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13. ABSTRACT *(Maximum 200*

Over the past four years we followed Desert Storm veterans from two Connecticut National Guard units. Studies focused on the evolution of trauma-related symptoms and the longitudinal consistency of memory for traumatic events. Results indicate an increase in PTSD symptoms among Desert Storm veterans over the first two post-war years. Level of combat exposure was significantly associated with Mississippi score at two years but not at one and six months. There were many instances of inconsistent recall for highly traumatic events. The same methodology will be continued for the eighth post-war year.

The second part of the grant is based on findings in Vietnam War veterans who underwent memory testing and MRI. Veterans with PTSD had an 8% decrease in right hippocampal volume relative to healthy subjects. Deficits in short-term verbal memory were associated with decreased right hippocampal volume in PTSD patients. Data suggest broad-based memory problems associated with decreased hippocampal volume. Twenty Desert Storm veterans with PTSD will be compared to 20 Desert Storm Veterans without PTSD and 20 non-deployed National Guard Reservists. Results of this study would help determine whether these abnormalities are present across combat populations.

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FOREWORD

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5. Introduction:

DoD grant " Psychological and Neurobiological Consequences of the Gulf War Experience" examines memory function, hippocampal volume, and the evolution of trauma-related symptoms in veterans of Operation Desert Storm. Based on previous work it was predicted that memory dyfsunction and reduction in hippocampal volume would be present in Desert Storm veterans with PTSD and that memory for traumatic events in many veterans of the Gulf war would lack consistency over time. It was further predicted that levels of trauma-related symptomatology would gradually increase over time. It was not possible to predict when the level of trauma-related symptoms would plateau. The purpose of the study was to better understand the natural course of trauma-related symptoms and to further delineate potential alterations in memory that typically accompany trauma. The grant is divided into two parts. The title of the first part is " Longitudinal Course of Trauma-Related Symptomatology. The title of the second part is " Memory Function and Hippocampal volume."

6. Body:

Thus far we have completed two manuscripts as part this DoD grant.
Both manuscripts involve Part I of the grant on the evolution of trauma-related symptoms. We have appended a copy of one manuscript that has recently been published.

The first manuscript, " Anniversary Reactions in Veterans of Operation Desert Storm, " recently has been published in the American Journal of Psychiatry. Please see appended copy of the published manuscript. The goal of this study was to assess the occurence of anniversary reactions in Gulf War veterans six years after the conclusion of the war. Subjects were administered questionnaires and asked to identify specific months of best and worst functioning and months of least and most symptoms of posttraumatic stress disorder for the twelve months before the study. Months of negative experiences were compared with previously documented dates of exposure to traumatic events during the war. Similar reports were also obtained from veterans' spouses in order to assess corroborative evidence for the occurrence of anniversary reactions. Anniversary reactions occurred with a frequency greater than chance and most often in individuals exposed to a greater number of traumatic events. Overall, spouse reports matched the veterans' reports of anniversary reactions. In addition, spouses identified anniversary reactions that were not endorsed by their veterans. These data suggest that anniversary reactions occur in numbers greater than those expected by chance, are correlated with the occurrence of traumatic events and may be part of the syndrome of PTSD.

The second manuscript " Inconsistency of memory for traumatic events: Replication and clarification six years after the Gulf War." is about to be submitted for publication. Six years after returning from the Gulf, subjects completed questionnaires about current trauma-related symptoms and about traumatic events experienced during Operation Desert Storm. Subjects had completed the same questionnaire one and again two years

after the Gulf War. All subjects had one or more inconsistencies in their reports of previously experienced traumas. Inconsistencies were noted on the Desert Storm Trauma Questionnaire and on the Combat Exposure Scale. Inconsistencies were noted for both objective and subjective events. Individuals with a greater number of PTSD symptoms were more likely to change their reports of exposure to trauma (up and down) compared to those veterans with fewer symptoms. Subjects provided multiple explanations for changes in their 1 month, 2 year and 6 year reports.

With regard to Part II of the grant, " Memory function and hippocampal volulme, thus far we have nearly completed data collection. In our grant application, we proposed to study 20 Desert Storm veterans who met criteria for PTSD, 20 Desert Storm veterans who did not meet criteria for PTSD and 20 National Guard reservists who did not serve in the Gulf War and who did not meet criteria for any axis I DSM-IV disorder.. All subjects were to receive SCID diagnostic testing, a battery of neuropsychological tests that focused on memory function and an MRI to measure volume of the hippocampus and comparison brain structures. It was hypothesized that hippocampal volume would be smaller and that memory dysfunction would be present in Desert Storm veterans with PTSD compared to the other two study groups. Thus far we have completed data collection for 12 Desert Storm veterans with PTSD, 20 Desert Storm veterans without PTSD and 20 national guard reservists who did not serve in the Gulf War. We have had greatest difficulty in recruiting veterans with PTSD compared to those without PTSD because only 7-9% of veterans in our previous Gulf War studies have met criteria for PTSD and because some veterans with PTSD have pronounced symptoms of hypervigilance and avoidance which keeps them from signing up for the study. Over the last year we have expanded our recruiting efforts and currently have 5 veterans with PTSD who have expressed strong interest in the study and have either been enrolled in the study or are in the process of enrolling. We will begin data analysis as soon as data collection is complete.

7. Key Research Accomplishments

Thus far the following key research accomplishments have emanated from this work:

1. Anniversary reactions were identified by Desert Storm veterans and their spouses. This report represents some of the only empirical data available in the scientific literature on anniversary reactions. These reactions occurred with greater frequency than chance and were most often observed in veterans exposed to a greater number of traumatic events. The data suggest that anniversary reactions may be part of the syndrome of PTSD.

