Response to Missile Attacks on Civilian Targets in Patients With Panic Disorder

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Background: The complex interaction that exists between biological and cognitive factors determines the reaction of panic-disorder patients to stressors. The current study was conducted to systematically assess the behavioral effects of a real, life-threatening event on panic-disorder patients.

Method: Sixty-five panic-disorder patients completed structured telephone interviews during the first 4 weeks of the Persian Gulf War. Evaluation included frequency of panic attacks, anxiety levels, and function levels both during and between air raid alarms.

Results: The findings indicate that panic-disorder patients, despite high levels of anxiety, did not demonstrate an increased frequency of panic attacks during the Persian Gulf War. In addition, the majority of patients reported good-to-high levels of functioning during the crisis in both everyday and alarm-related functioning. Grouping of subjects according to proximity to risk or current antipanic treatment did not produce significant differences in the frequency of panic attacks or levels of anxiety.

Conclusion: The findings suggest that vulnerability of patients with panic disorder to a "panic-stricken" response does not increase during real-life stressors. The lack of increased frequency of panic attacks observed under these circumstances provides additional support for the opinion that panic and fear are two distinct entities.

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Panic attacks can be provoked in experimental situations by a number of pharmacologic challenges. Agents used in these challenges include sodium lactate,[1] carbon dioxide,[2] yohimbine,[3] caffeine,[4,5] isoproterenol,[6] norepinephrine,[7] cholecystokinin (CCK),[8] and *m*-chlorophenylpiperazine (*m*CPP).[9] These agents have been shown to affect several neurotransmitter systems, such as the adrenergic, serotonergic, and dopaminergic systems.[10] However, they were also associated with peripheral autonomic changes such as increased heart rate and respiration, which themselves may provoke panic attacks in panic-disorder patients who are preoccupied with body and particularly respiratory and cardiac sensations.[11] Consequently, it is difficult to conclude whether these laboratory-provoked panic attacks are stimulated primarily by the activation of specific panicogenic mechanisms or by the catastrophic misinterpretation of nonspecific peripheral changes.[10]

However, not all laboratory stressors induce panic. Roth et al.[12] report that cognitive stress such as that of a mental arithmetic test, although inducing anxiety, does not seem to provoke panic attacks. Pain and hypoglycemia are also stressors that have not demonstrated any special panic-inducing properties in panic-disorder patients.[13,14] Furthermore, Roth et al.,[12] who examined the psychological and physiologic reactivity of panic-disorder patients to carbon dioxide (CO_2) challenge, reported that the degree of anticipatory anxiety can be an important factor in panic provocation. A more recent study employing CO_2 challenge showed that the degree to which the subject perceived control over the test paradigm had a significant effect on the outcome of the challenge.[15] Taken together, these findings suggest a complex interaction between biological and cognitive factors in determining the reaction of panic-disorder patients to stressors.

The reaction of panic-disorder patients to real life-threatening situations has only recently been studied. Many patients with panic disorder believe that they will panic in situations of actual life endangerment, and this belief has considerable impact on their self-esteem. The Persian Gulf War provided us with an opportunity to examine, in a structural manner, the interaction between panic disorder, peripheral autonomic changes, and real life-threatening events in a group of panic-disorder patients.

THE PERSIAN GULF WAR

The missile attack on Israeli cities on the night of January 17, 1991, abruptly hurled the civilian population into the Gulf War, which lasted 6 weeks. During the conflict, the Israeli civilian population was subjected to 18 separate missile attacks, in which a total of 38 missiles landed on Israeli soil. Due to the potential threat of biological and chemical warfare, gas masks and atropine autoinjectors were distributed to the civilian population in the months preceding the war. In addition, the public was instructed to prepare a "sealed room" to be used in the event of a missile attack. The preparation of this room included the sealing of windows and doors with plastic sheets and sealing tape and stocking the room with drinking water and food supplies as well as a radio to keep the civilian population informed and advised. The population was instructed to enter their sealed rooms upon hearing the air raid sirens, don their gas masks, and listen to the radio for instructions from the authorities. After each missile strike, a special team was sent into the area of impact to determine the type of warhead deployed.

In the interim, the population was ordered to remain in their sealed rooms with their gas masks in place for periods that lasted from 15 minutes to several hours. Almost all of the missile attacks occurred after dark and were directed mainly at the Tel Aviv coastal region. In this "high-risk" area, physical signs of danger were present, such as missile blasts, the wailing of emergency vehicles, and property damage. During the crisis period, essential civilian services were maintained without interruption. However, nonessential activities were minimized to allow workers to reach home before nightfall. By late afternoon, the majority of the civilians were to be found at home, anxiously awaiting a possible missile attack.

