

# Physiological Evidence of Exaggerated Startle Response in a Subgroup of Vietnam Veterans With Combat-Related PTSD

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*One of the diagnostic criteria for posttraumatic stress disorder (PTSD) is an exaggerated startle response; however, this phenomenon has not been verified empirically. The authors compared 20 Vietnam combat veterans with PTSD and 18 combat veterans without PTSD on the eyeblink reflex electromyographic response of the startle reaction. Subjects in both groups who failed to show an eyeblink response to the startle stimuli were eliminated from further analyses. Among the remaining subjects, the 13 with PTSD had a significantly greater startle response amplitude than the 12 control subjects at intermediate intensities of acoustic stimuli. The relationship between startle responsivity and both negative and positive symptoms was also investigated.*

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The introduction of posttraumatic stress disorder (PTSD) into the psychiatric nomenclature was accompanied by conflicting opinions over the validity of the diagnosis. Now, nearly 10 years later, PTSD remains in the diagnostic nosology (*DSM-III-R*), and there is evidence that Vietnam combat veterans may be at high risk for developing the disorder (1). Empirical studies suggest that there are significant differences between veterans with PTSD and both psychiatric control groups (2) and veterans who have had equal exposure to combat but have not sought psychiatric help (3). In general, these findings suggest that the development of chronic PTSD may be influenced by the veteran's degree of combat exposure, substance abuse, and experience of adverse events upon returning to the United States. Furthermore, in reviewing research on the MMPI and combat-related PTSD, Penk et al. (4)

found a relatively high degree of consistency in MMPI profiles across varying samples of subjects. Thus, a considerable amount of evidence has been accumulated in support of the overall validity of PTSD as a diagnostic entity. Much of this evidence, however, is based on self-report measures.

One of the critical symptom clusters necessary for a diagnosis of PTSD involves the persistent presence of increased arousal. Specific criterion symptoms are difficulty sleeping, irritability/anger, difficulty concentrating, hypervigilance, exaggerated startle response, and physiological reactivity upon exposure to events or thoughts similar to those during the traumatic event (*DSM-III-R*). The last two criteria are particularly important because they can be confirmed without using self-report measures. Furthermore, the first three criteria overlap considerably with symptoms of major depressive disorder.

Increased physiological reactivity to events or thoughts relating to the trauma in PTSD has been well researched. There is well-documented evidence of higher heart rate, skin conductance, blood pressure, respiration, and electromyographic (EMG) activity under conditions of reexposure in PTSD patients than in control subjects (5-8). Kolb (9) hypothesized that these results suggest the possibility of a subgroup of combat veterans who suffer from a chronic form of PTSD characterized by persistent conditioned emotional responsivity and perceptual abnormalities. Further evidence supporting this idea was reported by Mueser and Butler (10), who identified a small subgroup of chronic PTSD patients who manifested auditory hallucinations in the absence of other evidence of a psychotic process. These patients also reported significantly greater amounts of arousal than did nonhallucinating PTSD patients. While considerable effort has been directed toward verifying increased physiological reactivity, remarkably little work has been directed toward validating the presence of exaggerated startle responses in PTSD.

Landis and Hunt (11) reported that the human startle response can be reliably and validly measured by monitoring the amplitude of eyeblinks elicited by acoustic stimuli, the eyeblink being the major measurable component of the startle reflex in human beings. Other researchers have verified eyeblink amplitude as a

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valid measure of startle responsivity (12, 13) and pointed out this measure's methodological advantages (14). Additionally, evidence has suggested that the eyeblink startle reflex in response to acoustic tones may be associated with affect and is relatively independent of generalized arousal at the time of measurement (15).

Given that an apparently valid and reliable physiological measure of startle reactivity exists, use of this measure would appear to be an excellent way in which to empirically verify exaggerated startle responses in persons with chronic combat-related PTSD. In reviewing the literature, however, we were unable to locate any study that had directly investigated these responses in such subjects. We hypothesized that Vietnam combat veterans with chronic PTSD would exhibit larger eyeblink responses to startling acoustic or tactile (air puff) stimuli than would combat veterans without PTSD. The clinical observations of exaggerated startle responsivity might reflect lowered thresholds for startle rather than increases in the magnitude of responses to normally startling stimuli. Hence, the study was designed also to test the hypothesis that veterans with chronic PTSD would exhibit measurable startle responses at lower sound intensities than those required for eliciting startle responses in veterans without PTSD. We further hypothesized that PTSD patients with exaggerated startle responses would also show evidence of greater perceptual abnormalities.