2. Comparisons of 1month, 2 year and 6 year reports of exposure to traumatic events revealed one or more inconsistencies for each of 32 Desert Storm veterans. Inconsistencies were noted for objective and subjective events and were noted on both the Desert Storm Trauma Questionnaire and the Combat Exposure Scale. Individuals with a greater number of post-traumatic stress disorder symptoms were more likely to change their reports of exposure to trauma (up or down) compared to those veterans with fewer symptoms. Subjects presented multiple explanations for

the inconsistencies in reporting. However, most subjects had doubts about their explanations. This data adds to our understanding of memory for traumatic events.

3. The MRI and memory portion of the grant will add to our understanding of the hypothesized relationship between severe psychological trauma, hippocampal volume, memory function and PTSD.

8. Reportable outcomes:

1. Morgan CA III, Hill S, Fox P, Kingham P, Southwick SM: Anniversary reactions in Gulf War Veterans: A follow-up inquiry 6 years after the war. American Journal of Psychiatry 156, 1075-107: 1999.
2. Southwick SM, Morgan CA III, Vojvoda D, Lipschitz D: Stress effects of the Persian Gulf War. In Fink,G (ed) Encyclopedia of Stress. Academic Press, San Diego. In press.
3. Morgan CA III, Southwick SM: Inconsistency of memory for traumatic events: Replication and clarification six years after the Gulf War. In preparation
4. Southwick SM: Inconsistency of memory for combat trauma in veterans of Operation Desert Storm. Presentation at the International Society for Traumatic Stress Studies meeting November, Montreal Canada, November, 1997
5. Southwick SM, Morgan CA III: Memory for traumatic events. Presentation at the Yale Department of Psychiatry Grand Rounds, New Haven, Connecticut, April, 1998

9. Conclusions:

Thus far the results of data collected as part of this grant have provided empirical evidence for anniversary reactions in war veterans. These data add to the understanding of the longitudinal effects of war-related traumas. The data also have treatment implications. It is likely that learning about and recognizing anniversary dates can help veterans to better understand and control their psychological distress. Thus, relapse prevention treatment models may benefit by instructing patients to anticipate anniversaries. Through anticipation and preparation it may be possible to lessen the deleterious effects of recurrent exacerbation in PTSD symptoms.

Our report on inconsistency in reporting of traumatic events has relevance for the understanding of the nature of memory for stressful events. The data suggest that inconsistencies in reporting of traumatic events is common among healthy non-treatment seeking veterans. The majority of subjects in this study inconsistently reported at least some aspect of their traumatic experiences. The data suggest that inconsistencies in reports of trauma should not be viewed as evidence that an individual is unreliable or failing to tell the truth.

10. References: See section # 8 Reportable Outcomes

11. Appendices:

1. Morgan CA III, Hill S, Fox P, Kingham P, Southwick SM: Anniversary reactions in Gulf War Veterans: A follow-up inquiry 6 years after the war. American Journal of Psychiatry 156, 1075-107: 1999.
2. Southwick SM, Morgan CA III, Vojvoda D, Lipschitz D: Stress effects of the Persian Gulf War. In Fink,G (ed) Encyclopedia of Stress. Academic Press, San Diego. In press.

13. Final Report: Not applicable.

Anniversary Reactions in Gulf War Veterans: A Follow-Up Inquiry 6 Years After the War

Charles A. Morgan III, M.D., M.A., Susan Hill, C.I.S.W., Patrick Fox, M.D., Peter Kingham, B.A., and Steven M. Southwick, M.D.

Objective: The goal of this study was to assess the occurrence of anniversary reactions in Gulf War veterans 6 years after the conclusion of the war. **Method:** Subjects were administered questionnaires and asked to identify specific months of best and worst functioning and months of least or most symptoms of posttraumatic stress disorder (PTSD) for the 12 months before the study. Months of negative experiences were compared with previously documented dates of exposure to traumatic events during the war. Similar reports were also obtained from the veterans' spouses in order to assess corroborative evidence for the occurrence of anniversary reactions. **Results:** Anniversary reactions occurred with a frequency greater than chance and most often in individuals exposed to a greater number of traumatic events. Overall, spouse reports matched the veterans' reports of anniversary reactions. In addition, spouses identified anniversary reactions that were not endorsed by their veterans. **Conclusions:** These data suggest that anniversary reactions occur in numbers greater than those expected by chance, are correlated to the occurrence of traumatic events, and may be a part of the syndrome of PTSD.

(Am J Psychiatry 1999; 156:1075–1079)

An anniversary reaction has been described as a specifically timed, emotionally invested episode during which an individual experiences significant psychiatric or medical symptoms (1). It has been theorized that individuals suffering from such reactions have been sensitized by exposure to a specific traumatic event and that the effects of this sensitization are experienced later under circumstances that are reminiscent of the event. A review of the literature suggests that authors have differed quite significantly in their opinions about which circumstances or triggers are more important in precipitating anniversary reactions. While some have placed emphasis on the patient's age, others have focused on the date and nature of the stressful event (2–6). Regardless of emphasis, there is a consensus that the patient's distress is meaningfully connected to a specific, previously experienced traumatic event (1, 2, 4, 7–10).

Despite limited empirical data on anniversary reactions, it has become routine for many war-related posttraumatic stress disorder (PTSD) treatment programs to ask veterans about combat traumas and corresponding annual exacerbations of psychiatric symptoms (personal communication from American Lakes Program, Tacoma, Wash.; PTSD Program, Veterans Administration [VA] Medical Center, West Haven, Conn.; PTSD Program, Menlo Park VA Medical Center, Palo Alto, Calif.). It is believed that by learning about and recognizing anniversary dates, veterans can better understand, and control, their psychological distress. Models of treatment meant to prevent relapse instruct patients to anticipate anniversaries so that PTSD symptoms can be dealt with more effectively.