METHOD

Subjects

Sixty-five patients, 53 women and 12 men, who had been attending the outpatient panic-disorder clinic of the Beer-Sheva Mental Health Center for at least 1 month, participated in the study. The patients met DSM-III-R criteria for panic disorder. The mean age of subjects was 37.3 years (range, 20–65 years), and the mean education level was 11.2 years (range, 9–21 years). Thirty-eight of the subjects (58%) were receiving drug therapy (31 were receiving tricyclic antidepressants or selective serotonin reuptake inhibitors [SSRIs], 6 were receiving alprazolam, and 1 was receiving phenelzine) at the time of the interview. Ten of the subjects (15%) were being treated with behavioral modification only, and 17 (26%) were receiving a combination of pharmacotherapy and behavioral modification. Sixteen of the subjects (25%) resided in the Tel Aviv area where the actual missile strikes occurred, and 49 (75%) resided in "low-risk" areas.

Procedure

During the first 4 weeks of the Persian Gulf War, telephone interviews were conducted by personnel of the panic-disorder clinic (M.T., M.F., and J.Z.), according to a 17-item self-report questionnaire developed by the authors, to assess the response of panic-disorder patients to the war situation (see Appendix 1). The patients were asked to report on the number of panic attacks per week suffered prior to the onset of the crisis and the number of panic attacks per week suffered during the crisis. They were also asked to rate the change in their mental health during the crisis on a scale ranging from 7 (greatly improved) to 1 (exceedingly worse). The same 7-level scale was used to measure their level of general and alarm-related functioning during the crisis, the levels of anxiety between alarms, and the degree of return to the pre-alarm level of functioning.

RESULTS

No difference in the number of panic attacks per week prior to the crisis (mean ± SD = 0.53 ± 1.12) compared with the number of panic attacks during the war (mean ± SD = 0.68 ± 1.47) was found ($z = -1.15$, $p = .2491$). There was also no significant difference between the high-risk and low-risk areas, as studied by 2 × 2 (time × area of residence) factorial analysis of variance (ANOVA), which revealed no significant difference for main effect ($F = 2.38$, $df = 1$, $p = .1282$) and no interactions ($F = 0.27$, $df = 1$, $p = .60$). Furthermore, no significant main effects or interactions were observed when the treatment paradigms (pharmacologic, N = 38; behavioral, N = 10; combined, N = 17) were analyzed by time × treatment factorial ANOVA. However, a comparison between the groups demonstrated a significantly higher level of functioning during the alarms in the group residing in the high-risk area (N = 16) compared with the group residing in the low-risk area (N = 49) (mean ± SD score = 5.56 ± 0.51 vs. 4.98 ± 1.11; $t = 2.03$, $df = 63$, $p = .047$).

DISCUSSION

The frequency of panic attacks during the crisis was not significantly different from that of the precrisis period. In addition, the majority of subjects reported high levels of functioning during the crisis, both between and during the alarms. Moreover, when the subjects were grouped according to residential area, i.e., high-risk versus low-risk, no differences were found between the groups in regard to frequency of panic attacks or levels of anxiety. Nevertheless, the high-risk area group reported

significantly higher levels of functioning during the alarms than did the low-risk group. No significant differences in frequency of panic attacks, anxiety, or functioning levels were observed when the subjects were grouped according to treatment regimen.

Limitations in the methodology employed by this study include both subject selection and procedure. The vast majority of subjects participating in the study (63/65; 97%) were in remission, and many were receiving antipanic treatment (pharmacotherapy, behavioral therapy, or combined therapy) during the crisis. Since some studies have demonstrated that antipanic therapy may be effective in blocking panic attacks during laboratory challenge paradigms,[16,17] it is plausible to assume that therapy may have a similar effect in blocking the panic response to a naturalistic stressor.

Moreover, Schatzberg and Ballenger[18] reported that both length of treatment and duration of panic-free intervals appear to be important factors in the relapse rate in panic-disorder patients and in subsequent response to stressors. In our study, only 3% of the subjects reported having panic attacks prior to the crisis. This low incidence may have influenced the subjects' response to the stressor. Indeed, the 2 patients in our study who had panic attacks during the crisis also reported having them prior to the crisis.

