



PTSD and Vietnam Veterans

Eric Vermetten, *et al.*

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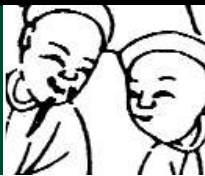
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LETTERS

edited by Etta Kavanagh

PTSD and Vietnam Veterans

IN HIS PERSPECTIVE "PSYCHIATRIC CASUALTIES OF WAR" (18 AUG., P. 923), R. J. McNALLY NOTES THAT a new study by B. P. Dohrenwend *et al.* ("The psychological risks of Vietnam for U.S. veterans: a revisit with new data and methods," Reports, 18 Aug., p. 979) revised downward from 15.2 to 9.1% the rates of chronic posttraumatic stress disorder (PTSD) from the Vietnam War estimated by the National Vietnam Veterans' Readjustment Study (NVVRS). He notes that this "confirmed the suspicions of the skeptics" but fails to observe that the new study confirmed that the 2.2% prevalence rate reported by the U.S. Centers for Disease Control (CDC) (1) was a serious underestimate.

In numbers, this new rate means that 236,000 veterans currently have PTSD from the Vietnam War, an enormous long-term emotional and human cost of war. Recently, the director of the National Center for PTSD warned about the "psychiatric cost" of deployment in war zones,

noting that we "underestimate the eventual magnitude of this clinical problem" (2). The Ex-Services Mental Welfare Society "Combat Stress" group in the United Kingdom saw 944 new referrals last year, an increase of 40% in recent years (3). The average period between discharge from the military and first contact was 12.7 years.

McNally cited a study (4) of 100 treatment-seeking veterans, claiming that only 41% of them had documented "combat exposure." Another 52% had

clearly served in Vietnam, but "combat exposure status (was) unclear (20)" or there was "no evidence of combat exposure (32)" [(4), table 1, p. 469]. Given the general unreliability of military records in a war zone, the old statistical rule that "absence of proof is not proof of absence" applies. We want to stress that the nature of modern warfare, evident in the current news, is such that danger and destruction do not occur only in places designated as "combat zones."

Lastly, in addition to Dohrenwend *et al.*'s valuable service, we think it is time that scientists design studies to increase the accuracy of our prevalence estimates by applying the knowledge of over two decades of research that includes measures of biomarkers. Studies like Dohrenwend *et al.*'s in combination with new knowledge about neurobiological correlates of PTSD will contribute to science and help us to plan effectively to treat the true costs of war.

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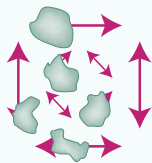
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I WISH TO CORRECT A MISCHARACTERIZATION OF my position that R. J. McNally made in his Perspective, "Psychiatric casualties of war" (18 Aug., p. 923). McNally stated that, in a column I wrote (1) as president of the International Society of Traumatic Stress Studies (ISTSS), I "urged critics to muffle their dissent, lest the intensity of scientific controversy distract us from attending to the needs of trauma victims." I did not say that we should stifle critics or scientific dissent. I specifically stated that "research and treatment ideas benefit from being subjected to the crucible of criticism via the scientific method" (1). As someone who has been conducting traumatic stress research for almost 30 years, I have consistently argued that good research is the best way to resolve controversial policy issues and that researchers also have a duty to report research results responsibly and accurately (2).

McNally's Perspective did not provide a balanced assessment of B. P. Dohrenwend *et al.*'s findings ("The psychological risks of Vietnam for U.S. veterans: a revisit with new data and methods," Reports, 18 Aug., p. 979), which refuted most of the prior criticisms of the National Vietnam Veterans' Readjustment Study (NVVRS). Instead, McNally focused on a misleading comparison of PTSD prevalence estimates for the entire NVVRS sample with those obtained from a clinically assessed subsample of the NVVRS that used extremely conservative criteria to determine PTSD status. Dohrenwend *et al.*'s findings show that NVVRS critics [e.g., (3-5)] were wrong when they argued that only veterans in combat roles could experience war zone stressors sufficient to produce PTSD and that veterans' reports of exposure to war zone stressors could not be independently verified.

