
Treating Gulf War Veterans’ Illnesses—Are More Focused Studies Needed?

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THE VETERANS AFFAIRS (VA) COOPERATIVE STUDY #470, a trial of cognitive behavioral therapy (CBT) and aerobic exercise for Gulf War veterans’ illnesses (GWVI) reported in this issue of THE JOURNAL,1 is a remarkable achievement. It is the first credible trial of an intervention for symptomatic Gulf War veterans, and with 1092 individuals randomized at 20 sites, it is one of the largest trials of a psychotherapeutic intervention ever published. The study used a factorial design to randomize symptomatic veterans who received usual care, CBT, graded exercise therapy, or both in combination. The results suggest that CBT leads to a modest reduction in physical disability (the primary outcome measure), graded exercise therapy has no such effect, and the combined treatments can lead to improvements in fatigue and cognitive symptoms but not pain. The modest effects shown in the primary outcome are difficult to interpret. Should all symptomatic veterans now be offered CBT or should further research attempt to refine the treatment? If graded exercise therapy is effective for some symptoms, are there subgroups of patients who would benefit from it more than from CBT?

The trial is remarkable in another respect. In developing complex interventions, it is unusual to conduct the “definitive” pragmatic multicenter trial before small exploratory trials have taken place. The reason is partly because, under most circumstances, funding bodies are unlikely to risk the immense resources necessary without some reassurance that the intervention could work. But another good reason small trials are usually performed first is that for CBT to work, it is necessary to develop a clear model to understand the cognitive and behavioral factors underlying continuing symptoms. In GWVI, such models are still lacking.

The researchers instead make links between GWVI and other chronic multisymptomatic conditions such as chronic fatigue syndrome (CFS) and borrow heavily from current thinking on treatment of this disorder. There are certainly similarities. Epidemiological studies of veterans indicate patterns of symptoms similar to those experienced by patients with CFS; fatigue, widespread pain, and cognitive symptoms (subjective memory impairment and poor concentration) dominate in both groups.5-3 Clinical studies on both sides of the Atlantic indicate that veterans’ symptoms have not been explained by clearly defined biomedical diagnoses,4,6 and in CFS such conditions are, by definition, absent.

Symptoms of CFS have been understood by CBT theorists using the influential fear avoidance model,7,8 which emphasizes maintaining factors for the disorder. The theory suggests that as the illness progresses, patients learn to respond to symptoms by avoidance of feared triggering factors. In CFS, the key factors are physical and mental exer-

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tion. Avoidance of physical exertion leads to a short-term improvement in symptoms at the cost of longer-term physical deconditioning and disability. The 2 therapies that have been shown to improve symptoms in patients with CFS, graded exercise therapy and CBT, probably work by breaking this cycle. For example, some evidence suggests that CBT is most effective when cognitions linking physical exertion to physical harm are addressed.

Is this model appropriate for explaining symptoms experienced by Gulf War veterans? It is not hard to find a catalog of understandable fears in Gulf War veterans, in particular relating to exposure to hazards that were widely publicized in the lay and scientific media, such as nerve gas attacks, immunizations, pesticides, and depleted uranium. What is less clear is what, if anything, is being avoided. A UK Gulf War veterans epidemiological study indicated that while most health outcomes were dramatically affected by service in the Persian Gulf, physical functioning was only marginally affected, in marked contrast to civilians with CFS. One explanation for this finding is that despite being significantly symptomatic, Gulf War veterans are not greatly avoidant of physical exertion. This may be due to a greater emphasis on physical fitness in military culture and may be one reason for the lack of effect of exercise therapy on physical functioning in the VA Cooperative Study. The CBT intervention predominantly concentrated on activity scheduling, problem solving, and sleep hygiene. Although such general approaches are useful, they may not get close enough to the specific anxieties of veterans. Richer qualitative data are required in Gulf War veterans to better understand the cognitions and behaviors associated with symptoms and to develop coherent models for GWVI.

Another reason why CBT may have had less effect in Gulf War veterans is that this intervention was weaker than that provided in trials of civilians with CFS. Such CFS trials have taken place in specialty centers, often with single therapists with a special interest in the condition providing individual therapy. In the VA trial, therapy was provided in a group setting, and therapists, while experienced in the use of CBT, may not have had an equivalent depth of understanding of unexplained physical symptoms. For CFS patients, aspects of CBT that may be helpful are the opportunities it affords to develop a therapeutic alliance and to describe in detail the consequences of a complex illness. This process of engagement allows the patient and therapist to collaborate and form new understandings of symptoms, which may lead to adaptive behavioral responses. It is likely that these components of therapy are less readily achieved in a group setting. Furthermore, there may be barriers to groups succeeding in a male-dominated culture like the military. These problems are reflected in the poor adherence to therapy in the VA Cooperative Study: participants randomized to CBT attended a median of 5 of 12 sessions offered, and only 7% randomized to this treatment attended all 12 sessions.

Despite the importance of large pragmatic trials, additional small trials of focused treatments in specialty settings are required to develop and assess appropriate treatments for GWVI. Even before conducting focused trials to refine the components of CBT that may help, qualitative work is necessary to build a coherent model for symptoms. In addition to its important results, a lesson from the VA Cooperative Study is that it is necessary to establish whether a treatment can work under ideal conditions before attempting to determine whether it does work in the real world.

REFERENCES