of extinction is high and steadily increasing, and (iii) invasive species are a major threat to biodiversity (*2*). Publicity materials occasionally use imprecise language when conveying this information, but how this "can have serious consequences… for the ability of scientists to comprehend ecological phenomena" is unclear.

> "Scientists often use metaphors to symbolize complex ideas, yet behavioral ecologists talk about 'arms races' without imagining deer and lions stocking nuclear weapons."
>
> –PERRY AND SCHUELER

Control efforts focus on a small minority of destructive pests, such as the brown treesnake. These are often described as having no "natural enemies," a term Chew and Laubichler object to as vague and unhelpful. Yet the phrase offers a precise inclusive description of an ecological interaction in which one species reduces the fitness of another. Terms such as "symbiosis" are in fact used to represent "natural allies."

Scientists often use metaphors to symbolize complex ideas, yet behavioral ecologists talk about "arms races" without imagining deer and lions stocking nuclear weapons. Chew and Laubichler counsel caution when using metaphors. Postmodern philosophers, deconstruct thyselves!

> "It is not evolutionary biologists 'imagining deer and lion stocking nuclear weapons' we are concerned about, but fundamentalists of all stripes seeing a supposedly scientific endorsement for their attitudes and actions."
>
> –CHEW AND LAUBICHLER

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Response

WE APPRECIATE BRÜMMER'S comment about the metaphorical origins of the term "parasite." Indeed, our argument about the double-edged role of metaphors in science could just as easily have been made about the use and abuse of the concepts of parasite or parasitism. Those studies that we criticized for their unreflective use of "natural enemies" with all the consequences outlined in our essay did, however, describe ecological relationships between organisms that exemplify a mathematically precise dynamic referred to as parasitism [e.g., (*1*, *2*)]. We agree with Brümmer that the term "parasite" has been (and is) frequently abused to advance political or social positions and that its metaphorical currency is also readily spent in other scientific contexts, such as molecular biology. We intended our essay to stimulate exactly the kind of discussion about the rich historical and metaphorical origins of scientific concepts that Brümmer provided, and we hope that this is not the last contribution to this debate.

As Perry and Schueler misrepresent the views expressed in our article, we will briefly revisit two of our arguments in the context of his comments.

First, we argued that metaphorical language is both necessary for and dangerous to scientific research—necessary because it allows us to conceptualize new and/or complex phenomena, and dangerous, because if we, as scientists, are careless in applying metaphors, we invite their misrepresentation. Perry argues that such misrepresentation and exaggeration is an inevitable function of "publicity material," suggesting that it does not affect the development of scientific work. For better or worse, scientists, like anyone else, are also prone to

believing their own press releases. The story of how "invasive species" became the "second greatest threat to biodiversity" is a revealing case. Originally proposed in 1992 by E. O. Wilson (*3*), based on a vast intuitive extrapolation from unpublished data about North American fishes, the idea's emotional appeal allowed it to "blossom" into dogma without rigorous quantitative support (*4*). That dogma is only gradually being reevaluated [e.g., Davis (*5*), whom Perry and Schueler cite but also seem to misapprehend].

Second, in the case of "natural enemies," we are particularly concerned that the reification of this category as a naturally occurring object (again without any precise definition of how, for instance, one species lowers the fitness of another species or what the fitness of a species actually is) contributes to dangerous misunderstandings of ecological and evolutionary processes. It is not evolutionary biologists "imagining deer and lions stocking nuclear weapons" we are concerned about, but fundamentalists of all stripes seeing a supposedly scientific endorsement for their attitudes and actions.

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CORRECTIONS AND CLARIFICATIONS

Reports: "A microRNA as a translational repressor of *APETALA2* in *Arabidopsis* flower development" (*Science* Express, published online 31 July; 10.1126/science.1088060). The author has noted an error in the paper. In engineering silent mutations into the miRNA172 binding site in the AP2 cDNA—to abolish miRNA-binding but not change the amino acid of the protein (and therefore not affect its function or stability)—an amino acid change was inadvertently introduced (Phe to Leu at codon seven in Fig. 1). Experiments are under way to determine whether this mistake changes the conclusions of the paper.

TECHNICAL COMMENT ABSTRACTS

COMMENT ON "Molecular Correlates of Primate Nuclear Transfer Failures"

R. Lanza, Y. Chung, M. D. West, K. H. S. Campbell

Simerly *et al.* (Brevia, 11 April 2003, p. 297) reported important new data but have overstated their conclusions. They transferred only 33 primate embryos and concluded that reproductive cloning with current approaches may be unachievable. We suggest that conclusions regarding the efficiency of human cloning extrapolated from animal data be tempered with abundant caution.

Full text at www.sciencemag.org/cgi/content/full/301/5639/1482b

RESPONSE TO COMMENT ON "Molecular Correlates of Primate Nuclear Transfer Failures"

G. Schatten, C. Navara, C. Payne, S. Capuano, G. Gosman, K.-Y. Chong, D. Takahashi, C. Chace, D. Compton, L. Hewitson, T. Dominko, C. Simerly

Space constraints precluded publication of aligned chromosomes on bovine nuclear transfer (NT) mitotic spindles—a condition not seen after rhesus NT. Without benefit of this knowledge, Lanza *et al.* fairly raise the uncertainty in extrapolating results between species. Regardless, realizing the medical potential of stem cells requires further studies, as well as consideration of the peer-reviewed data.

Full text at www.sciencemag.org/cgi/content/full/301/5639/1482c

COMMENT ON "Hexapod Origins: Monophyletic or Paraphyletic?"

Frédéric Delsuc, Matthew J. Phillips, David Penny

Nardi *et al.* (Reports, 21 March 2003, p. 1887) suggested that extant hexapods might be diphyletic based on the analysis of amino acid sequences of mitochondrial genes. However, improved phylogenetic analyses of nucleotide sequences (RY-coding) from the same genes consistently retrieve the classical hypothesis of hexapod monophyly.

Full text at www.sciencemag.org/cgi/content/full/301/5639/1482d

RESPONSE TO COMMENT ON "Hexapod Origins: Monophyletic or Paraphyletic?"

Francesco Nardi, Giacomo Spinsanti, Jeffrey L. Boore, Antonio Carapelli, Romano Dallai, Francesco Frati

Reanalyses of our data set that more explicitly models among-site rate variation continue to support the view that Collembola are basal to the assemblage of other hexapods and crustaceans. However, further taxon sampling along with improved methods of analysis will be required for a completely convincing reconstruction of arthropod relationships.

Full text at www.sciencemag.org/cgi/content/full/301/5639/1482e