## METHOD

Data were initially collected on 56 veterans screened for potential entry into the study. Eighteen of these veterans were eliminated from the study for one or more of the following reasons: 1) no combat experience, 2) suspected presence of schizophrenia, psychosis, or major affective disorder, 3) history of significant head trauma or other neurological impairment, and 4) inability to provide discharge papers or other independent verification of service in Vietnam. Thus, the remaining 38 subjects had verified service in Vietnam, did not report histories of major neurological disturbance, and did not meet criteria for an additional clinically significant *DSM-III-R* axis I disorder. Additional diagnoses were verified by administering to all subjects the Schedule for Affective Disorders and Schizophrenia—Change Version (SADS-C) (16). Each subject was also rated with the Scale for the Assessment of Negative Symptoms (17) and the Scale for the Assessment of Positive Symptoms (18).

All of the subjects were nonhospitalized men recruited from a local veterans' center who were tested after they responded to an advertisement for research volunteers. The entire procedure lasted 2–3 hours, and each subject was paid \$5 per hour for participation. Descriptive data concerning the subjects' characteristics are presented in table 1.

Of the 38 veterans who met the inclusion criteria for the study, 20 met the *DSM-III-R* criteria for chronic

TABLE 1. Characteristics of Combat Veterans With and Without Diagnoses of PTSD Who Were Tested for Startle Response

Characteristic	PTSD Subjects (N=20)			Control Subjects (N=18)		
	N	Mean	SD	N	Mean	SD
Age (years)	—	40.2	3.3	—	40.9	4.4
Education (years)	—	13.6	2.2	—	13.3	2.2
Unemployed	14	—	—	9	—	—
Race/ethnicity						
Black	4	—	—	1	—	—
Hispanic	1	—	—	1	—	—
White	15	—	—	16	—	—
Service branch						
Marines	9	—	—	3	—	—
Army	9	—	—	9	—	—
Navy	1	—	—	5	—	—
Air force	1	—	—	1	—	—
Months in Vietnam	—	15.4	7.8	—	13.2	8.3
Self-report on current alcohol use (1–9, Likert scale)	—	2.6	2.2	—	2.8	2.1

PTSD that was clearly combat-related. The other 18 were used as control subjects because they did not have diagnoses of PTSD. Diagnoses were made by the first author on the basis of clinical interviews and the subjects' responses to a PTSD symptom checklist (2). At the time of diagnosis, the first author was blind to the startle and other symptom variables.

As an independent check on diagnostic validity, the subjects also completed the Mississippi Scale for Combat-Related Posttraumatic Stress Disorder (19). The groups were significantly different on this measure in the expected direction (mean±SD score=119.94±14.30 for the PTSD subjects and 88.30±8.95 for the control subjects;  $t=7.2$ ,  $df=36$ ,  $p<0.001$ ). The PTSD group also had a significantly higher mean±SD score on the Vietnam Combat Exposure Scale (20) than the control group (PTSD group, 5.80±0.75; control group, 3.89±1.05;  $t=6.3$ ,  $df=36$ ,  $p<0.001$ ). This finding was not unexpected, as degree of combat exposure is highly predictive of PTSD symptoms in Vietnam veterans (2).

All subjects were given a brief hearing test with a Saico SCR-2 audiometer to ensure that their auditory abilities were intact. For the startle response measurement, after the subject was seated comfortably, two Beckman miniature silver/silver chloride electrodes were positioned below and to the right of his right eye, over the orbicularis oculi muscle. Electrode placement was selected so as to minimize potential electro-oculograph (EOG) artifact. Specifically, one electrode was positioned 1 cm lateral to and ½ cm below the lateral canthus, and the other electrode was placed 1½ cm below and slightly medial to the first electrode. Placement was such that the electrodes were equidistant from the center of the eye and as close to each other as possible; Beckman adhesive collars were used. Additionally, recorded EMG activity was high-pass filtered (1–1,000 Hz) to minimize EOG artifact. A 60-Hz notch filter was also used to eliminate 60-Hz interference. A ground electrode was placed behind the right