McNally states that Frueh *et al.* (6) consulted "the same archival sources" as Dohrenwend *et al.* However, Dohrenwend *et al.*'s verification procedures were much more rigorous than Frueh *et al.*'s. McNally also stated that Frueh *et al.* were only able to verify combat exposure in 41% of veterans. This is true but misleading in that 93% of veterans had documented service in Vietnam. Dohrenwend *et al.*'s findings suggest that exposure to war zone stressors, not





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just combat stressors, increases risk of PTSD, so the latter percentage is more applicable than the former.

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THE REPORT "THE PSYCHOLOGICAL RISKS OF Vietnam for U.S. veterans: a revisit with new data and methods" by B. P. Dohrenwend et al. (18 Aug., p. 979) and the accompanying Perspective "Psychiatric casualties of war" by R. J. McNally (18 Aug., p. 923) confirm what many in the academic community suspect about the epidemiological estimates of posttraumatic stress disorder (PTSD) generated by the National Vietnam Veterans' Readjustment Study (1): that the estimates are unreasonably high and uncorroborated by other scientific evidence. Indeed, a less frequently cited study commissioned by the U.S. Centers for Disease Control (CDC) yielded a modest estimate of PTSD in veterans (2). Looking at the data presented by Dohrenwend et al. (Table 1), one might argue that the new estimates are still high if "impairment" is a key criterion in defining disability.

Missing from the analyses of Dohrenwend et al. and McNally is the concern that PTSD as a construct is not well supported by data reduction techniques such as principal components analysis. Also absent from the discussion was the fact that clinical trials with civilians reveal that psychiatric symptoms secondary to trauma, when present, are quite responsive to treatment; yet, the largest treatment outcome study commissioned by the Department of Veterans Affairs (VA) revealed almost no salutary impact on symptoms in veterans with PTSD (3). Research on the effects of the VA disability system suggests that the current treatment and disability programs for PTSD promote disincentives

for veterans to work toward functional outcomes, while at the same time promoting incentives to report psychiatric symptoms (4). It may be time for the VA to disassemble its current PTSD programs and embrace programs that promote rehabilitation and functional outcomes rather than disability. Our returning veterans deserve the promise of a productive future beyond a disability paycheck. Such a change will not be politically popular, but it will be scientifically defensible.

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IN THEIR REPORT "THE PSYCHOLOGICAL RISKS OF Vietnam for U.S. veterans: a revisit with new data and methods" (18 Aug., p. 979), B. P. Dohrenwend et al. provide startling new data from their re-analysis of the National Vietnam Veterans' Readjustment Study (NVVRS), which indicate surprisingly little current impairment in Vietnam veterans with lifetime or current combat-related posttraumatic stress disorder (PTSD). The measure of functioning they used was a 9-point Likert-scale clinician rating, ranging from a high level of functioning, that is, "good functioning in all areas" to the lowest level, that is, "persistent danger to self or others." The scale is heavily skewed toward identifying impairment—all but the highest value represent some degree of compromised functioning—yet very few of the veterans were rated at the lower end of the scale.

Among veterans with lifetime (but not current) PTSD, over 90% were rated within the top three categories of functioning; none were rated in any of the four lowest categories. As Dohrenwend et al. note, this level of functioning was as good as that of the "no-PTSD" group. It seems appropriate to conclude that veterans who recovered from

PTSD were functioning approximately at levels comparable to the general population.

Veterans with current PTSD at the time of the survey evidenced greater functional impairment. However, even among these current cases, only a small minority (7.4%) were rated in any of the four lowest categories of functioning; the majority (55.6%) experienced only slight impairment or some difficulties in role functioning.

Disability claims and payments to the Department of Veterans Affairs (VA) for combat-related PTSD, predicated on severe functional impairment, have risen dramatically and asymmetrically since 1999 (1). These new data suggest that the VA is further justified in its current review, in consultation with the Institute of Medicine, of its existing disability policies and procedures.