To date, only two longitudinal studies have empirically examined the timing of, and the symptoms experienced during, anniversary reactions to traumatic events. In the first, Borstein and Clayton (11) interviewed 92 widows and widowers on the first anniversary of their spouse's death and identified anniversary reactions in four subjects. Each subject suffered from clinically significant depression and identified the anniversary date as the nidus of his or her psychological distress. While the study is promising, it has been difficult to interpret the precise meaning or implication of these data, since the incidence of anniversary reactions in this study is well within the range of occurrences that would be expected by chance (N=7.6).

Received May 15, 1998; revision received Nov. 30, 1998; accepted Jan. 4, 1999. From the Department of Psychiatry, Yale University School of Medicine, New Haven, Conn.; the National Center for Post Traumatic Stress Disorder, VA Medical Center; and the State University of New York at Stony Brook, Long Island. Address reprint requests to Dr. Morgan, 116A, VA Medical Center, 950 Campbell Ave., West Haven, CT 06516; charles.a.morgan@yale.edu (e-mail).

In the second study (12), we investigated the frequency of anniversary reactions in a group of Gulf War veterans 2 years after the war. Veterans were invited to report on their psychological symptoms during the year (12 months) before their participation in the study. Each was asked to select, if applicable, the month during the previous year when he or she felt the worst and the month, if applicable, when he or she experienced the most stress symptoms (i.e., the specific PTSD symptoms according to DSM-III-R). If either of these months corresponded with the date during which a veteran experienced his or her most traumatic event while in the Persian Gulf, then the veteran was identified as having an anniversary reaction. Of the 59 subjects who participated in the study, 18 had anniversary reactions, twice the number that would be expected by chance. Moreover, veterans with anniversary reactions were more symptomatic on measures of PTSD compared with veterans who did not have anniversary reactions. This study was limited by the absence of third-party reports and by the fact that the veterans were asked about functioning and dates of trauma in the same setting.

The present study is a follow-up to our previous investigation of anniversary reactions in Gulf War veterans. It is also part of a larger investigation that has focused on the evolution of trauma-related symptoms in Gulf War veterans (13, 14). Using questionnaires based on DSM-III-R nosology, the current study evaluated the relationship between traumas experienced during the Gulf War and the timing and nature of postwar psychiatric distress.

More specifically, the current follow-up investigation was designed to evaluate whether anniversary reactions would still be present in the individuals who had them at the 2-year evaluation, determine whether the occurrence of anniversary reactions at 6 years would exceed that expected by chance, assess whether anniversary reactions would be found in individuals with greater levels of PTSD symptoms, and understand the relationship between the reports provided by the veterans and those provided by the veterans' spouses. The rationale for examining the relationship between anniversary reactions and the level of PTSD symptoms was based on the findings of a previous study indicating that individuals with anniversary reactions also exhibited more PTSD symptoms (12). Self-report data were compared with spouse report data in order to evaluate whether anniversary reactions were observable by others.

In order to minimize bias in their reporting, the veterans were not asked about, nor asked to provide a date of, trauma. Instead, this information was obtained from the initial questionnaires completed by the veterans in May 1991—1 month after their return from the Gulf War.

METHOD

The subjects of the study were a subgroup of 119 soldiers, who, during their first monthly training session after the Gulf War, were recruited from two Connecticut Army Reserve units (the 142nd Medical and the 143rd Military Police) to participate in a longitudinal study of war-related symptoms (14, 15). Fifty-nine soldiers continued to participate in the longitudinal study at 2 years and were the subjects of our previous investigation of anniversary reactions to war-related stressors (12). Thirty-two of the 59 were available at the 6-year time point. Each had been a subject in previous investigations at our site (12–14). Subjects were contacted by telephone and agreed to participate in the current investigation. All subjects gave written informed consent.

Measures

As reported in the investigation of the 2-year time point (12) to assess emotional functioning within the past 12 months, subjects were asked to indicate during which month of the previous year they had felt the best and during which month they had felt the worst. Additionally, each subject was asked to indicate during which month, if any, he or she experienced the most stress-related symptoms—i.e., the 17 symptoms of DSM-III-R for PTSD. Subjects also rated the month during which they experienced the least stress-related symptoms.

The initial questionnaire was administered in 1991, 1 month after their return from the war. Subjects had been asked to give the date and description of the most traumatic event they had experienced during their tour in the Persian Gulf. In this report, unlike in the previous report, subjects were not asked about the date of their most traumatic event so as not to create bias. Instead, the date noted in their original 1991 surveys, which specified his or her most traumatic event, was used to determine the presence or absence of anniversary reactions.

As in the earlier investigation, an anniversary reaction was defined as either 1) a match between the month of the most severe war-related traumatic event and the month identified as worst during the previous year or 2) a match between the month of the most severe war-related traumatic event and the month during which PTSD specific symptoms were most prominent. All subjects completed the questionnaires as well as the interviews during August and September 1997. Neither of these months corresponded to the dates of military deployment or to exposure to military trauma.

Subjects were also administered the PTSD Symptom Scale (13, 14), a valid self-report inventory consisting of 35 items derived from DSM-III-R. It provided a measure of both frequency and intensity of PTSD symptoms within the 30 days before participation in the study. After completing the questionnaire, subjects participated in a direct interview with the principal investigator (C.A.M.). Each was asked about his or her responses to the questionnaire in order to gain a more complete understanding of the nature of the responses.

Finally, married subjects or those who lived with a significant other were given a questionnaire for his or her spouse or significant other to fill out without the veteran's assistance. The questionnaire was identical to the one given the veterans, except that it asked the spouse to identify which months, if any, over the past year the veteran had felt the best and the worst and had experienced the least and most symptoms of stress.

Data Analysis

Since an anniversary reaction was defined as either a match between the date of most severe trauma and the month of feeling worst or a match between the date of trauma and the month of greatest PTSD-specific symptoms, there was a two in 12 (17%) probability that an anniversary reaction would exist by chance alone. The number of anniversary reactions within the group as a whole, and within each unit, was compared with this probability factor in order to determine whether these matches occurred at a greater frequency than that expected by chance.