## EXAGGERATED STARTLE RESPONSE IN PTSD

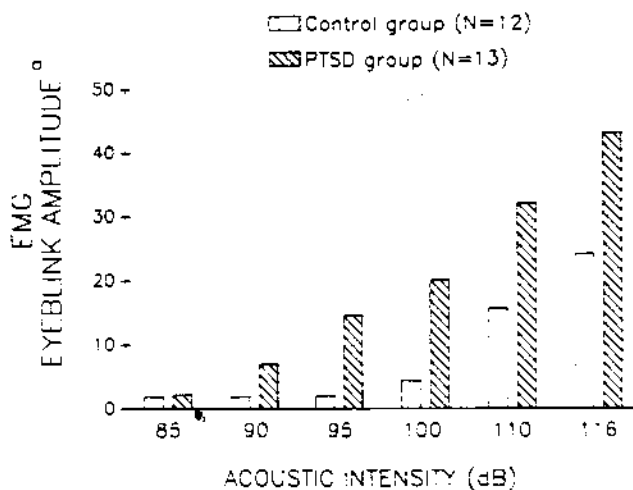
ear over the mastoid. EMG activity recorded by the electrodes was directed through a custom-made EMG amplifier (21) to a computerized startle response monitoring system (SR-LAB, San Diego Instruments, Inc.) for digitization and analysis. The system permanently recorded 250 1-msec readings starting at the onset of the startle stimulus. The software parameters by which voluntary and spontaneous eyeblinks were recognized and excluded have been described in detail elsewhere (13). The magnitude of each startle response was defined as the largest of the peak values beginning between 20 and 80 msec after the onset of the startle stimulus, expressed in digital units (each unit = 15  $\mu$ V).

Acoustic startle stimuli were presented binaurally through Telephonics (model TDH-39-P) headphones. Each test session began with a 5-minute acclimation period consisting of 70-dB(A) broadband noise, which continued throughout the session. The session had two components, one acoustic and one tactile. In the first component, seven different trial types were presented in a pseudorandom order, each trial type occurring six times. Although the order of trials was randomized within each subject's test session, it did not vary across subjects. Thus, all subjects were tested under identical conditions. Six of the trial types presented 40-msec noise bursts at different sound levels: 85, 90, 95, 100, 110, and 116 dB(A). The seventh trial type presented a 20-msec burst of 85-dB(A) noise (prepulse) 120 msec before the 116-dB(A) startle stimulus. Such a prepulse stimulus normally inhibits the response to a subsequent startle stimulus, a phenomenon referred to as prepulse inhibition (12); it was included as a confirmatory test of the subjects' ability to detect the relatively weak 85-dB(A) stimulus. The background noise and acoustic stimuli were generated by the SR-LAB system and measured with a calibrated Quest sound pressure level meter (model 215). Sound level was calibrated on a monthly basis by means of a 6-cc coupler in an artificial ear (model EC-9A) and continuous noise.

In the second component of the session, 30-psi air puffs (40 msec in duration) were presented to the subject's neck through a small rubber tube. A total of 30 air puff trials were presented. Air pressure delivery was regulated at the air supply. The internal tube diameter was 4 mm, and the end of the tube was placed approximately 5 mm from the subject's suprasternal notch. On 10 of these trials, the 85-dB(A) prepulse stimulus was presented 120 msec before the air puff. Again, all subjects were tested under identical conditions during this component. The interval between trials in both components varied from 9 to 23 seconds, with a mean interval of 15 seconds.

As in other studies of human startle response (22), in some subjects in each group there was a relative lack of eyeblink EMG activity elicited by the startle stimulus. Therefore, the subsequent analyses of startle data did not include data from these subjects. The criterion for inclusion in the subsequent analyses was an eyeblink EMG amplitude of 8 units or more in the 116-dB(A)

FIGURE 1. Startle Response Reactivity in Subjects With Combat-Related PTSD and in Control Subjects



\*Expressed in digital units (1 unit = 15  $\mu$ V).

condition. Thirteen (65%) of the 20 PTSD subjects and 12 (67%) of the 18 control subjects were responders, suggesting no appreciable differences between groups in responsivity to the startle paradigm.