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Response

ACCORDING TO DOHRENWEND ET AL.'S reanalysis, the National Vietnam Veterans' Readjustment Study (NVVRS) (1) overestimated the prevalence of posttraumatic stress disorder (PTSD) by 40%, thereby confirming the central claim of its critics. Moreover, contrary to what Kilpatrick states, Dohrenwend et al. did not use "extremely conservative criteria to determine PTSD status." Instead, they accepted a case as PTSD-positive if the veteran received a score from one through seven on the nine-point Global Assessment of Functioning (GAF) scale. Nine is the highest possible level of functioning, whereas one is the lowest. The typical (apparent) PTSD case received a GAF score of seven, defined as "[s]ome difficulty in social, occupational, or school functioning, but generally functioning pretty well, has some meaningful interpersonal relationships OR some mild symptoms (e.g., depressed mood and mild insomnia, occasional truancy, or theft within the household)" [(2), p. 2]. Clearly, a seven does not indicate clinically significant impairment, as noted by Buckley. Had they been slightly more stringent (i.e., GAF rating from one through six), the prevalence would have dropped by 65%, not 40%. Thus, the estimate for current (late 1980s) prevalence would have been 5.4%—substantially lower than either Dohrenwend et al.'s estimate of 9.1% or the original NVVRS estimate of 15.2%. But even this

figure is more than twice as high as the 2.2% rate reported by the U.S. Centers for Disease Control (CDC) (3). The flawed methods of the CDC study almost certainly underestimated the true prevalence of PTSD, as emphasized by Vermetten *et al.* and many other PTSD experts (as I mentioned in my Perspective).

Kilpatrick misunderstands other criticisms of the NVVRS. The critics never claimed that self-reports of traumatic events could not be independently verified; they complained that the NVVRS researchers had not verified them. Moreover, the critics never claimed that only those serving in combat roles could be exposed to PTSD-inducing danger. Rather, the critics were puzzled how 53.4% of male veterans could develop either partial or full-blown PTSD when only between 12.5% (4) and 15% (5) had served in direct combat roles (e.g., infantry rifleman) and when the vast majority of individuals exposed to traumatic events, including combat (6), do not develop PTSD (7). As everyone, including me (8), acknowledges, those serving in other capacities sometimes got in harm's way. Nevertheless, as the dose-response effect implies, combat infantrymen were more at risk than supply clerks working at airbases.

To corroborate reports of trauma exposure, Dohrenwend *et al.* used a range of indicators, most of which were obtainable from veterans' DD-201 personnel files. When the DD-201 was ambiguous, they consulted additional archival sources. Using the DD-201 files, Frueh *et al.* (9) corroborated the trauma reports of only 41% of 100 men recently seeking treatment for PTSD. Although Vermetten *et al.* question the adequacy of military records, Dohrenwend *et al.* found the DD-201 to be a very useful corroborative source. It is unclear whether further archival inquiry would have increased the number of corroborated cases in Frueh *et al.*'s study. Frueh *et al.* found that many uncorroborated cases reported events seemingly inconsistent with their DD-201 file (e.g., uncorroborated cases reported exposure to battlefield atrocities at twice the rate of corroborated cases).

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 through the Web (www.submit2science.org) or by 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.

Finally, Kilpatrick says that I mischaracterized his views as expressed in his essay entitled "Our Common Bonds" (10). Likening our field to a "family" that often quarrels, Kilpatrick surmises that trauma victims, whose welfare constitutes our common bond, "would rather see us work together than to squabble and bicker." And despite his mentioning the importance of critique in science, he contradicts himself in his take-home message: "In my view, our field would do well to focus more on our common bonds and less on our differences." But if we downplay our differences, muffle our dissent, or curb our critique, studies like Dohrenwend *et al.*'s might never get launched.

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Response

IN HIS PERSPECTIVE ON OUR REPORT, McNally nominated as our "most newsworthy" finding the discrepancy between our somewhat lower rates of posttraumatic stress disorder (PTSD) and the original National Vietnam Veterans' Readjustment Study (NVVRS) rates (1). Buckley commends us for findings that he suggests indicate that the NVVRS estimates "are unreasonably high and uncorroborated by other scientific evidence." This choice of emphasis is highly selective and ignores considerations that are more important than our differences with the original NVVRS rates.