Data from the 6-year time point were compared with data from the 2-year time point in order to determine whether identified cases

were new or chronic in nature. Comparisons between the 2- and 6-year data also permitted a determination as to whether any of the identified anniversary reactions at 2 years no longer existed at 6 years. We performed t tests between the total PTSD Symptom Scale scores to determine whether individuals with anniversary reactions differed from unit members without anniversary reactions.

Finally, spouse reports were examined in order to determine whether there was agreement between the veteran and his or her spouse about the existence of anniversary reactions. The number of anniversary reactions identified by the spouse only—and not the veteran—was also calculated.

RESULTS

In the total group (N=32), the observed number of subjects who had an anniversary reaction at 2 years was 12. The observed number of subjects in the group who had anniversary reactions at 6 years was also 12 (38%). This was more than twice the number of occurrences (N=5.4, 17%) that would be expected by chance alone. Eight of the 12 cases identified at the 6-year time point represented chronic cases, whereas four were new.

Within the group of 20 subjects who were from a medical unit, one would expect 3.4 anniversary reactions by chance alone. By contrast, 10 subjects selected a month corresponding to his or her previously identified date of trauma. This occurrence was three times greater than that expected by chance. Similarly, in the group of subjects from a military police unit (N=12), one would expect two anniversary reactions because of chance alone. Within this group, only two subjects selected a month corresponding to their identified date of trauma. Thus, the occurrence of anniversary reactions was greater than that expected by chance in the group of veterans as a whole and in the group from the medical unit but not in the group from the military police unit.

Comparisons of the total PTSD scores between the group of individuals with anniversary reactions and the group without anniversary reactions (mean=12.7, SD=12.6, and mean=5.8, SD=1.3, respectively) revealed a statistically significant effect of group ($t=-2.07$, $df=30$, $p<0.05$). Thus, individuals with anniversary reactions had more symptoms of PTSD than those who did not have anniversary reactions. In the group as a whole, only four (12.5%) of the 32 subjects met the criteria for PTSD on the PTSD Symptom Scale. All four of these subjects with PTSD were identified as having anniversary reactions.

In 11 of 12 subjects with an anniversary reaction, the associated trauma involved witnessing the death or serious injury of another human being. Exposure to mines while in a war zone constituted the associated trauma for the remaining subjects who had anniversary reactions.

Thirteen of the 32 subjects were married. Of these, five reported anniversary reactions. Four of the five respective spouses matched their veteran's report and identified their veteran as suffering from an anniversary reaction. The spouse whose report did not match that of her veteran identified her husband as suffering from an anniversary reaction during the month of February—not January, as the veteran had indicated. This appeared to be a negative finding. However, examination of the veteran's narrative description of his worst trauma, which was logged in his January 1991 questionnaire, revealed that he had incorrectly paired his date of trauma (January 1991) with an incident that was documented by the military (and by other members of his unit) to have occurred during the month of February 1991. Thus, by his own report, he suffered from an anniversary reaction during the month in which he believed the incident had occurred, whereas by his wife's report, he suffered an anniversary reaction during the month of February—the month during which the trauma had actually occurred.

Four of the married subjects who did not personally endorse one were identified as suffering from an anniversary reaction by his or her spouse. None of these veterans had previously endorsed anniversary reactions at the 2-year time point, and each was from the military police unit. When these veterans were asked about the apparent inconsistency between their data and those provided by their spouse, each suggested to the interviewer that the spouse's report was a more accurate description of his or her behavior. If these third-party spouse reports are considered equal in validity to those given by the veterans where anniversary reactions are concerned, nine (69%) of the 13 married subjects would be identified as suffering from anniversary reactions. Such a percentage would represent a sizable (albeit speculative) increase from that calculated from self-report data alone (31%–38%).

The most frequently endorsed symptoms of PTSD that were identified by veterans as being associated with an anniversary reaction were irritability, sleep disturbance, intrusive memories, efforts to avoid thinking about the war, emotional numbness, and reactivity to reminders of war-related events. The spouses did not mention symptoms of memories, intrusive thoughts, or avoidance of thinking but instead endorsed (in descending frequency) irritability, sleep disturbance, emotional distance, emotional numbness, and reactivity to reminders of war-related events. Thus, the spouses reported what might be considered more objective symptoms of PTSD compared with subjective items such as intrusive memories. This supports the idea that the reports provided by the spouses are valid and not simply copies of the veterans' reports.

Only three subjects (9%) selected a feeling-best month and one subject (3%) a least-symptoms-of-stress month that corresponded to their previously reported dates of most severe trauma. This frequency of endorsement is cumulatively less than that expected by chance alone (17%) and supports the idea that anniversary reactions are predominantly distressing experiences.

Of note, no significant differences were observed when comparing total PTSD Symptom Scale scores between the subjects who dropped out of the study (N=27) and those who remained in the study at the 6-year

time point. Similarly, of the original 18 veterans identified as having anniversary reactions, six dropped out and 12 remained in the study. Thus, the occurrence of anniversary reactions in the dropout group also exceeded, albeit modestly, the number expected by chance alone (N=4.5).

DISCUSSION

This follow-up study provides empirical evidence for anniversary reactions in Gulf War combat veterans. As in our earlier report (12), anniversary reactions occurred in the group as a whole with a frequency that was nearly twice that expected by chance alone. Of note, all but two of the anniversary reactions occurred in members of the medical unit, where the number of such reactions (N=10) was approximately three times greater than that expected by chance (N=3.4). In contrast, only two members of the military police unit experienced anniversary reactions, the frequency expected by chance (N=2.0).