## RESULTS

For the 25 responders, eyeblink EMG amplitudes for the six different acoustic intensities were analyzed by the nonparametric Mann-Whitney U test, as variances were quite heterogeneous across the PTSD and control groups. Startle reactivity data for the two groups are presented in figure 1. The two groups were not significantly different in eyeblink EMG amplitude in the 85-dB(A) and 90-dB(A) conditions, but the PTSD group exhibited significantly higher eyeblink EMG amplitudes than the control group at 95 dB(A) ( $U=123$ ,  $N=25$ ,  $p=0.01$ ) and 100 dB(A) ( $U=124$ ,  $N=25$ ,  $p=0.01$ ). While the PTSD group continued to manifest higher EMG amplitude than the control group in the 110-dB(A) and 116-dB(A) conditions, these differences did not achieve significance at the designated alpha criterion of  $p=0.01$  (corrected for familywise error rates). The 85-dB(A) prepulse effectively reduced the startle response to the subsequent 116-dB(A) stimulus in both the PTSD and control groups; mean  $\pm$  SD = 65.0%  $\pm$  28.9% and 40.0%  $\pm$  86.7%, respectively. Within each group, these amounts of prepulse inhibition were statistically reliable (binomial probability,  $p<0.001$ ). The two groups did not differ significantly on this measure of prepulse inhibition.

In the second component of the test session, no significant differences were found between the two groups of subjects in their response to tactile startle stimuli. In this component only two subjects in each group were nonresponders (i.e., eyeblink EMG ampli-

tude < 8 units, or 120  $\mu$ V, in response to the air puffs). For the remaining subjects, the mean  $\pm$  SD responses to the 20 tactile trials were  $32.6 \pm 32.1$  and  $32.4 \pm 23.5$  units for the PTSD and control groups, respectively. Comparable results were found when only the subjects who were responders in the acoustic component were examined (PTSD group,  $41.5 \pm 33.7$  units; control group,  $33.5 \pm 26.1$  units). Similarly, both groups exhibited robust amounts of prepulse inhibition: the 85-dB(A) prepulse inhibited the response to the air puffs by  $63.4\% \pm 29.2\%$  in the PTSD group and  $41.6\% \pm 38.8\%$  in the control group (binomial probability for each group,  $p < 0.01$ ). These group means did not differ significantly.

Within the PTSD group, the acoustic startle responders and nonresponders were compared on the Scale for the Assessment of Negative Symptoms to determine whether nonresponsivity to the startle paradigm was associated with negative symptoms such as greater levels of emotional numbing, withdrawal, and affective blunting. This difference approached significance ( $U = 71$ ,  $N = 25$ ,  $p = 0.04$ ), with the responders showing evidence of more negative symptoms (mean  $\pm$  SD =  $13.9 \pm 11.0$ ) than the nonresponders ( $4.9 \pm 4.2$ ). The difference between the acoustic startle responders and nonresponders also approached statistical significance ( $U = 69$ ,  $N = 25$ ,  $p = 0.07$ ) on the Scale for the Assessment of Positive Symptoms, with the responders having a higher mean  $\pm$  SD score ( $8.4 \pm 6.4$ ) than the nonresponders ( $2.9 \pm 3.9$ ), indicating greater levels of perceptual aberration and atypical thought.

## DISCUSSION

The results of this study provide empirical evidence for increased startle reactivity in a subgroup of veterans with chronic, combat-related PTSD. It appears that the startle threshold for acoustic stimuli may be reduced in PTSD. The significant differences between the PTSD and control groups were found with 95- and 100-dB(A) acoustic stimuli; neither lower nor higher intensities resulted in statistically reliable differences in startle response magnitudes. There was a trend, however, for the PTSD group to respond with exaggerated responses to the more intense acoustic stimuli. With tactile stimuli, the two groups exhibited virtually identical startle response magnitudes. This unexpected result may be a reflection of stimulus-specific increased startle reactions in persons with combat-related PTSD. This interpretation has clinical appeal, since many veterans report that auditory stimuli, such as an automobile "backfire," will result in an exaggerated startle response. An alternative hypothesis, however, may be that as the strength of the eliciting stimuli increases, all subjects begin to show exaggerated startle responses. Thus, nonsignificant differences between the groups on the relatively strong tactile stimuli may be consistent with the lack of statistically significant differences in response to the more intense acoustic stimuli. Fur-

ther research will be required in order to address these possibilities.