First, the discrepancies are attributable to differences in the definitions of disorder rather than to inflationary measurement error in the original NVVRS rates. To estimate rates of first onsets of war-related PTSD and rates of these onsets that were current at follow-up 10 to 12 years after the war, we used diagnostic histories obtained by experienced NVVRS clinicians from a subsample of the

veterans. By contrast, self-report symptom scales were used in the full-sample NVVRS measure to provide a less time-consuming and expensive approximation of current PTSD. This approximation did not specify whether or not PTSD was war-related. However, if you take the NVVRS rate of 2.5% current PTSD for veterans who did not serve in Vietnam as an estimate of non-combat-related current PTSD, double it as per the 2:1 ratio of lifetime to current PTSD (see our Table 2 and the original NVVRS rates showing this ratio), and subtract the resulting rates from the original NVVRS 30.9% lifetime and 15.2% current PTSD rates, the result is 25.9% lifetime and 12.7% current war-related PTSD. These rates are very close to our war-related PTSD rates before adjustments for impairment and documentation of exposure (see our Table 2). This correspondence is what you would expect if, as was its aim, the NVVRS symptom scales were successfully calibrated against the subsample diagnoses.

Second, skepticism about the NVVRS rates has been stimulated by a number of factors: the discrepancy with much lower rates reported in a CDC study (2), a belief that only 15% of Vietnam veterans saw combat [e.g., (3)], and the related assumption that many veterans were either fabricating their combat experiences or that the dose-response relation between self-reports of exposure and PTSD risk was due to recall bias [e.g., (4-6)]. We pointed out that the CDC measure grossly underreports diagnosable PTSD [(7), Appendix E]. We demonstrated that the prevalence of combat exposure was much higher than 15% in this "war without fronts" (8). We found little evidence of fabrication. We showed that our record-based measure of severity of exposure to war-zone stressors, which is independent of veterans' reports of their combat experiences, is positively associated with self-reported exposure and with clinical diagnoses of PTSD. The dose-response relationship with this record-based measure of exposure is strong evidence of the validity of war-related PTSD and, we think, our most important finding.

When the NVVRS was conducted, a PTSD diagnosis did not require, as it does now, the presence of impaired functioning. Skeptics speculated that the PTSD symptoms measured in the NVVRS might indicate relatively mild psychological distress rather than true disorder [e.g., (9)]. The subsample diagnoses included ratings of severity and impairment useful for addressing this question. Frueh interprets our findings on functioning as indicating "surprisingly little current

impairment” among veterans with war-related PTSD. However, our results in Table 1 are for impairment at time of diagnosis, 10 to 12 years after the war. As we show, the large majority of war-related PTSD involved substantial impairment when the disorder was at its worst, even for veterans whose onsets had remitted (our Report and SOM text). We concluded that the Vietnam War took a severe psychological toll on U.S. veterans.

An epidemiological study like ours cannot speak to the treatment and compensation issues raised by Buckley and Frueh. Follow-up of the NVVRS sample could, however, provide longitudinal information on the natural history of this disorder that would be invaluable for our understanding of the nature of war-related PTSD and the factors that reduce its psychological costs.

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Disbelievers in Evolution

IN THEIR POLICY FORUM “PUBLIC ACCEPTANCE OF EVOLUTION” (11 Aug., p. 765), J. Miller, E. Scott, and S. Okamoto show that Americans are less likely to accept evolution than citizens of other industrial nations, and that U.S. attitudes are strongly tied to fundamentalist religious beliefs. This replicates earlier results (1). They hint that American views on evolution may be related to political liberalism and conservatism.

The validity of their conjecture can be seen in earlier surveys. In 1993, 1994, and 2000, the General Social Surveys asked

how true is the statement, “Human beings evolved from earlier species of animals.” Of 3673 American respondents offering an opinion, a majority (53%) called the statement definitely or probably not true (2). Respondents also reported their political views, ranging from extremely liberal to extremely conservative. Political liberals were significantly more likely than conservatives to believe that humans evolved.

In Fig. S1 (3), the percentage of respondents believing in human evolution is plotted simultaneously against political view (conservative, moderate, liberal), education (high school or less, some college, graduate school), and respondent's religious denomination (fundamentalist or not) (2). Belief in evolution rises along with political liberalism, independently of control variables.

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3. See Supporting Online Material available at www.sciencemag.org/cgi/content/full/315/5809/187a/DC1.