In addition, limitations inherent in the assessment procedure may have influenced the results. The circumstances surrounding the crisis dictated that the interviews be carried out by telephone. This type of interview setting might play a role in decreasing the sensitivity of the assessment,[19] possibly contributing to the low levels of panic attacks reported during the crisis, although a recent study found excellent agreement between telephone and face-to-face interviews for anxiety disorders.[20] However, we believe that the previous familiarity of the subjects with the interviewers and the use of the same terminology in the questionnaire that had been used in the regular clinic visits contributed to the accuracy of this assessment procedure.

Furthermore, during the threat of missile attacks, families stayed together, and the lack of increase in frequency of panic attacks may reflect the beneficial effect of familial and social support on perceived stress.[21] Another possible explanation is the ability of the hypothalamic-pituitary-adrenal axis to accommodate chronic stress, which is typical during wartime. The response of acute stress that appears against the background of chronic stress seems to be blunted because of the relatively rapid adaptation of the neuroendocrine system.[21,22]

Numerous studies have suggested that panic-disorder patients tend to catastrophically misinterpret normal physiologic responses.[23] These cognitive misinterpretations generate increasing levels of anxiety that result in a panic attack. If this is the case, the question then arises: how is it that patients with panic disorder who stayed in a sealed room, wearing a gas mask (which restricts free breathing and may thus induce a panic attack[24–28]), hearing explosions and waiting to be informed if chemical warfare was involved, and experiencing tachycardia, hypertension, and hyperpnea[29–31] (also the vivid personal experience of all the authors of this article), did not develop panic attacks? One possible explanation is that in order to develop a panic attack, not only is the sense of a catastrophic event necessary, but dissonance between feelings, the inner experience of a panic attack and the surrounding environment, is also needed. During the Persian Gulf War, this type of dissonance did not exist, since the external stress shared by others agreed with the internal stress of panic-disorder patients.

Another complementary explanation might be related to the hypothesis that conditioned fear activates the dorsal raphe nucleus serotonin system, which inhibits the fight/flight (i.e., panic) component of the defense reaction.[32] Along these lines, i.e., that panic corresponds to spontaneous activation of brain flight/defense systems, fear (or lack of dissonance) should indeed inhibit panic reaction.[32]

CONCLUSION

In conclusion, the results of the present study suggest that real warfare-associated events that threaten the lives of civilians are not associated with an increased frequency of panic attacks.

These findings may have important clinical implications. First, they are supportive of a previously proposed distinction between panic and fear.[24,32] Second, and perhaps most importantly, many patients with panic disorder believe that they will be immobilized by panic during a real life-threatening situation. Due to this belief, they are often reluctant to pursue occupations or lifestyles that require the ability to cope during stressful situations. These self-imposed limitations add to the already considerable morbidity of the disorder. If the findings of the present study are substantiated in subsequent studies, they could prove helpful in disputing these beliefs.

Drug names: alprazolam (Xanax and others), phenelzine (Nardil), yohimbine (Yocon and others).

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Appendix 1. 17-Item Structured Telephone Interview Employed to Assess Response of Panic-Disorder Patients to the Persian Gulf War

1. Has there been any change in your general state during the Persian Gulf War?

1	2	3	4	5	6	7
very much improved	much improved	slightly improved	no change	slightly worse	much worsened	very much worsened

2. What medication are you currently receiving?

3. Has there been any change in your medication during the crisis?
   Decrease
   No change
   Increase

4. How would you grade your level of general functioning?

7	6	5	4	3	2	1
excellent	very good	good	moderate	poor	very poor	incapacitation

5. Did you enter the sealed room during the alarms as instructed?
   Yes
   No

6. Did you don the gas mask as instructed?
   Yes
   No

7. Did you exit the sealed room when instructed to do so?
   Yes
   No

8. Did you have a panic attack during the alarm?
   Yes
   No

9. Did you have a panic attack while donning the gas mask?
   Yes
   No

10. Did you have a panic attack while in the sealed room?
    Yes
    No

11. Did you have a panic attack during the first hour after leaving the sealed room?
    Yes
    No

12. Did you have a panic attack during the first 2 hours after leaving the sealed room?
    Yes
    No

13. How would you grade your level of functioning during the alarms?

7	6	5	4	3	2	1
excellent	very good	good	moderate	poor	very poor	incapacitation

14. How would you grade your level of anxiety during the alarms?

7	6	5	4	3	2	1
extremely high	very high	high	moderate	low	very low	none

15. How many panic attacks per week did you have prior to the crisis?

16. How many panic attacks per week did you have during the crisis?

17. Have you returned to your precrisis level of functioning?
    Yes
    No