In both the acoustic and tactile components of the test session, an 85-dB(A) prepulse stimulus was effective in inhibiting the startle response. These results confirm that there was no difference between groups in subjects' ability to perceive and respond to the 85-dB(A) noise bursts. Although we had screened all subjects for hearing difficulties, the demonstration of prepulse inhibition confirms the sensitivity of the subjects to stimuli that were qualitatively similar to those used to elicit startle responses in the same test session. Hence, the differences in the responses of the PTSD and control groups to 95- and 100-dB(A) stimuli are unlikely to have been due to differences in hearing thresholds. More detailed analyses using larger samples and startle responses in a measurable physiological paradigm such as ours will be needed to confirm the specificity of the apparent change in acoustic startle response threshold. It is too early to state whether the measure we used will have diagnostic utility, although the results are encouraging. Before criterion cutoff levels of startle reactivity can be determined, we need to extend the database and cross-validate the findings of this study. Nevertheless, our results provide initial evidence to support the exaggerated startle responses reported by many patients with combat-related PTSD.

In addition to the data on startle reactivity, the issue of responsivity to the startle paradigm in PTSD may be of interest. Research on unmedicated schizophrenic subjects (23) has suggested that physiological nonresponsivity to measures such as skin conductance tends to be associated with more negative symptoms (e.g., affective blunting, social withdrawal). To the extent that nonresponsivity on the startle paradigm might mirror other physiological modalities, PTSD appears to be characterized by a converse phenomenon. Specifically, the PTSD subjects in this study who were responders tended to have a greater degree of negative symptoms than the nonresponders. It should be noted that the responders and nonresponders were not significantly different on other variables, including self-report about substance abuse.

The fact that the PTSD responders manifested an exaggerated startle response and a strong trend toward more positive symptoms (e.g., perceptual aberration, atypical thought) is quite consistent with Kolb's hypothesis (9) that a subgroup of patients with chronic, combat-related PTSD have persistent emotional hyperresponsivity and perceptual abnormalities. Kolb also proposed that central adrenergic overactivity might mediate these symptoms, and our results provide indirect support for this possibility. Certainly, central catecholaminergic neurotransmitters have been implicated in the modulation of startle reactivity in animal studies (24, 25). Our inferences, however, assume that startle responsivity is correlated with other indexes of physiological responsivity. This is a speculation that needs empirical verification. The relationship between physiological variables and symptom clusters in PTSD

appears to be complex, but our results suggest that this relationship may be meaningful. Continued data collection, including neurotransmitter metabolite measurements, may be fruitful.

Several cautions should be raised regarding our results. We purposely restricted the number of statistical comparisons and raised the alpha level to help compensate for familywise error rates. Nevertheless, the sample size was modest, and the results need to be replicated. Additionally, we attempted to ensure that our control group had been exposed to combat, and all subjects reported some degree of combat involvement. The PTSD group, however, had significantly greater combat exposure than the control group, and this remains a potential confounding factor. As our work has progressed, we have also become increasingly dissatisfied with simple self-report about substance abuse; thus, we do not think that questions of how alcohol and other drug abuse might have influenced our results were adequately addressed. More sophisticated and detailed measures of substance abuse are needed to answer these questions.

Finally, we are again struck by the apparent high base rates of PTSD in Vietnam combat veterans who are not psychiatrically hospitalized. In this study approximately 50% of the subjects met the *DSM-III-R* criteria for PTSD. Previous studies (3, 26) have also documented the high prevalence of PTSD in outpatient and nonpsychiatric veterans. It is important to attempt to collect information on Vietnam veterans with high combat exposure who do not have PTSD to fully understand etiological factors in this disorder.