The higher frequency of anniversary reactions in the medical unit may be related to the types of traumatic events experienced by members of that unit. It appears that some events are more likely than others to be matched with anniversary reactions. The majority of anniversary reactions (N=11 of 12) were associated with events involving loss of life, suggesting that witnessing the loss of life may serve as a powerful stimulus for the development of anniversary reactions. Consistent with this notion is the observation that the four cases of anniversary reactions that were no longer present at the 6-year time point had developed in response to SCUD missile attacks or to being activated for the war. In addition, the four new cases that were identified at the 6-year time point were linked to events that included witnessing the loss of human life.

Individuals with anniversary reactions reported significantly greater symptoms of PTSD as measured by the PTSD Symptom Scale. This raises an important question about the relationship between anniversary reactions and PTSD. Of the four subjects in the study who met the criteria for PTSD, all four (100%) had anniversary reactions. Of the subjects who did not have PTSD, only 29% had anniversary reactions. Eight of the 12 anniversary reactions in this study had been identified at 2 years and continued to be present at 6 years. At 6 years, there were four new cases, suggesting that anniversary reactions, like PTSD symptoms, may be chronic or show a delayed onset. Taken together, these findings raise the possibility that anniversary reactions may be an important aspect of PTSD that has not been included in the formal DSM-IV criteria.

Four anniversary reactions that existed at 2 years were no longer reported at 6 years. It is not possible to know the number of cases that may have subsided in the dropout group; however, in the group that remained in the study, 22% (four of the original 18 cases) were no longer endorsed 6 years after exposure to trauma.

The veterans' spouses provided information that both coincided and diverged from that given by the veterans. There was a high degree of agreement (four out of five) between the veterans who endorsed an anniversary reaction and their respective spouses. These third-party reports lend credibility to the idea that anniversary reactions may be pronounced enough that they can be observed by others. In fact, there is evidence that, at times, they may be more apparent to others than to the veterans themselves. This raises the question as to whether anniversary reactions are conscious or nonconscious processes. Evidence for a nonconscious process may be found in the fact that several of the spouses identified anniversary reactions in veterans who personally did not endorse such reactions. These women (and a man) each mentioned relatively objective symptoms (irritability, sleep disturbances, or emotional numbness) as evidence for their claims.

It is consistent with our clinical observations that men in these military units may downplay symptoms and emotional reactions. It is possible that some individuals did indeed have anniversary reactions but did not report them. Among the 13 married subjects, where one would expect the occurrence of anniversary reactions to be 2.2 by chance, they numbered nine—when the spouse's report was used. This suggests that future investigations exploring the nature and existence of anniversary reactions should involve third-party reports.

The limitations of this study are clearly those of a small study group size. The small group size reflects the inherent difficulties encountered in a longitudinal study. Many subjects from the original group of veterans were unavailable for participation in the study at the 6-year time point. However, it is likely that the current data are representative of the group as a whole, since we have previously found that subjects who dropped out of the study did not differ in the degree of symptoms from those who continued to participate (14).

The empirical evidence for anniversary reactions is robust. However, the current data must be viewed with caution, since the study of anniversary reactions is nascent. The data from the present study do not permit a conclusion as to whether such reactions are the result of conditioned response, trauma sensitization, or an unconscious time-keeping process—all of which have been proposed in the literature. However, it is theoretically possible to design studies that might address this issue. For example, it may be fruitful to assess psychobiological responding (e.g., as sensory processing, conditioned responding, acoustic startle, yohimbine challenge studies) before, during, and after anniversary reactions in victims of trauma. It seems plausible that psychobiological responses, and perhaps responses to medications, may be significantly different depending on time of year (15).

The current data are relevant to psychotherapy as well. Psychotherapeutic issues may also be approached

with the concept of anniversary reactions in mind. Clinicians and patients might reasonably expect that at least 30% of trauma-exposed individuals have a likelihood of experiencing or exhibiting significant psychiatric distress (including more symptoms of PTSD) on the anniversary of their trauma. Clinicians and patients might acknowledge the trauma-related source of the distress rather than assuming that the patient's distress reflects a non-trauma-related contemporary issue. This understanding might result in a therapeutic clinical focus on the index trauma and the corresponding symptoms of reexperiencing (36, 17).

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Stress Effects of the Persian Gulf War

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I. Health Risks of the Gulf War

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Posttraumatic Stress Disorder (PTSD) results from situations where an individual believes that he/she or someone else is in danger of being seriously injured or killed. Symptoms of PTSD included repetitive reexperiencing of the trauma in the form of intrusive memories, nightmares and flashbacks; persistent avoidance of stimuli reminiscent of the trauma; a general numbing of emotions; and increased arousal as expressed by hypervigilance, exaggerated startle, irritability and insomnia.

In the present chapter we will review published studies related to the effects of war stress on American and Israeli civilians and American veterans during Operation Desert Shield/Storm. While the primary focus will be on "psychological" symptoms and syndromes, we recognize that the distinction between physical and psychological illness is often unclear and at times artificial.

I. Health Risks of the Gulf War

In 1990 the United States and allied countries responded to the Iraqi invasion of Kuwait by deploying a large number of soldiers to the Persian Gulf. Operation Desert Storm began in 1991 when Allied Forces launched a five-week intensive air attack on Iraq. This was followed by a four-day ground war. The number of deaths to American and Allied forces during the Gulf war was limited compared to World War I and II, the Korean War and the Vietnam war. Nevertheless, since the end of the Gulf War a substantial number or Desert Storm veterans have experienced a host of physical and psychological symptoms that in some cases have had a pronounced impact on psychosocial functioning.

Military personnel stationed in the Gulf were exposed to a wide variety of potential health risks. These included a hostile environment (e.g., extreme temperatures, humidity and rainfall, blowing sand, crowded living conditions), infectious agents (e.g., leichmaniasis, sandfly fever), medical prophylaxis (e.g., pyridostigmine bromide, anthrax and botulinum toxin vaccines), occupational exposures (e.g., chemical exposures associated with routine maintenance and repair of equipment, fuels), environmental hazards (e.g., pesticides, smoke from oil well fires), depleted uranium (used in some artillary shells), the possibility of chemical and biological warfare agents (e.g.,

organophosphate nerve agents, sulfur mustard, anthrax, botulinus toxin) and repetitive physiological and psychological stress.

