

EDITORIAL

Adding to our understanding of Gulf War health issues^{1,2}

In this edition of *Psychological Medicine*, research findings are reported from two studies of British Gulf War veterans (David *et al.* 2002; Everitt *et al.* 2002). Both studies were carried out at King's College 'Gulf War Illness Research Unit', which was established in 1996. The two studies were conducted to examine the causes of unexplained symptoms among Gulf War veterans. The results presented in these papers are important because they were derived from well-designed studies that employed a randomized sample of Gulf War veterans and two control populations of non-deployed 'era' veterans who served in the early 1990s and troops who participated in another hazardous deployment to Bosnia.

In one study, cognitive function and mood disturbances were evaluated using a comprehensive battery of neuropsychological tests and rating scales (David *et al.* 2002). A significant proportion of Gulf War veterans reporting ill health were found to have both lower cognitive function scores and depressed mood compared to well Gulf War veterans, era veterans and Bosnia troops. Importantly, a strong association was found between depressed mood and poor performance on cognitive function tests. It is noteworthy that among ill Gulf War veterans, most cognitive function measures were within the normal range, although they were significantly lower than those of controls.

Based on these and related research findings, the study investigators concluded that lower performance on cognitive function tests could be explained primarily by mood disturbances. However, they could not rule out the possibility that cognitive difficulties had led to depressed mood or that a neurotoxic environmental exposure had caused both health problems. Despite these uncertainties, the study findings clearly indicate that mood disturbance has to be considered as a potential confounder in studies of cognitive function among Gulf War veterans.

In the second published study, the researchers used cluster analysis to determine whether Gulf War and Bosnia veterans can be distinguished by the pattern of their medically unexplained symptoms (Everitt *et al.* 2002). In contrast to other surveys of Gulf War veterans, which used another sophisticated statistical technique, factor analysis, to try to identify a unique 'Gulf War syndrome', this survey attempted to group study participants with related symptoms by geographic location of deployment. Gulf War and Bosnia veterans were asked about the presence during the prior month of 50 non-specific symptoms and about the severity of any symptoms. A unique syndrome could not be distinguished among veterans deployed to the Persian Gulf by this analysis of self-reported symptoms.

The results of these two studies are in agreement with other large, randomized and controlled studies of Gulf War veterans. A consistent pattern of either symptoms or clinical signs has not been identified that points to the presence of a unique, war-related physical disease. Moreover, similar non-specific symptoms have been reported in these studies by control groups of veterans who were not deployed to the Persian Gulf.

The research methodologies employed in the two studies deserve comment because they have been used frequently in the search for a unique Gulf War syndrome. Both studies utilized symptom reports to group study subjects and complex statistical techniques to analyse clinical data. Studies that rely on

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self-reported data and exploratory statistical techniques to identify a new physical disease are based on several fundamental assumptions. Although research studies of Gulf War veterans have provided an immense amount of useful information, these underlying assumptions have not been systematically assessed and verified. Enough data is now available from the numerous Gulf War research studies to begin to evaluate these assumptions.

One unverified assumption is that subjective symptoms, as reported in epidemiological surveys, can be treated as discrete and comparable variables for analysis. For example, in the search for symptom patterns, complaints of fatigue, forgetfulness, headaches and joint pains have been considered equivalent among different age groups, from young male and female military personnel in their twenties to 40 and 50 year-old retired veterans. But as the two authors of this Editorial can attest, the causes and severity of common somatic complaints often change in middle age. Also, it frequently is unclear in epidemiological studies of Gulf War veterans whether reported symptoms were occurring together as a single illness or instead were present at different points in time during a specified time interval.

In some studies of Gulf War veterans, symptom scales have been incorporated into survey checklists to obtain more precise data. This approach still may not ensure that comparable data is being collected because there is no objective standard for standardizing internally perceived experiences. For instance, it is not possible to determine whether a participant's report of 'moderately' severe headaches is qualitatively or quantitatively different from reports of 'slight' or 'severe' headaches among other study participants. As shown by prior research and practical clinical experience, there is an enormous degree of individual variability in the internal perception of symptoms and in subsequent impairment of normal daily activities.

Another underlying but untested assumption is that recall or reporting bias is not a problem in studies that rely on self-reported data. However, the findings from epidemiological surveys of Gulf War veterans suggest that recall bias could be important because of repeated media and Internet reports about the possibility of adverse health effects and toxic exposures. In multiple surveys of varied populations of Gulf War veterans almost every symptom and health problem has been reported at higher rates than in control populations. Although it is conceivable that an undetected health problem could be responsible for these findings, the potential role of recall bias should be specifically assessed in future studies.

In searching for a unique war-related syndrome at least two assumptions underlie the use of complex statistical techniques, like factor analysis and cluster analysis. The first is that reports of non-specific symptoms by themselves can provide enough information to identify a postulated physical disease. The second is that exploratory statistical analysis of clinical data can identify a new physical disease when the physician-patient interaction, the most discriminating tool, has failed to uncover a diagnosis. Neither of these assumptions has been carefully assessed. Indeed, the historical record shows that complex statistical techniques may provide a misleading picture of scientific certainty, as occurred in the early part of the twentieth century when factor analysis erroneously identified racial difference in studies of intelligence test data (Gould, 1981).

Even though these assumptions need further study, much has been learned about the health status of this war veteran population. The 750 000 US, UK and Canadian Gulf War veterans arguably have been studied more extensively than any other large population of adults. Over 200 million dollars has been spent in the US alone to evaluate the health status of Gulf War veterans. Both clinical and epidemiological studies have been funded (Research Working Group of the Military and Veterans Health Coordinating Board, 2002). The only essential kinds of study that have not been performed – because the Gulf conflict ended just 12 years ago – are long-term follow-up investigations of veterans with unexplained symptoms. In addition to numerous research studies, more than 100 000 Gulf War veterans have undergone a clinical 'registry' examination in these three countries to identify war-related health problems.

Substantial research efforts are still in progress to address Gulf War health questions. Of 224 federally-funded Gulf War research studies in the USA, 88 are still on-going as of January 2002 (Research Working Group of the Military and Veterans Health Coordinating Board, 2002). One area

of current research is focusing on the possibility that some veterans are suffering from a neurological disease caused by a toxic exposure during the Gulf War (Haley *et al.* 1997). Additional research is being conducted to explore whether certain individuals have a genetic pre-disposition to the toxic effects of organophosphorus compounds, like insecticides and chemical warfare nerve agents.

This massive clinical and research effort clearly demonstrates that Gulf War veterans have experienced a wide range of both medical and psychological health problems. No single type of illness predominates. A primary underlying cause therefore is not evident and treatment has had to vary depending on individual assessment and diagnosis. There are, nevertheless, some encouraging research findings. Most notably, the overall mortality rate of US Gulf War veterans has been found to be less than one-half that of the general civilian population matched for age and gender (Kang & Bullman, 2001).

Despite a concerted research and clinical assessment effort, the search for a unique war-related syndrome has been frustratingly inconclusive. It is therefore time to assess current research findings and to determine what types of studies are likely to add to the large body of accumulated data on the health status of this deserving population of war veterans.

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