## REFERENCES

1. Kaylor JA, King DW, King LA: Psychological effects of military service in Vietnam: a meta-analysis. *Psychol Bull* 1987; 102: 257-271
2. Foy DW, Sippelle RC, Rueger DB, et al: Etiology of posttraumatic stress disorder in Vietnam veterans: analysis of premilitary, military, and combat exposure influences. *J Consult Clin Psychol* 1984; 52:79-87
3. Butler R, Foy DW, Snodgrass L, et al: Combat-related posttraumatic stress disorder in a nonpsychiatric population. *J Anxiety Disorders* 1988; 2:111-120
4. Penk W, Keane T, Robinowitz R, et al: Posttraumatic stress disorder. in *The MMPI: Use With Specific Populations*. New York, Grune & Stratton, 1988
5. Kolb LC, Maltipassi LR: The conditioned emotional response: a sub-class of the chronic and delayed post-traumatic stress disorder. *Psychiatr Annals* 1982; 12:979-987
6. Blanchard EB, Kolb LC, Pfallmeyer TP, et al: A psychophysiological study of posttraumatic stress disorder in Vietnam veterans. *Psychiatr Q* 1982; 54:220-229
7. Blanchard EB, Kolb LC, Gerardi RJ, et al: Cardiac response to relevant stimuli as an adjunctive tool for diagnosing posttraumatic stress disorder in Vietnam veterans. *Behavior Therapy* 1986; 17:592-606
8. Pitman RK, Orr SP, Forgue DF, et al: Psychophysiological assessment of posttraumatic stress disorder imagery in Vietnam combat veterans. *Arch Gen Psychiatry* 1987; 44:970-975
9. Kolb LC: A neuropsychological hypothesis explaining posttraumatic stress disorders. *Am J Psychiatry* 1987; 144:989-995
10. Mueser KT, Butler RW: Auditory hallucinations in combat-related chronic posttraumatic stress disorder. *Am J Psychiatry* 1987; 144:299-302
11. Landis C, Hunt WA: *The Startle Pattern*. New York, Farrar & Rinehart, 1939
12. Hoffman HS, Ison JR: Reflex modification in the domain of startle. I: some empirical findings and the implications for how the nervous system processes sensory input. *Psychol Rev* 1980; 87:175-189
13. Graham FK: The more or less startling effects of weak prestimuli. *Psychophysiology* 1975; 12:238-248
14. Braff DL, Geyer MA: Sensorimotor gating and schizophrenia: human and animal model studies. *Arch Gen Psychiatry* 1990; 47:181-188
15. Vrana SR, Spence EL, Lang PJ: The startle probe response: a new measure of emotion? *J Abnorm Psychol* 1988; 97:487-491
16. Spitzer RL, Endicott J: *Schedule for Affective Disorders and Schizophrenia—Change Version, 3rd ed.* New York, New York State Psychiatric Institute, Biometrics Research, 1978
17. Andreasen NC: *Scale for the Assessment of Negative Symptoms (SANS)*. Iowa City, University of Iowa, 1984
18. Andreasen NC: *Scale for the Assessment of Positive Symptoms (SAPS)*. Iowa City, University of Iowa, 1984
19. Keane TM, Caddell JM, Taylor KL: *Mississippi Scale for Combat-Related Posttraumatic Stress Disorder*: three studies in reliability and validity. *J Consult Clin Psychol* 1988; 56:85-90
20. Lund M, Foy DW, Sippelle RC, et al: The Combat Exposure Scale: a systematic assessment of trauma in the Vietnam war. *J Clin Psychol* 1984; 40:1323-1328
21. Fridlund AJ, Price AW, Fowler SC: Low noise, optically isolated electromyographic preamplifier. *Psychophysiology* 1982; 19: 701-705
22. Geyer MA, Braff DL: Habituation of the blink reflex in normals and schizophrenics. *Psychophysiology* 1982; 19:1-6
23. Venables PH: Cerebral mechanisms, autonomic responsiveness, and attention in schizophrenia, in *Theories of Schizophrenia and Psychosis*. Lincoln, University of Nebraska Press, 1984
24. Davis M: Neurochemical modulation of sensory-motor reactivity: acoustic and tactile startle reflexes. *Neuroscience Biobehavioral Reviews* 1980; 4:241-263
25. Davis M, Astrachan D, Kehne J, et al: Catecholamine modulation of sensorimotor reactivity measured with acoustic startle, in *Catecholamines: Neuropharmacology and Central Nervous System—Theoretical Aspects*. Edited by Usdin E, Carlsson A, Dahlstrom A, et al. New York, Alan R Liss, 1984
26. Card JJ: *Lives After Vietnam: The Personal Impact of Military Service*. Lexington, Mass, Lexington Books, 1983