Soldiers serving in the Persian Gulf were exposed to numerous potential psychosocial stressors. Stressors associated with deployment included uncertainty about parameters of deployment (e.g, the period of waiting for deployment, unknown length of tour and return date), over estimation of Iraqi military forces, media anticipation of high casualty rates and separation from home and family. As in all wars, soldiers described the anticipation of combat as being highly stressful. In a study of 1,524 deployed military personnel, 80% of subjects reported feeling stressed by the persistent threat of SCUD missile attacks, terrorist attacks and biological and chemical warfare. Many experienced strong emotional responses to repeated missile warnings and the rapid donning of protective gear that they did not fully trust would be effective against all possible toxic agents.

Reports of directly experienced traumatic events vary depending on the units studied. In a series of scientific investigations commissioned by the Department of Defense, Marlowe found that 40% of soldiers in the units studied experienced incoming indirect fire, between 40% and 70% reported exposure to mines and booby traps, 40% in two units recalled firing rounds at the enemy, and 80% in one unit and 60% in another claimed to see enemy killed or wounded in action. In two units more than 20% of soldiers believed they were in imminent danger of being killed at some point during their tour in the Persian Gulf. Reports of seeing an American wounded by friendly fire had great emotional impact as did work in grave registration units. Sadly some traumas

experienced in the Gulf, such as sexual harrassment and assault, were inflicted by Americans on their own fellow soldiers.

Other frequently cited Gulf War stressors include austere physical environment and severe climatic conditions, heavy workload, sleep deprivation, inadequate supplies and equipment, lack of information, poor leadership and unit morale, and unsatisfactory living conditions.

II. Mental Health

The psychological consequences of war have been described for centuries and have been referred to by a variety of different terms including shell shock, irritable heart of soldiers, physioneurosis and most recently posttraumatic stress disorder. Posttraumatic stress disorder (PTSD) results from situations where the individual believes that he/she or someone else is in danger of being seriously injured or killed. Symptoms of PTSD include repetitive re-experiencing of the trauma in the form of intrusive memories, nightmares, and flashbacks; persistent avoidance of stimuli reminiscent of the trauma; a general numbing of emotions; and increased arousal as expressed by hypervigilance, exaggerated startle, irritability and insomnia. Depression, anxiety, substance use and changes in personality traits are other frequently cited consequences of trauma.

A. Psychological symptoms in Persian Gulf Veterans

Prior to the ground war it was estimated that acute psychiatric casualties might reach as high as 50,000. This estimate was based on experience from previous wars. However, during the Gulf war there appeared to be very few psychiatric casualties. Between August 1990 and August 1991, 476 soldiers were evacuated from Southwest Asia for psychiatric reasons. This number constituted only 6.5 % of all medical evacuations from

the Persian Gulf. Similarly, only 158 soldiers from the US Army 7th corps received mental health treatment while stationed in the Gulf and 99% were returned to duty after brief treatment. These low rates lead to the belief that psychiatric problems in Gulf veterans would be lower than expected. Explanations for low rates included the brief nature and success of the war, limited exposure to traditional combat stressors, and high levels of perceived social support.

Since the end of the Gulf war, however, a number of different research groups have reported rates of psychiatric symptoms and disorders in Persian Gulf veterans that are high in light the above evacuation figures. The Fort Devons Operation Desert Storm Reunion Survey was conducted within five days of return to this country before soldiers rejoined their families. The most commonly endorsed war zone stressors were: formal alert for chemical or biological attack (approximately 75%), receiving incoming fire from large arms (approximately 73%) and witnessing death or disfigurement of enemy troups (approximately 48%). Four percent of 2136 men and nine percent of 208 females met a presumptive diagnosis of PTSD. Symptoms of hyperarousal and exaggerated startle were the most commonly endorsed PTSD symptoms. Twenty-eight to thirty-one percent had General Severity Index (GSI) Scores on the Brief Symptom Inventory (BSI), which reflects general psychological stress, in the clinically significant range.

Approximately six months after Operation Desert Storm, Labatte and Snow administered a self-report questionnaire to fifty-seven soldiers stationed in Germany who were members of a single mechanized infantry unit that suffered four casualties during the brief ground war. Fourteen soldiers (25%) reported traumatic nightmares within two

months of the war. Nightmares began two to six months after the war for an additional nine soldiers (16 %).

Two other studies assessed PTSD symptoms and general psychopathology in a large number of reservists within the first year of their return from the Persian Gulf. In a study of 591 Army, Navy and Marine reservists, Perconte and colleagues found that those who had been deployed to the Gulf War combat zone had significantly higher Mississippi PTSD scores, Beck Depression scores and higher levels of global distress as measured by the Symptom Check List-90 (SCL-90) than reservists who had been activated but not deployed to combat zones. Over fifteen percent of deployed reservists met Mississippi cut off scores for PTSD compared to less than 4% of non-deployed reservists. Sutker and colleagues reported low levels of psychological distress in their overall group of 775 combat deployed Reserve and National Guard troops. However, 12.5% of the sample were diagnosed with PTSD.

Approximately one year after the war, Holmes and colleagues evaluated 179 members of an Air National Guard unit who were never deployed to the Persian Gulf and compared them to 296 members of the same who were deployed. Most members of the deployed group did not experience any traditional combat stressors, although they were exposed to non-traditional combat stressors such as anticipation of missile attacks and biological warfare. Compared to the non-deployed, the deployed group had statistically higher mean scores on the Mississippi PTSD scale and on the GSI as well as the obsessive-compulsive, depression, hostility, phobic anxiety and paranoia subscales of the BSI. 6.8% of deployed and 1.7% of nondeployed were identified as having increased risk for PTSD. The findings of this study suggest that multiple non-combat stressors

were distressing enough to cause both PTSD and non-PTSD psychological symptoms in some deployed veterans.

