Correction

LETTER (ONLINE ONLY). For the letter "Reply to Blazer *et al.*: Flawed challenges to 'Acetylcholinesterase inhibitors and Gulf War illnesses'," by Beatrice A. Golomb, which appeared in issue 33, August 19, 2008, of *Proc Natl Acad Sci USA* (105:E53; first published August 11, 2008; 10.1073/pnas.0805246105), the author notes that the following sentences were omitted from the end of the first paragraph of the letter: "Their statements are counter to fact. They mischaracterize the evidence, employ the introduction of irrelevant material, and exemplify flaws in inference, as I will illustrate." The corrected letter appears below.

LETTER

Reply to Blazer *et al.*: Flawed challenges to ''Acetylcholinesterase inhibitors and Gulf War illnesses''

Blazer *et al.* (1) challenge my PNAS article (2) connecting acetylcholinesterase inhibitor (AChEi) exposure and Gulf War veterans' (GWV) illness (GWI). Their statements are counter to fact. They mischaracterize the evidence, employ the introduction of irrelevant material, and exemplify flaws in inference, as I will illustrate.

Excess amyotrophic lateral sclerosis (ALS) in GWV was not represented as central to the inferences drawn (ref. 2, p. 4299); moreover, the ALS excess is shown by not one but three independent studies (3–5) (including two in the supporting information). Although rarity of ALS reduces power for risk factor identification, mounting evidence supports a role for AChEi-relevant exposures (pesticides, paraoxonase genotypes regulating organophosphate detoxification) in sporadic ALS (6–8). While ALS remains rare and not a dominant contributor to neurological deaths, a significant ALS excess is still important.

Lack of EMG/NCV abnormalities "in numerous large, representative, controlled, investigations" of GWV (for which they cite one study with 49 symptomatic veterans) is incompatible how? No evidence suggests that EMG/NCV abnormalities follow low-level AChEi exposure either.

The assertion that the article did not "pay any attention to recall bias" in epidemiological studies is false: I expressly stated "the results may be influenced by self-report bias" (p. 4295) (subsuming recall bias) and also exposed other study flaws that "limit confidence in causal inferences across AChEi classes from epidemiological studies viewed in isolation" (p. 4296). Moreover, when airing relative advantages of genetic/enzyme studies, I note that those are (in contrast) "difficult to ascribe to recall or reporting bias" (p. 4296).

I agree that my conclusions differed from prior reports. It is true too that I considered only original evidence and not opinion or authority: the mischaracterizations of the article throughout by Blazer *et al.* (1) ably illustrate why, when primary sources are available, secondary representations of evidence should be eschewed.

Beatrice A. Golomb*
Department of Medicine, University of California at San Diego, La Jolla, CA 92093-0995

1. Blazer D, *et al.* (2008) Acetylcholinesterase inhibition and Gulf War illnesses: Conclusions are not supported by independent reviews of the same evidence. *Proc Natl Acad Sci USA* 105:E20.
2. Golomb BA (2008) Acetylcholinesterase inhibitors and Gulf War illnesses. *Proc Natl Acad Sci USA* 105:4295–4300.
3. Haley RW (2003) Excess incidence of ALS in young Gulf War veterans. *Neurology* 61:750–756.
4. Horner RD, *et al.* (2003) Occurrence of amyotrophic lateral sclerosis among Gulf War veterans. *Neurology* 61:742–749.
5. Coffman CJ, Horner RD, Grambow SC, Lindquist J (2005) Estimating the occurrence of amyotrophic lateral sclerosis among Gulf War (1990–1991) veterans using capture–recapture methods. *Neuroepidemiology* 24:141–150.
6. Slowik A, *et al.* (2006) Paraoxonase-1 Q192R polymorphism and risk of sporadic amyotrophic lateral sclerosis. *Clin Genet* 69:358–359.
7. Saeed M, *et al.* (2006) Paraoxonase cluster polymorphisms are associated with sporadic ALS. *Neurology* 67:771–776.
8. Morahan JM, Yu B, Trent RJ, Pamphlett R (2007) A gene-environment study of the paraoxonase 1 gene and pesticides in amyotrophic lateral sclerosis. *Neurotoxicology* 28:532–540.

Author contributions: B.A.G. wrote the paper.

The author declares no conflict of interest.

*To whom correspondence should be addressed. E-mail: bgolomb@ucsd.edu.

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Author contributions: B.A.G. wrote the paper.

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