TECHNICAL COMMENT ABSTRACTS

COMMENT ON “A Common Genetic Variant Is Associated with Adult and Childhood Obesity”

Christian Dina, David Meyre, Chantal Samson, Jean Tichet, Michel Marre, Beatrice Jouret, Marie Aline Charles, Beverley Balkau, Philippe Froguel

Herbert *et al.* (Reports, 14 April 2006, p. 279) reported an association between the *INSIG2* gene variant rs7566605 and obesity in four sample populations, under a recessive model. We attempted to replicate this result in 10,265 Caucasian individuals, combining family-based, case-control, and general population studies, but found no support for a major role of this variant in obesity.

Full text at www.sciencemag.org/cgi/content/full/315/5809/187b

COMMENT ON “A Common Genetic Variant Is Associated with Adult and Childhood Obesity”

Ruth J. F. Loos, Inês Barroso, Stephen O'Rahilly, Nicholas J. Wareham

Herbert *et al.* (Reports, 14 April 2006, p. 279) found that the rs7566605 genetic variant, located upstream of the *INSIG2* gene, was consistently associated with increased body mass index. However, we found no evidence of association between rs7566605 and body mass index in two large ethnically homogeneous population-based cohorts. On the contrary, an opposite tendency was observed.

Full text at www.sciencemag.org/cgi/content/full/315/5809/187c

COMMENT ON “A Common Genetic Variant Is Associated with Adult and Childhood Obesity”

Dieter Rosskopf, Alexa Bornhorst, Christian Rimbach, Christian Schwahn, Alexander Kayser, Anne Krüger, Grietje Tessmann, Ingrid Geissler, Heyo K. Kroemer, Henry Völzke

Contrary to the findings of Herbert *et al.* (Reports, 14 April 2006, p. 279), homozygous carriers of the C allele of the rs7566605 variant near the *INSIG2* gene did not exhibit a significantly increased risk for obesity in a large population-based cross-sectional German study. A subgroup analysis, however, revealed that this allele significantly increased the risk for obesity in already overweight individuals.

Full text at www.sciencemag.org/cgi/content/full/315/5809/187d

RESPONSE TO COMMENTS ON “A Common Genetic Variant Is Associated with Adult and Childhood Obesity”

Alan Herbert, Norman P. Gerry, Matthew B. McQueen, Iris M. Heid, Arne Pfeufer, Thomas Illig, H.-Erich Wichmann, Thomas Meitinger, David Hunter, Frank B. Hu, Graham Colditz, Anke Hinney, Johannes Hebebrand, Kerstin Koberwitz, Xiaofeng Zhu, Richard Cooper, Kristin Ardlie, Helen Lyon, Joel N. Hirschhorn, Nan M. Laird, Marc E. Lenburg, Christoph Lange, Michael F. Christman

Identification of genetic variants affecting complex traits such as obesity is confounded by many types of bias, especially when effect sizes are small. Given our findings of a positive association between rs7566605 and body mass index in four out of five separate samples, a false positive finding cannot be ruled out with certainty but seems unlikely. Meta-analyses of multiple large studies will help refine the estimate of the effects of rs7566605 on body mass index.

Full text at www.sciencemag.org/cgi/content/full/315/5809/187e

CORRECTIONS AND CLARIFICATIONS

Reports: “Relating three-dimensional structures to protein networks provides evolutionary insights” by P. M. Kim *et al.* (22 Dec. 2006, p. 1938). In note 32, the funding acknowledgment should read, “This work was supported by NIH grants N01-HV-28186 and RR19895.” Additionally, on page 1939, a maximum degree of 14 was reported for the SIN v1; this number refers to an earlier version of the SIN (v0.9). The SIN v1 as reported in the paper has one node with a degree of higher than 14. All versions of the SIN and current statistics on them are available at <http://SIN.gersteinlab.org>.

Special Section: Breakthrough of the Year: “Minute manipulations” (22 Dec. 2006, p. 1855). This item incorrectly described Piwi-interacting RNAs (piRNAs) as binding to Piwi genes, when in fact piRNAs bind to Piwi proteins.

Perspectives: “The brain's dark energy” by M. E. Raichle (24 Nov. 2006, p. 1249). The author's affiliation was incorrect. It should be Department of Radiology, Washington University School of Medicine, St. Louis, MO 63110, USA. E-mail: marc@npg.wustl.edu.