In a follow-up study of the Fort Devons sample 18-24 months after the war nearly half of the sample reported no physical or psychological symptoms. Twenty-seven percent believed that their psychological health had deteriorated since the war. PTSD symptomatology was significantly associated with high health symptom endorsement. Twenty-two percent of soldiers with high combat exposure met a presumptive diagnosis of PTSD compared to 8.1% with low combat exposure. The data was consistent with a number of recent studies suggesting that an apparent association between combat exposure and health is significantly mediated by a diagnosis of PTSD.

In a survey administered approximately two years after the war to 1,524 deployed and 2,727 nondeployed military personnel from Hawaii and Pennsylvania, Stretch and colleagues reported possible PTSD in 8.0% of active duty veterans and 9.35% of reserve veterans who had been deployed to the Persian Gulf. By comparison, 1.3% of active duty nondeployed and 2.1% of reservist nondeployed met possible criteria for PTSD. The sample was also compared to a large group of deployed active duty Army veterans from the XVIIIth and VIIth Corps. Possible risk for PTSD in these groups was 15.2% and 12.9% respectively. The authors speculate that these units had higher rates of possible PTSD because their duty was more dangerous and because they were evaluated one year earlier. Deployed personnel also scored significantly higher on the somatization, obsessive-compulsive and hostility subscales of the BSI and the GSI.

As part of a follow along study of Gulf veterans from two National Guard units, Southwick and colleagues reported a rate of presumptive PTSD in 8.3% of 84 subjects

six months after the war and in 10% of 64 subjects two years after the war. Greatest increase in overall PTSD symptoms occurred between one month and six months after the war and symptoms of hyperarousal were elevated above re-experiencing and avoidance symptoms at one-month, six-month and two-year evaluations. Morgan and colleagues found evidence for anniversary reactions in this same group of veterans.

Approximately five years after the war, the Iowa Persian Gulf study group conducted telephone interviews with 1896 Gulf War veterans and 1799 personnel who served in the military during the war but who were not stationed in the Persian Gulf. Persian Gulf War personnel reported higher rates of PTSD (1.9% vs.0.8%) depression (17.0% vs. 10.9%) cognitive dysfunction (18.7%vs. 7.6%) asthma (7.2%vs. 4.1%) fibromyalgia (19.2% vs. 9.6%) alcohol abuse (17.4% vs. 12.6%) chronic fatigue (1.3% vs. 0.3%) and sexual dysfunction compared to non-Persian Gulf War military personnel. Symptom levels were generally higher in Persian Gulf War National Guard reserve personnel than Persian Gulf War regular military personnel.

Finally, in a report of 18,495 Gulf War veterans who presented for evaluation to the Department of Defense Comprehensive Clinical Evaluation Program, 36% met ICD-9-CM diagnoses for psychological conditions. In most cases symptoms did not develop until after the war. There was no apparent association between individual physical or psychological symptoms and specific exposures. Compared with a referent group of patients having no symptoms, excess prevalence of disorders was highest for psychological conditions compared to a variety of physical conditions such as digestive and skin conditions.

B. Psychological symptoms in civilians affected by the Persian Gulf War

Clearly the Gulf War had profound stress-related effects on Iraqi military personnel and civilians living in Iraq and surrounding Middle Eastern countries. In general, the rates of death, physical and psychological injury have not been reported accurately in the scientific literature. However, there have been a number of publications related to the effects of the Gulf war on American and Israeli civilians as well as Vietnam veterans and Holocaust survivors.

In American civilians, it has been reported that the Gulf war was associated with mild to moderate symptoms of anxiety and depression particularly in those who had a relationship with a deployed soldier. In children of deployed American soldiers, a major predictor of psychological symptoms was level of symptoms in other household members. Although deployment rarely provoked pathological levels of symptoms in healthy children, it was associated with increases in symptoms of depression especially among younger children. In a study of Israeli civilians that was conducted during the war, Solomon and colleagues found that 80% of individuals whose homes had been destroyed by Iraqi missiles described symptoms consistent with DSM-III-R criteria for PTSD. Similarly, Laor and colleagues reported elevated levels of Gulf war stress-related symptoms in children and mothers who were displaced from their homes due to damage from SCUD missiles and in young children living in families characterized by inadequate cohesion.

In Vietnam veterans no consistent response to the Gulf war has been described. Reported responses have included support for the war, anger at the US government for starting another war, irritability, intrusive thoughts, and increased depression and

suicidality. In a study of 76 female Vietnam veterans with PTSD, Wolfe and colleagues reported some exacerbation of symptoms in most subjects, with the greatest increases in those who had high levels of pre-existing PTSD symptoms. In a study of Holocaust survivors living in Israel during the Gulf war, Robinson reported that many were still vulnerable 50 years after WWII and reported a revival of feelings and memories associated with the Holocaust.

III. Predictors of PTSD

Numerous investigations of WWII, Korean and Vietnam veterans have shown that not all individuals develop PTSD and/or other psychological disorders after life threatening traumas. Given an equal degree of traumatic exposure, some individuals are more likely than others to develop subsequent trauma-related psychopathology. In order to explain such individual differences in veterans of the Gulf war, researchers have studied a number of potential risk factors or predictors for the development of PTSD. These have included characteristics of the traumatic event, as well as available personal and environmental resources.

The most commonly cited risk factor for the development of PTSD is the nature and severity of the trauma itself. Many war-related investigations, including a number of Desert Storm studies, have demonstrated a clear dose-response relationship between severity of psychological trauma and subsequent psychopathology (i.e. the more severe the trauma the greater the likelihood of developing PTSD and/or other mental disorders). When traumatic exposure involves actual physical injury, the risk for subsequent psychopathology is even greater. In a hospital chart review study of medical and surgical patients who were evacuated from the Gulf to the Walter Reed Hospital, Brandt and

colleagues reported a significantly higher rate of Axis I disorders (and psychiatric symptoms of concern) in the hospital records of soldiers with traumatic injuries (e.g., shrapnel, gunshot wounds, motor vehicle accidents, SCUD missile attack) compared to soldiers without traumatic injuries (e.g., gastrointestinal bleeding, chest pain, malignancies). Other trauma-related risk factors identified in Gulf war veterans include exposure to dead or dying bodies, having a buddy wounded or killed in action, exposure to American soldiers killed or wounded by friendly fire, being in the reserve (e.g. lack of psychological preparation for deployment), and handling of human remains.

Personal variables that have been studied in Gulf war veterans include gender, race, intelligence, personality hardiness, coping style, and perceived social and family support. In a study of 653 Persian Gulf war-zone exposed veterans, Sutker and colleagues reported significantly greater psychological distress and PTSD symptoms in minority men compared to white men but no differences between war zone males and females. In a separate report, Sutker and colleagues found more avoidance, wishful thinking and self-blame coping strategies, fewer problem-oriented coping strategies, lower scores on hardiness dimensions of commitment, control and challenge, and less perceived social and family support among Gulf war veterans with PTSD (n=97) compared to those without psychopathology (n=484). No differences in intellectual sophistication as measured by the Shipley Institute of Living Scale were found between the two groups.

IV. Physical Symptoms

Since the end of the Gulf war, a large number of veterans have reported an array of troubling physical symptoms including fatigue, joint pain, gastrointestinal problems, skin

rash, headache, memory loss, insomnia and shortness of breath. In a relatively small percent of veterans, specific etiologies for physical complaints have been linked directly to military service in the Gulf (e.g. leishmaniasis, malaria, and embedded fragments of uranium). However, for the majority of veterans with physical complaints, a specific relationship between physical symptoms and biological, chemical or other environmental exposures has not been reported in the literature. Further, no specific medical diagnoses appear to explain most of the complaints. As a result, some have postulated a "Gulf War Syndrome" to account for these unexplained physical symptoms.

While some studies clearly report a greater number of physical complaints among military personnel who served in the Gulf compared to those who did not serve in the Gulf, most have not found high rates of any one medical disorder or conclusive evidence for a new syndrome. To date five expert panels (Defense Science Board Task Force, National Institutes of Health Technology, Institute of Medicine, Presidential Advisory Committee on Gulf War Veteran's Illnesses) have failed to identify a new "Gulf War Syndrome." For example, in 1996 the Institute of Medicine reported that " the committee has not identified scientific evidence to date demonstrating adverse health consequences linked with PGW service other than the documented incidents of leishmaniasis, combat-related or injury-related mortality or morbidity, and increased risk of psychiatric sequelae of deployment." Similarly, in 1995 Coate reported no increased risk of pre-war or post-war hospitalization for any cause among 547,076 PGW veterans compared to 618,335 non-deployed. PGW veterans did have higher rates of psychiatric hospitalization that appeared to be related to the use of drugs and alcohol. Two large-scale mortality studies have reported no increased mortality as a result of medical diseases in PGW veterans.

However, an excess number of deaths due to accidents and unintentional injury have been reported.

V. Relationship Between Physical and Psychological Complaints

In a recent comprehensive literature review on the relationship between psychological trauma, posttraumatic stress disorder and physical health in diverse trauma populations, Friedman and Schnurr reported that exposure to catastrophic events (independent of actual physical injury) was frequently associated with adverse health reports and increased medical utilization, morbidity and mortality. Based on work by Wolfe and others, Friedman and Schnurr suggested that PTSD-the reaction to a trauma-may serve as an important mediator in the association between traumatic exposure and perceived physical health. Baker and colleagues found support for this hypothesis in a sample of 188 Desert Storm veterans where fatigue, nausea, muscle aches, dizziness, back pain, stomach ache, and numbness were much more likely to be reported by Persian Gulf War veterans with PTSD compared to those without PTSD. Similarly, Stretch and colleagues reported a probable link between Gulf War Syndrome and PTSD even though they found the relationship between stress and physical health to be relatively weak in a large group of Desert Storm veterans. Approximately 30% of veterans with Gulf War Syndrome also met criteria for PTSD. In a study of female veterans conducted within one year of their return from the Gulf, Wolfe and colleagues found anxiety and PTSD, but not combat exposure, to be significant predictors of health symptoms.

Neurobiological, psychological and behavioral hypotheses have been offered to explain the relationship between PTSD and physical health. As noted by Friedman and Schnurr medical problems in trauma survivors may result from neurobiological

alterations characteristic of PTSD such as exaggerated cardiovascular reactivity, adrenergic dysregulation, disturbed sleep physiology, altered hypothalamic pituitary adrenal axis activity and enhanced thyroid function. It is also possible that these neurobiological alterations increase susceptibility to immunologic disorders and infections. Psychological and behavioral factors that may contribute to health problems and that are commonly seen in survivors with PTSD include hostility, depression, alcohol and drug use, smoking, poor social support, and avoidant and emotion-focused coping.

Summary

Soldiers serving in the Gulf war were exposed to a wide variety of potential health risks including traumatic stress. Across multiple studies it appears that between 6-10 percent of Gulf war veterans developed PTSD as a result of their service in the Middle East. A host of other psychological and physical symptoms have been reported and some researchers have proposed a Gulf war syndrome. In Gulf war veterans the precise relationship between stress, the neurobiological alterations that accompany stress and toxic or infectious exposure currently is poorly understood and the subject of intense scientific investigation.

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